BILAG 31

B 35

I have Asthma.

by Amanda Thomsen

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I have Asthma

Dear Parent/Carer

This book explains what asthma is to children 4 to 8 years old. The information is factual, as we have found that children are more trusting of adults if they are honest with them.

Children's treatment will vary, so you may need to explain to your child that some things in the book may not apply to them.

As you read this book with your child encourage them to ask questions. If you would like help with this, ask a health worker involved in your child's treatment.

This edition of "I Have Asthma" has been designed to be downloaded via the internet and printed by the recipient.

Please complete the questionnaire attached in the back of the book and return to me. Your feedback will be used to evaluate the usefulness of this book.

Amanda Thomsen

Amanda Thomsen
Clinical Nurse Consultant - Respiratory (Acute)
Sydney Children's Hospital, Randwick

Published in Australia by
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P.O. Box 32
Rozelle NSW 2039

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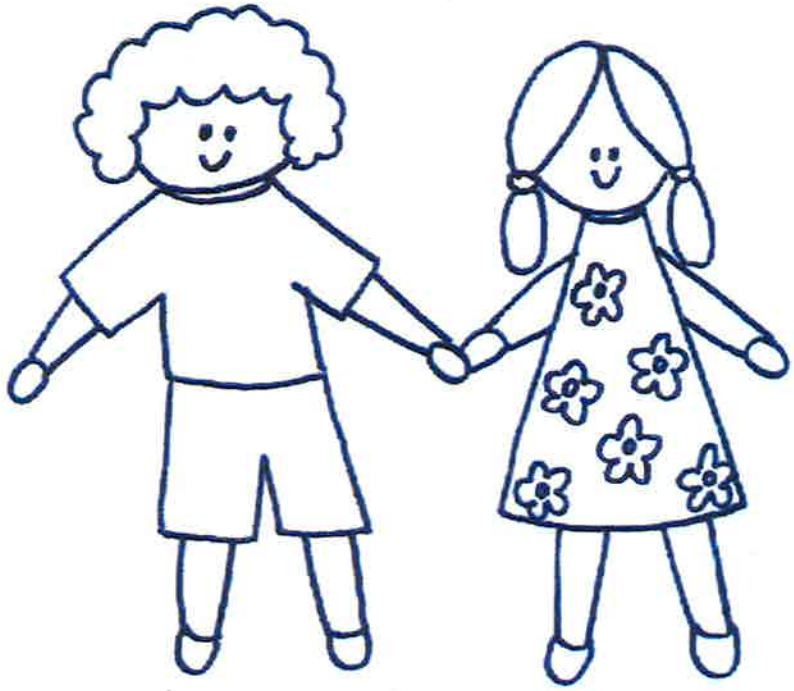
178

I have Asthma.



This book is written for you

It will tell you all about your asthma.

Colour in the pictures as you read the book.

This book belongs to...

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179

What is Asthma?

Asthma is a breathing problem.

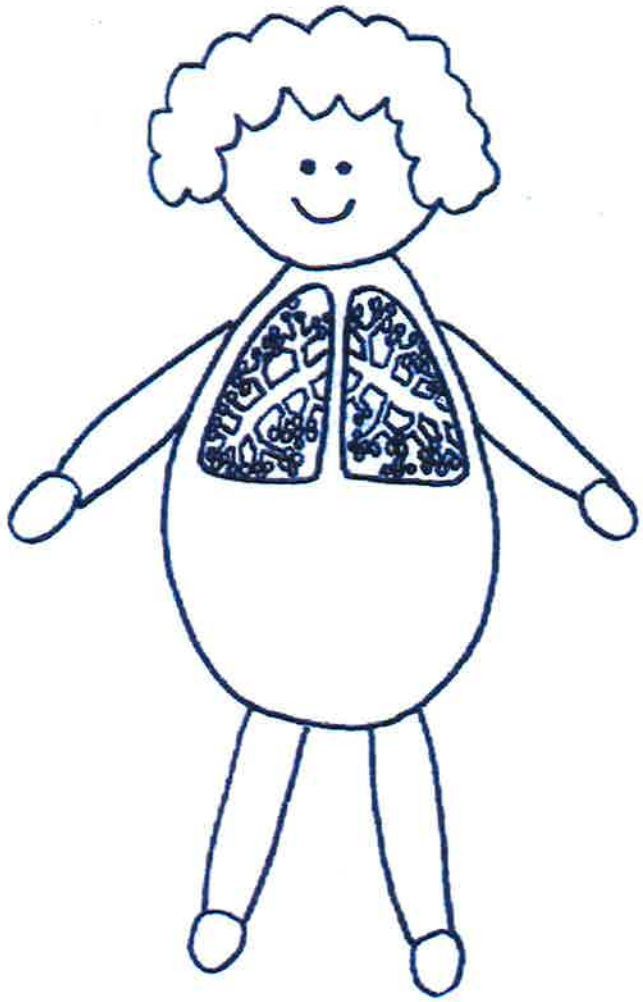
When you breathe air goes in and out of your lungs. Inside your lungs are lots and lots of breathing tubes, like drinking straws. At the end of the tubes are little balls that look like bunches of grapes.

When you have an asthma attack the breathing tubes become very skinny and blocked which makes it hard to breathe.

You may also cough and sometimes your breathing will sound strange like a whistle. This is called a 'wheeze'.

Breathing hard and coughing can sometimes make your tummy sore and you may even vomit.

Colour in your lungs



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180

Triggers.

Triggers are what start an asthma attack.
Not everyone has the same triggers.

Some triggers are:

- ☆ When you have a cold or have a runny nose
- ☆ Smoke, especially from cigarettes
- ☆ Cockroaches
- ☆ Dust mites. These are tiny bugs
- ☆ Animal fur, like cat and dog hair
- ☆ Running around, playing sport
- ☆ Plants and grass
- ☆ Changes in the weather – if one day it's sunny and the next day it's cold

Colour in these things that trigger or start your asthma

Weather

Cigarette smoke

Animal fur

Dust mites

Cockroaches

Grass and pollen

Colds

Exercise

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Puffers

You will need to take some medicine to make you feel better. If you have a bad asthma attack you may be given tablets or syrup to take for a few days, but most asthma medicines are puffers.

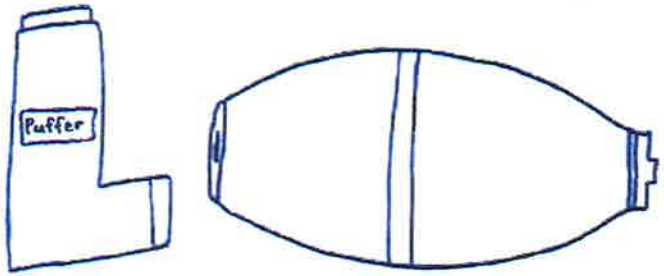
Puffers come in different colours and different shapes.

They can look like the letter L, they can look like a rocket, or they can look like a spaceship.

Some of the colours are:

blue
purple
red
orange
brown

Tablets or syrup



Puffer and spacer

Turbuhaler

Accuhaler

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Relievers.

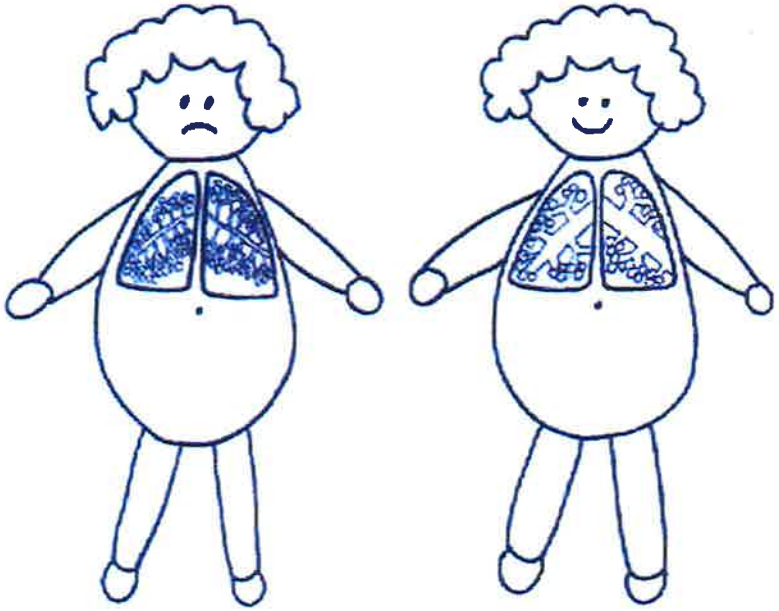
Reliever puffers are **blue**.

Use your blue puffer when it is hard for you to breathe or if you start coughing and wheezing.

You may need to use this one before sport or exercise.

The blue puffer relaxes the tight muscles around the breathing tubes - this makes it easier to breathe.

Spot the difference...



Hard to breathe

Easy to breathe

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183

Preventers.

Preventer puffers are yellow, orange or brown.

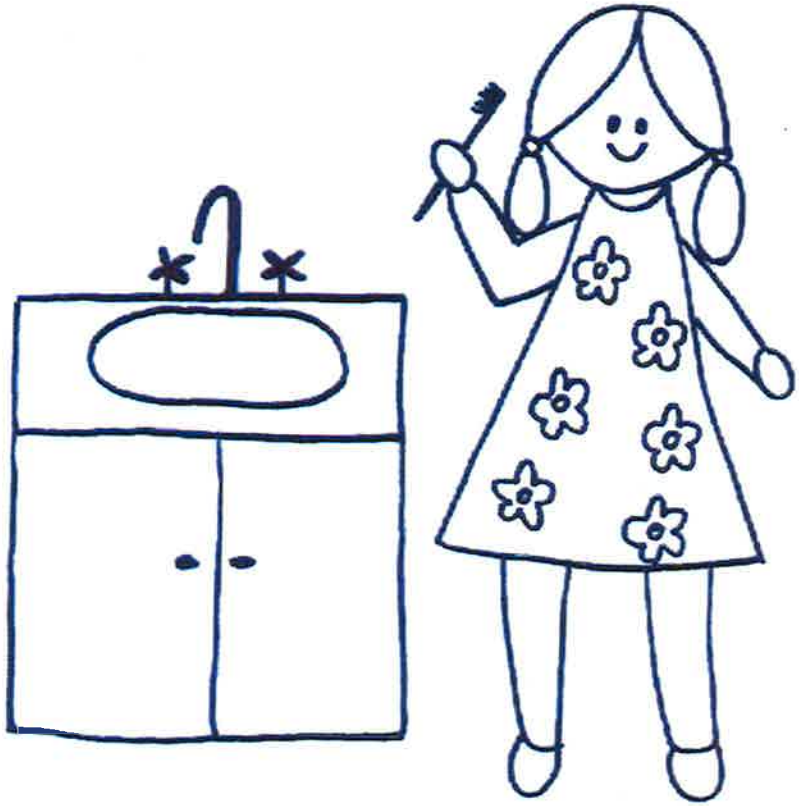
You will only need a preventer puffer if your asthma is a problem.

Preventers keep the inside of the breathing tube open, so it is easy for you to breathe. They need to be taken every day, even when you are feeling well.

Preventers can sometimes make the inside of your mouth sore.

It is very important not to have a drink straight after using your preventers but you should clean your teeth or rinse your mouth with water and then spit out.

Remember to clean your teeth or rinse your mouth



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184

Combination Therapy.

Combination therapy puffers are red or purple.

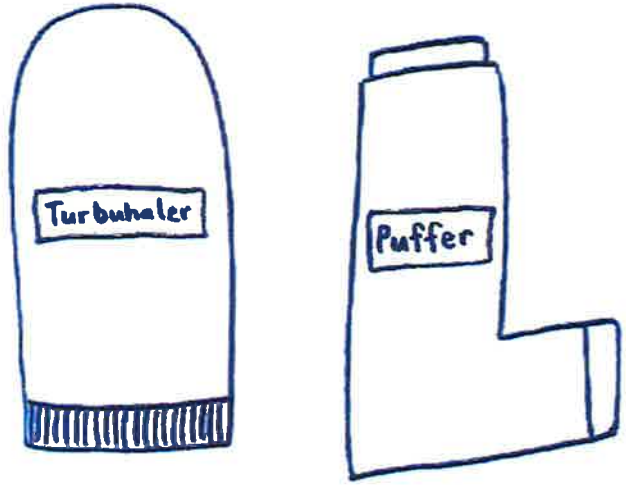
They have 2 medicines in them:

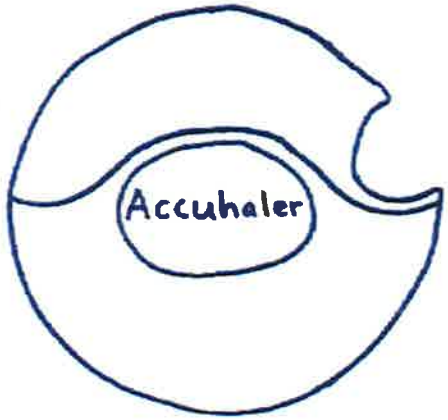
1. A preventer
2. A reliever that keeps your breathing tubes open for a long time.

Combination therapy puffers need to be taken every day even if you feel well.

Remember to clean your teeth or rinse your mouth with water and then spit out so you don't get a sore mouth.

What colour is your combination therapy puffer?





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185

Skinny Spacers.

A spacer is a plastic tube that helps you to use your puffers properly.

You will use a skinny spacer if you are 5 years old or younger.

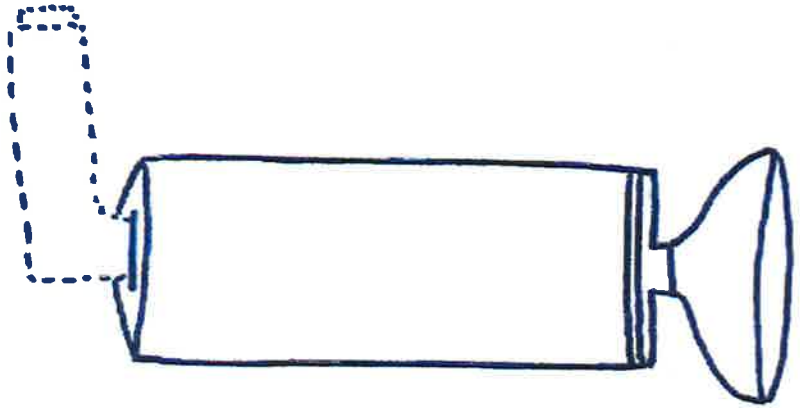
How old are you? ____

The puffer fits into one end of the spacer. At the other end is a face mask that goes over your nose and mouth.

The face mask may be a bit scary but it will not hurt you.

You need to breathe in and out 4 to 6 times after each puff.

Skinny Spacer



You may like to put the face mask on your teddy or doll and give them a puff to make them feel better.

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186

Football Spacers.

A spacer is a plastic tube that helps you to take your puffers properly.

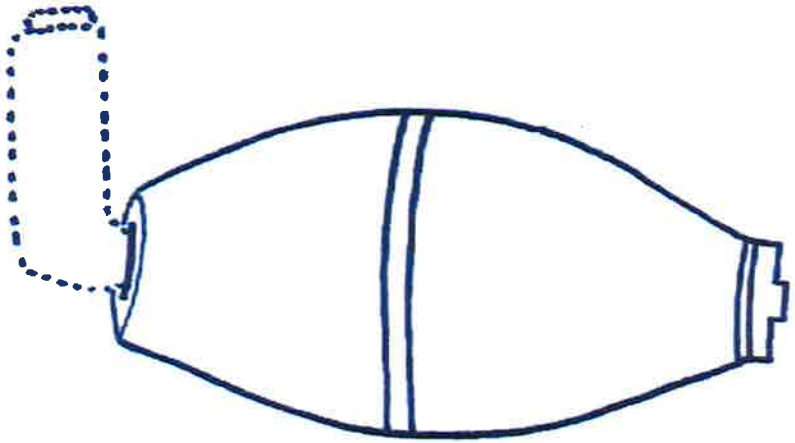
You will use the football spacer if you are 6 years or older.

How old are you? ____

The puffer fits into one end of the spacer and the other end goes into your mouth. It is important that you keep your lips closed over the mouthpiece.

You may be able to help press the puffer. You need to breathe in and out 4 to 6 times after each puff.

Football Spacer



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187

Turbuhalers.

Turbuhalers are puffers that look like rockets.

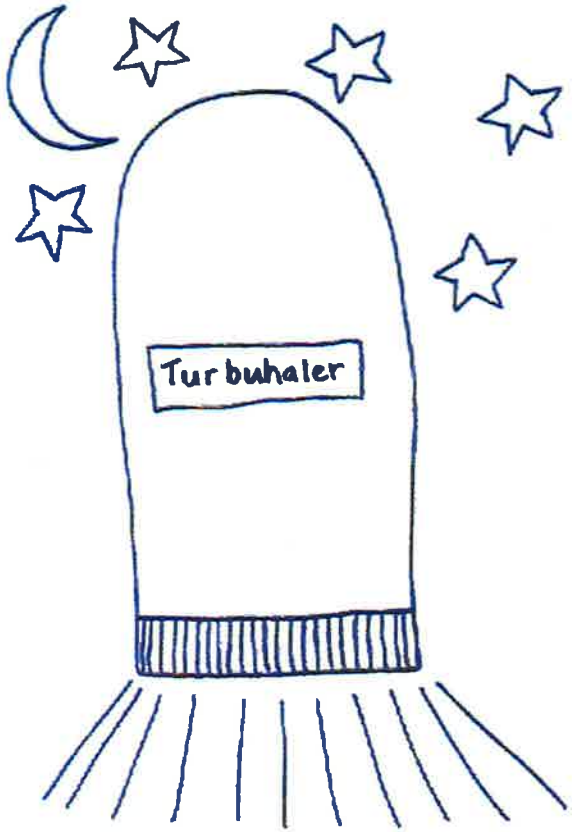
You need to be about 6 or 7 years old to use a turbuhaler properly.

It is very important that the turbuhaler is standing upright, just like a rocket, when you turn the bottom to get your medicine.

Before you use it, you need to turn the coloured base to the right and then back to the left until you hear a click.

Turbuhalers can fit into your pocket and are good if you need to take a puffer before sports or at school.

What colour is your turbuhaler?



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188

Accuhalers.

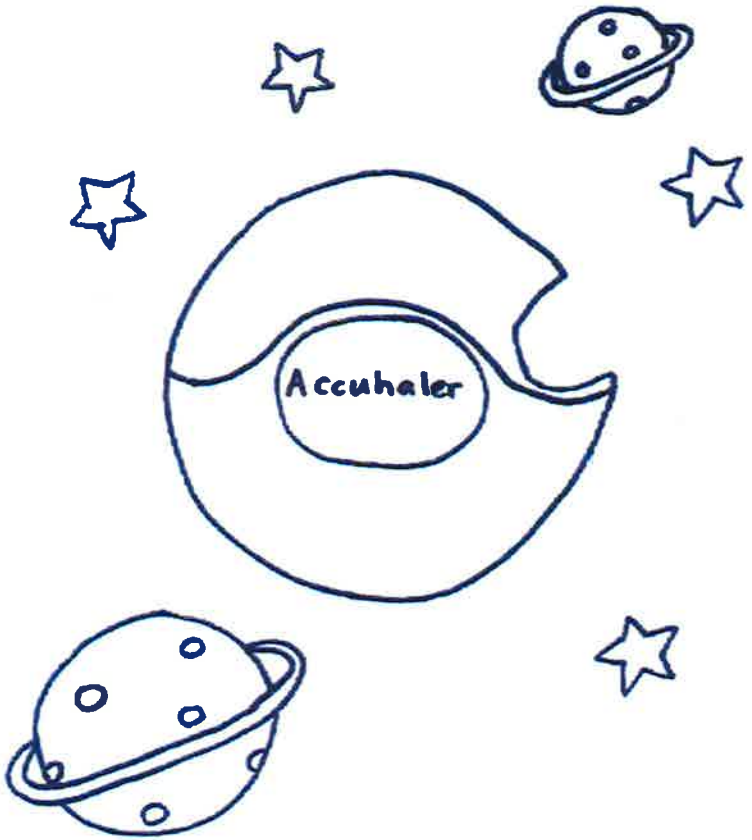
Accuhalers are a type of puffer that look like spaceships.

Accuhalers will not help you during an asthma attack, but are taken every day to help keep your asthma away.

You need to be about 7 years old to use an accuhaler properly.

Before you use it, you need to slide the cover back until you hear a click and then press the lever down until you hear another click.

What colour is your accuhaler?



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Playing Sport

Exercising or playing sport is very important. It keeps you healthy. But sometimes when you run around a lot or play sport you may begin to cough, wheeze or find it hard to breathe. This could be an asthma attack.

This kind of asthma attack can be helped by:

- ☆ doing warming up exercises before playing sport.
- ☆ take 1-2 puffs of your blue reliever puffer 5-10 minutes before warming up.
- ☆ doing cooling down exercises after.

If you get an asthma attack while exercising or playing sport, stop exercising and have 1-2 puffs of your blue reliever puffer.

Only start exercising or playing sport again if your asthma attack has finished.

Tell your doctor if you have asthma attacks when exercising or playing sport. They will tell you which is the best medication for you to take.

Visiting the Doctor.

It is very important to see your doctor often to make sure your asthma treatment is ok.

Don't forget to use your puffer as long as your doctor says to, even though you feel well. This will help to keep your asthma away so you can play and do all the things that your friends do.

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Cleaning Spacers

Spacers need to be cleaned every 1-2 weeks.

1. Pull the spacer apart.

2. Wash the spacer in warm soapy water.

3. Do not rinse the spacer.
The detergent leaves a slippery surface that prevents medication from sticking to the inside of the spacer.

4. Leave the spacer to air dry.
Spacers take a long time to dry. It may be convenient to wash the spacer in the evening and dry overnight.

For more asthma information

Contact your local Asthma Foundation
1800 645 130.

Questionnaire

Please take a few minutes to complete and return the following questionnaire. The questionnaire is strictly confidential, and there will be no method of identifying respondents. Therefore please do not write your name on the questionnaire.

The information gathered from the questionnaires will be used to evaluate the effectiveness and usefulness of this book.

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Parent/Carer Questionnaire
"I Have Asthma" - A Children's Colouring Book

Please tick the most appropriate response ie. (✔)	**Your post code:**
How old is your child? ..... *Years* .....*Months*	**Is your child a:** ( ) *Boy* ( ) *Girl*

Generally, did you find the booklet "I Have Asthma" useful?	( ) *Yes*	( ) *No*	
Did reading "I Have Asthma" help...			
you and your child identify what triggers his/her asthma?	( ) *Yes*	( ) *No*	( ) *Not sure*
you and your child use a puffer and spacer?	( ) *Yes*	( ) *No*	( ) *Not sure*
you and your child understand reliever medications?	( ) *Yes*	( ) *No*	( ) *Not sure*
you and your child understand preventer medications?	( ) *Yes*	( ) *No*	( ) *Not sure*

Fold here

Did reading "I Have Asthma" encourage you and your child to talk about Asthma?	( ) *Yes*	( ) *No*
Is the language in "I Have Asthma" suitable for your child?	( ) *Yes*	( ) *No*
Did your child like the pictures in "I Have Asthma"?	( ) *Yes*	( ) *No*

Do you or your child have any other comments regarding "I Have Asthma"? If yes, we would value them

.....

.....

.....

.....

.....

Fold here

Delivery Address:
PO Box 32
ROZELLE NSW 2039

No stamp required
if posted in Australia

I HAVE ASTHMA
Reply Paid 32
ROZELLE NSW 2039

First Aid for an Asthma Attack

Step 1.

- Sit child upright.
- Do not leave child alone.

Step 2.

- Immediately give 4 separate puffs of a reliever (blue puffer):
  - Give 1 puff at a time using a spacer.
  - Allow the child to breathe 4 times between each puff of medication.

If a spacer is not available, simply use the puffer on its own.

Step 3.

- Wait 4 minutes.

Step 4.

- If there is no improvement repeat steps 2 and 3.
- If still no improvement call an ambulance
- Keep repeating steps 2 and 3 whilst waiting for the ambulance.

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Factsheet - Asthma - Medications

Asthma Medications

PDF Version Available

Disclaimer: This fact sheet is for education purposes only. Please consult with your doctor or other health professional to make sure this information is right for your child.

Medications used in the treatment and management of asthma either relax the tight muscles around the airways and reduce or prevent inflammation of the inside airway lining. These medications relieve asthma symptoms and may prevent asthma attacks.

The most common way for your child to take their asthma medication is by inhaling it directly into their lungs through their mouth, or mouth and nose. **During an asthma attack, the best way for your child to take their medication is with a puffer and spacer.** For other times, e.g. before exercise or play, or in the daily management of asthma control, and depending on your child's age and ability to use them, other devices may be suitable available. Speak with your child's doctor or asthma educator to determine the most suitable device.

Inhaled asthma medications are grouped according to their use, and are easily identified by the type of colours associated with that group.

RELIEVERS - Blue/Grey Colours eg. Ventolin, Airomir, Asmol, Epaq, Bricanyl

USED WHEN SYMPTOMS ARE PRESENT OR DURING AN ASTHMA ATTACK

- Relieve asthma symptoms by relaxing the tight muscles and opening airways.
- Used when symptoms are present and may also be used before exercise or play.
- Work within minutes, and should be effective for up to 4 hrs.
- If needed more often than 3-4 times per week (excluding exercise or play) your child's asthma may not be well controlled and should be reviewed by their doctor.
- Always carry your child's blue reliever medication.

POSSIBLE SIDE EFFECTS

- Fast Heart Rate, Shaky Hands, Hyperactivity, Excitability.
  Vary between children and subside without any harmful effects.

PREVENTERS- Autumn Colours i.e. Yellow/ White/ Brown/ Burgundy/ Orange eg Intal Forte, Tilade, Pulmicort*, Qvar*, Flixotide*, Singulair**

USED IN THE DAILY MANAGEMENT OF ASTHMA CONTROL

- Prevents asthma symptoms and reduces the risk of an asthma attack, by decreasing the inflammation (swelling) and making the airways less sensitive to the trigger factors.
- To be effective, they need to be taken every day, even when symptoms are not present.
- May take up to two weeks before they start working.
- Not every child is on preventer medication.
- Often prescribed when symptoms are troublesome.

POSSIBLE SIDE EFFECTS

- Oral thrush (sore mouth).
- Voice change.

- Unpleasant taste and cough.
  To reduce the risk of side effects your child should use a puffer through a spacer device and also rinse their mouth with water and spit out after taking their inhaled preventer medication. They could also choose a suitable alternative device.

* **Pulmicort, Flixotide and Qvar** are inhaled corticosteroids. It is important to discuss with your doctor how to maximise the benefits of these medications whilst reducing the risk of side effects

** **Singulair** is a chewable tablet taken orally once a day. Potential side effects may include a headache.

SYMPTOM CONTROLLERS - Green/Blue Colours eg. Serevent, Oxis, Foradile.

USED IN THE DAILY MANAGEMENT OF ASTHMA CONTROL

- Work in a similar way to relievers by relaxing tight muscles.
- Usually take up to 30 minutes to start working, but last for up to 12 hours.
- May be prescribed when asthma is not controlled despite taking inhaled preventer medications (containing corticosteroid).

POSSIBLE SIDE EFFECTS

- Fast heart rate, shaky hands, hyperactivity, excitability, & headaches.
  Vary between children and subside without any harmful effects.

COMBINATION MEDICATIONS - Purple / Red & White Colours - eg. Seretide (Serevent + Flixotide), Symbicort (Oxis + Pulimcort)

- Contain a symptom controller and preventer in the one device, but are more convenient to take.
- May not be suitable for everyone
- Recommended when the use of an inhaled steroid (preventer) alone is not achieving control

POSSIBLE SIDE EFFECTS

- Same as for inhaled steroid preventers and symptom controllers

To reduce the risk of side effects your child should use a puffer through a spacer device and also rinse their mouth with water and spit out after taking their inhaled preventer medication. They could also choose a suitable alternative device.

RESCUE MEDICATION - Prednisone (Tablet); Prednisolone (Tablet or Syrup); Predmix, Redipred (Syrup)

- Called "rescue medications" because they are used in an asthma attack when there is little or no response to inhaled reliever medication.
- May be given to your child in hospital; may be required to be taken for a few days after discharge from hospital; or may be included as part of your child's asthma action plan when their asthma worsens.
- Generally used for short periods only - 3 to 5 days.

POSSIBLE SIDE EFFECTS

- Hunger, Puffy Face, Weight Gain, Mood Swings.

If the above side effects occur they are usually minimal and resolve once medication has stopped

Ensure optimal asthma control with the least side effects. Always discuss any concerns about medications and ensure your child is reviewed regularly.

Source: The Children's Asthma Resource Pack for Parents and Carers, June 2006
NSW Paediatric Network

The Children's Hospital at Westmead
Tel: (02) 9845 3585
Fax: (02) 9845 3562
www.chw.edu.au

Sydney Children's Hospital, Randwick
Tel: (02) 9382 1688
Fax: (02) 9382 1451
www.sch.edu.au

Kaleidoscope, Hunter Children's Health Network
Tel: (02) 4921 3670
Fax: (02) 4921 3599
www.kaleidoscope.org.au

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ASTHMA ATTACK

SAVING LIVES THROUGH St John FirstAid

What is asthma?

Asthma is a disease of the airways, the small tubes which carry air in and out of the lungs.

When you have asthma symptoms the muscles in the airways tighten and the lining of the airways swells and produces sticky mucus. These changes cause the airways to become narrow, so that there is less space for the air to flow into and out of your lungs.

Signs & symptoms

- Unable to get enough air
- Progressively becoming anxious, short of breath, subdued or panicked
- Focused only on breathing
- Coughing or wheezing
- Pale and sweating
- Blue around lips, ear lobes and fingertips
- Loss of consciousness or collapse

4:4:4

If someone is exhibiting difficulty breathing, but has not previously had an asthma attack, assist in giving four puffs of a blue reliever, followed by four breaths after each puff. Continue every four minutes if required, until an ambulance arrives.

Where permitted under local legislation/ regulations and if necessary, use another person's reliever inhaler or use one from a first aid kit to assist a patient with a severe asthma attack.

Management

▼ UNCONSCIOUS PATIENT

Follow DRSABCD action plan

▼ CONSCIOUS PATIENT

1. **Help the patient into a comfortable position**
   - Usually sitting upright and leaning forward
   - Be reassuring and tell patient to take slow, deep breaths
   - Ensure adequate fresh air
2. **Help with administration of patient's medication (4:4:4)**
   - Give four puffs, one at a time, of a blue reliever inhaler (use spacer if available)
   - Patient takes four breaths after each puff
   - Wait four minutes
   - If no improvement, give another four puffs
3. **If little or no improvement within minutes, keep giving:**
   - Children – four puffs every four minutes
   - Adults – six to eight puffs every five minutes
4. **If the patient still cannot breathe normally, call triple zero (000) for an ambulance**
   - Inform the operator that someone is having an asthma attack
   - Continue administering medication (4:4:4) until the ambulance arrives

In an emergency, call triple zero (000) for an ambulance

1300 360 455 stjohnnsw.com.au stjohnfirstaid stjohnnsw stjohnnsw

This information is not a substitute for first aid training. St John recommends that everyone is trained in first aid.

1401-BUS-FL-254

GlaxoSmithKline AS, Forskningsveien 2 A
Postboks 180 Vinderen, 0319 Oslo
Telefon: 22 70 20 00 - Telefaks: 22 70 20 04
www.gsk.no

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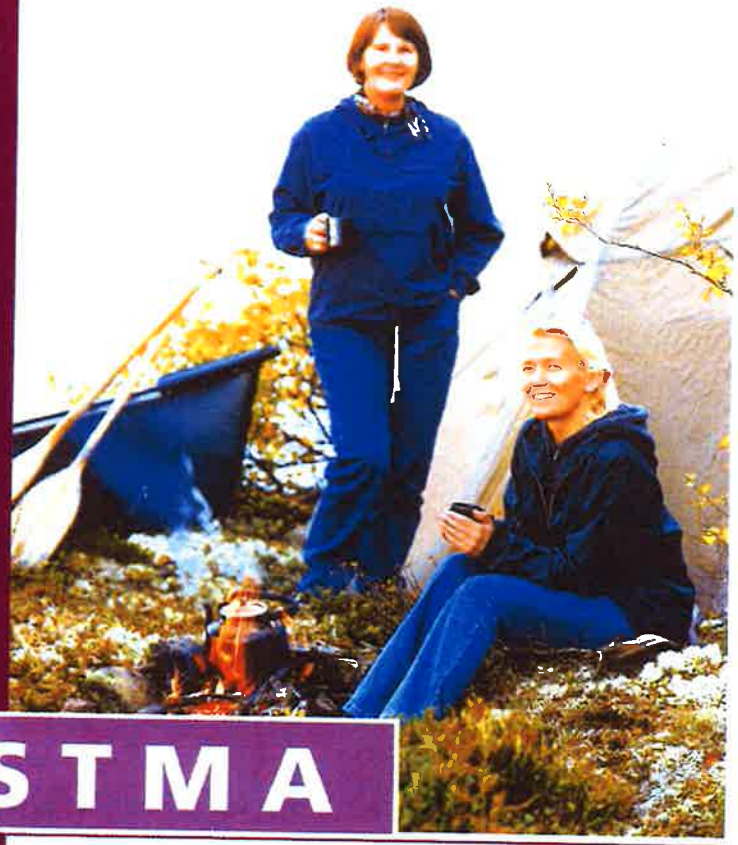

ASTMA

hos voksne

Utarbeidet av overlege Ragnar Dahle og overlege Per F. Ekholdt i samarbeid med GlaxoSmithKline AS

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Behandling av astma

Målsetning for astmabehandling
Målet for behandlingen er at du skal kunne leve et liv med minst mulig begrensning i dagliglivets aktiviteter på grunn av sykdommen; minst mulig oppvåkning om natten på grunn av hoste og tetthet og minst mulig astmasymptomer på dagtid.

Hva bør du gjøre selv?
Miljøsanering
Unngå eller fjern faktorer i miljøet som du reagerer på.

Kom i form
Det er viktig å holde seg i god fysisk form året rundt. Velg aktiviteter du trives med og mosjoner regelmessig. Les mer om fysisk aktivitet under avsnittene "Anstrengelsesutløst astma" (s.25) og "Hva kan fysioterapeuten hjelpe deg med?" (s. 27).

Røykekutt
Lær mer
Dersom du røker, bør du slutte med det.
Jo større kunnskap du skaffer deg om din astma, jo bedre blir resultatet av behandlingen.

Noen stikkord er:

Heve toleranse-terskelen - tilnærmet terskelen hos friske.

Normal lunge-funksjon.

Forebygge akutte astmaanfall.

Minst mulig fravær fra skole eller jobb.

Best mulig effekt og minst mulig uønskede effekter av behandlingen gjennom riktig medisinering.

Livskvalitet!

Medikamentell behandling av astma

Medisiner til inhalasjon er mest brukt ved behandling av astma. Det finnes tre hovedtyper inhalasjonsmedisiner. Disse har alle forskjellig funksjon. Derfor må du ikke kutte ut en type medisin du har fått forskrevet, selv om du føler deg bedre. Hvilke medisintyper du trenger og hvilke doser du skal ta, avhenger av hvor alvorlig astma du har.

1. Korttidsvirkende anfallsmedisin (korttidsvirkende $ß_2$-agonister, blå medisin). Tas ved behov

Disse ligner på kroppens eget adrenalin, men gir mindre bivirkninger på hjertet. Effekten inntrer raskt og løsner muskelkrampen i de små luftrørene, slik at det blir lettere å puste. Anfallsmedisin skal brukes når man blir tett og tungpustet. Den kan tas opptil 4-6 ganger i døgnet. Effekten varer i 2-4 timer. Anfallsmedisin kan også tas før man blir tett ved f. eks. fysisk aktivitet som løping, sykling og før gymnastikktimer. Ha alltid anfallsmedisinen med deg!

I Norge finnes slike medisiner med virkestoffene; Salbutamol, Terbutalin.

2. Sykdomsforebyggende medisin (kortison til inhalasjon, brun eller orange medisin). Tas morgen og kveld hver dag

A. Kortison til inhalasjon er et effektivt forebyggende medikament. Det er i slekt med kortisol som kroppen selv produserer. Effekten er direkte på slimhinnen på samme måte som kortisonsalve på eksem. Betennelse (inflammasjon) og hevelse i slimhinnen reduseres, og det produseres mindre slim. Det blir derfor lettere å puste, samtidig som overømfintligheten i slimhinnen reduseres. På den måten økes også toleranseterskelen i luftveiene (se side 12). Det tar gjerne 1-4 uker før man merker effekt av de sykdomsforebyggende medisinene. Bivirkninger forekommer, men er vanligvis beskjedne; Hes stemme eller soppbelegg i svelget. Plagene kan forebygges ved å skylle munn og svelg godt etter inhalasjon, eller ved å bruke plastkammer (spacer). Andre bivirkninger som benskjørhet og hudblødninger kan forekomme, men er svært sjeldne. Det kan tyde på at disse bivirkningene er doseavhengige. Så lenge man kan klare seg med 1000 mikrogram i døgnet eller mindre, er man på den trygge siden.

I Norge finnes slike medisiner med virkestoffene; Beklometason, Budesonid, Flutikason.

B. Leukotrien antagonister

Leukotrien antagonister er forebyggende medisin i tablettform. Også disse medisinene virker ved å redusere betennelse, slimdannelse og hevelse i slimhinnen. Kan også ha effekt på kronisk hoste ved astma. Bivirkninger er sjeldne, men hodepine og magesmerter kan forekomme. Skal tas en gang daglig.

C. Kortison tabletter

Kortison tabletter har mer alvorlig bivirkninger enn kortison til inhalasjon og skal derfor helst brukes i korte kurer på 2 - 4 uker. Men de er effektive til å få kontroll over alvorlige astmaplager. Bivirkninger er økt appetitt, væskeansamling i kroppen, økt syreproduksjon i magesekken og søvnvansker. Benskjørhet og hudblødninger kan forekomme dersom disse tablettene brukes daglig

over lang tid. Doseringen tilpasses alltid den enkelte pasient.

3. Anfallsbeskyttende medisin (langtidsvirkende ß2-agonister) Tas morgen og kveld hver dag

Også disse medisinene virker ved å løsne muskelkrampe i de små luftrørsgrenene, slik at det blir lettere å puste. Effekten varer i hele 12 timer. Disse medisinene inhaleres gjerne morgen og kveld. Kan beskytte mot nattlige astmasymptomer og mot anstrengelsesutløst astma. Når man bruker anfallsbeskyttende medisin, vil behovet for anfallsmedisin gå ned. Bivirkninger er sjeldne, men hodepine og muskelkrampe kan forekomme.

I Norge finnes slike medisiner med virkestoffene Formoterol og Salmeterol. Formoterol virker noe raskere enn Salmetereol, og kan brukes ved behov.

4. Kombinasjonsmedikamenter: Sykdomsforebyggende og anfallsbeskyttende medisin i én inhalator (kortison til inhalasjon/langtidsvirkende $ß_2$-agonist, lilla eller rød medisin). Tas morgen og kveld hver dag

Disse medisinene inneholder både kortison som virker forebyggende, og langtidsvirkende anfallsbeskyttende medisin. De skal vanligvis tas morgen og kveld. Vedrørende virkemåte og bivirkninger se under avsnittene 3 og 2A.

I Norge finnes slik medisin med virkestoffene: Flutikason/Salmeterol. Budesonid, Formoterol.

5. Anfallsbeskyttende medisiener

Teofyllinpreparater finnes som depot-tabletter, med 12 timers virkningstid. Disse medisinene finnes også som mikstur og til intravenøs bruk. Miksturen brukes til små barn og tablettene brukes som tilleggsbehandling til anfallsmedisin og forebyggende medisin ved alvorlig astma. Bivirkninger kan være magesmerter og søvnvansker.

6. Andre inhalasjonsmedisiner

Ipratropiumbromid er en annen type anfallsmedisin som brukes både ved astma og kronisk bronkitt. Effekten varer vanligvis 4-5 timer, og vi anbefaler å bruke den regelmessig 3-4 ganger daglig. Det tar 30 til 60 minutter før man merker effekt. Kromoglikat har en sykdomsforebyggende effekt, men er nok ikke så effektivt som kortison til inhalasjon. Medisinen brukes mest av barn og ved anstrengelsesutløst astma hos ungdom.

BILAG 35

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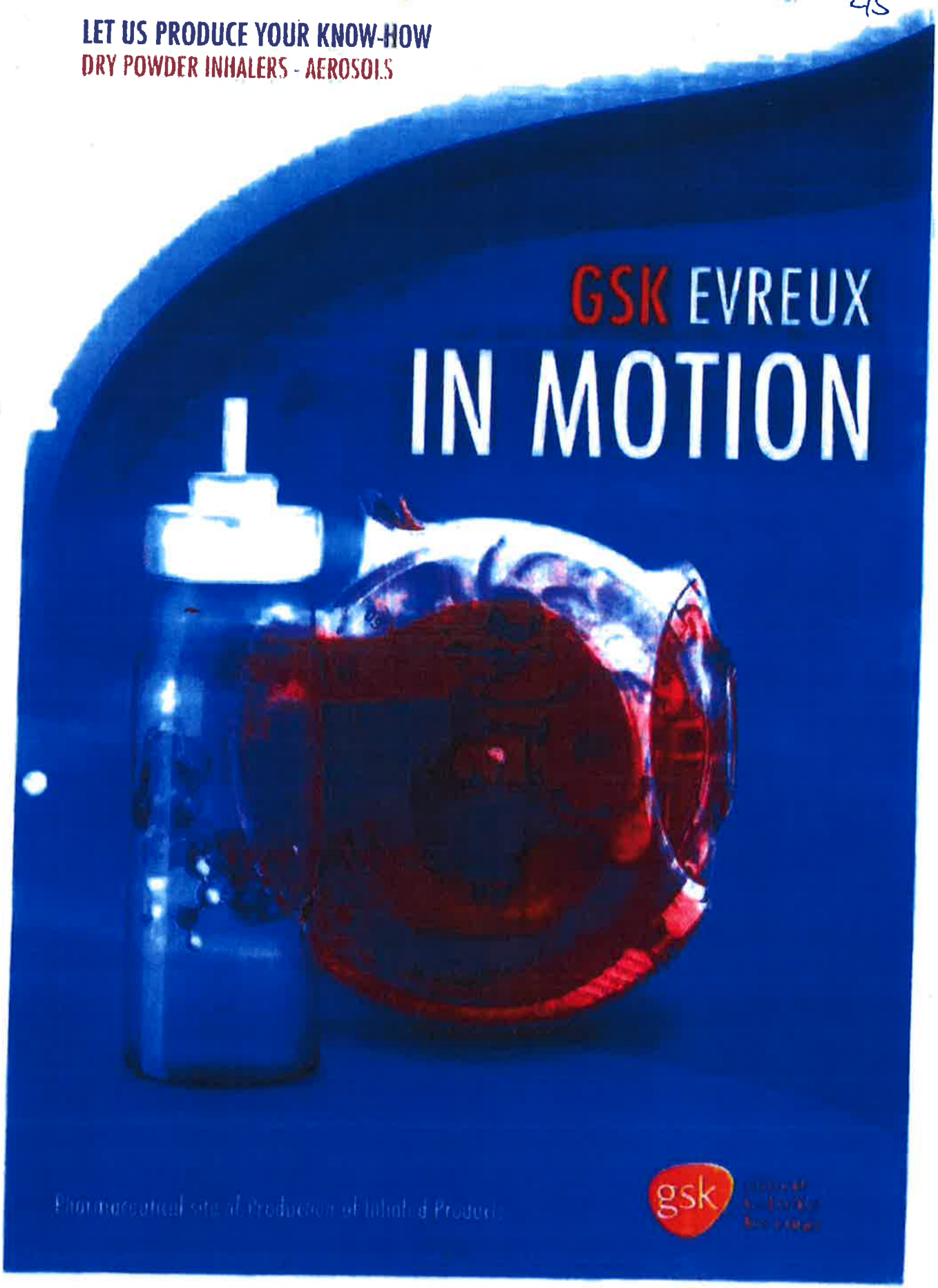
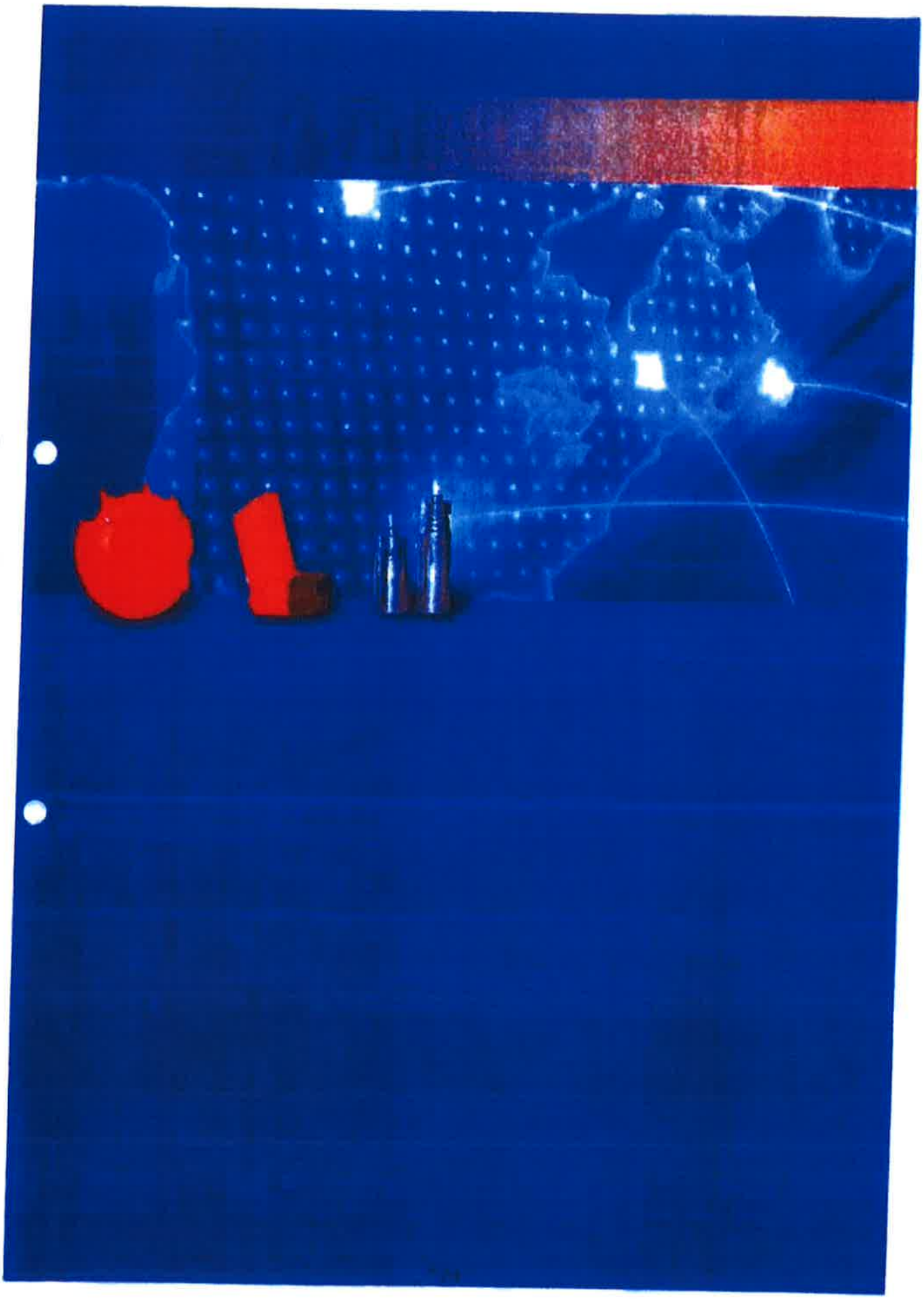
LET US PRODUCE YOUR KNOW-HOW
DRY POWDER INHALERS - AEROSOLS





GSK EVREUX

A site recognized all over the world for micronisation and production of inhaled products.
A multi-disciplinary team with broad experience to support your business needs from development to finished product supply, offering state-of-the-art technology and high process capabilities for your products.

DRY POWDER INHALERS PRODUCTION

Diskus® and Rotadisk® are devices containing multi dose medication to be inhaled. Dry Powder Inhalers are easy to use. Diskus® has a built-in dose counter to help patients accurately taking their dose and indicate when a replacement is needed.

AEROSOLS PRODUCTION

Each canister is comprised of a can and a valve.
The canister is filled under pressure with a predefined mixed quantity of active and propellant gas.
Each canister can be fitted with an actuator and a dose counter.

GSK Worldwide

- GlaxoSmithKline - one of the world's leading research-based pharmaceutical and healthcare companies - is committed to improving the quality of human life by enabling people to do more, feel better and live longer.
- We produce medicines that treat six major disease areas - asthma, virus control, infections, mental health, diabetes and digestive conditions.

In addition, we are a leader in the important area of vaccines and are developing new treatments for cancer.

- More than 108 000 employees, all over the world, in 116 different countries.
- 78 manufacturing sites, based in 33 countries.
- 2009 turn over: 34,1 Billions euros.

GSK, in France

In 2009, GSK France is the third largest pharmaceutical group in France. For GSK, France, in terms of trade, is the first European subsidiary and the second subsidiary in the world, behind the United States.

Our locations:

1 - EVREUX (Eure)	Manufacturing Site
2 - MARLY-LE-ROI (Yvelines)	Headquarter
3 - LES ULIS (Essonne)	R&D Center
4 - NOTRE-DAME DE BONDEVILLE (Seine Maritime)	Manufacturing Site
5 - MAYENNE (Mayenne)	Manufacturing Site
6 - SAINT-AMAND-LES-EAUX (Nord)	Biologicals Manufacturing Site

GSK Evreux

The Evreux site is dedicated to production of micronized and inhaled products. GSK Evreux employing over 1000 people, is manufacturing aerosols and dry powder inhalers for all markets. Our teams of experts and multi-skilled staff in respiratory processes (micronisation, filling, analytical, quality) are now available to support your challenges.

More than 500 Million of Ventolin HFA canisters have been supplied in the world over the last 10 years.

"We, at GSK Evreux are committed to your success.
Our team of experts and competent professional in production and development of respiratory products works everyday to improve our Quality, Service and Costs, for the benefit of million of patients worldwide. We base our performance on Technical mastery, team commitment and continous improvement, and are keen to work with you. Together we will embrace new opportunities."

Marc Santesmases - Site Director

Key figures

Foundation	1968
Location	Evreux ◆ Haute-Normandie
Forms	**Inhaled** ■ Aerosols ■ Rotadisks® ■ Diskus®
Distribution	120 customers including China, US, Japan....
Sales breakdown	15% France 85% Export

Services

Our strengths and key assets

Quality is our first priority

Quality is at the heart of all activities that support the development, manufacturing, supply and marketing of products to our patients and customers. It means doing what is right, first time every time.

Our Agreements:

Our excellent quality, regulatory status and compliance are endorsed by national and international following agreements for more than 20 years

- AFSSAPS (France)
- EMEA (Europe)
- FDA (US)
- MLHW (Japan)
- ANVISA (Brazil)
- MoH (Iran, Saudi Arabia, Yemen, Ouganda)
- SFDA (China)

A specific knowledge in inhaled products quality control

We have comprehensive laboratory facilities to support quality, product development, engineering, and physical properties analysis with state-of-the-art instrumentation.

Inhaled analytical expertise

Quality control analysts have developed a recognized expertise in respiratory physical and chemical analysis, for more than 40 years.

This expertise is also covering, analytical method development, stability studies, and specific respiratory equipments development.

SERVICES

Operational Excellence

We have a culture of continuous improvement coupled with operational excellence and lean sigma. We are committed to removing waste and complexity from our operations.

A highly skilled site

Staff and Training

- High level of qualifications and training
- 50% are graduated from higher education or master
- Partnerships developed with universities (Engineers, Pharmacists, ...)
- Continuous investment in people development

A site committed to the environment

Health, Safety and Environment

Reducing our impact on the environment is one of our priority through continuous improvement programs:

- Carbon foot print and COV reduction
- Water zero reject
- Waste reduction and recycling
- Energy consumption reduction

Our main equipments (micronizers, blenders and filling equipments) are Respiratory Free designed.

The site is certified OHSAS 18 001 and plans ISO 14001.

All Environmental, Health and Safety team have been trained and certified to conduct EHS audits (COV, carbon footprint assessment, certifications support, Zero access, Ergonomicity).

Active Pharmaceutical Ingredient

GSK Evreux is in charge of Active ingredient micronisation for all the other production sites. This process requires state-of-the-art technology and specific knowledge.

Aerosols

From filling to packaging, a fully dedicated area for aerosols manufacturing compliant with the highest worldwide regulatory expectations.

Dry Powder Inhalers (DPI)

State of the-art technology are used to manufacture pharmaceutical dry powder inhalers.

Development

A multi disciplinary team including representatives from quality, engineering, medical device design, process experts, operations and regulatory affairs available for your business.

BILAG 36

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Queen Elizabeth Hospital Birmingham NHS
Part of University Hospitals Birmingham NHS Foundation Trust

About your Accuhaler

It is important you use the inhaler correctly to make sure you have the full dose of the medication you need.

How does it work?

The accuhaler can be used to deliver different types of medication (different colours indicate different medication) depending on your problem and how severe it is. It is likely to be either: Salmeterol/Serevent (green), Fluticasone/Flixotide (orange), Seretide (purple) or Salbutamol (blue) and may include a steroid component (Fluticasone and Seretide include a steroid). These inhalers work by relaxing the muscles of the large airways and/or reducing the inflammation of the airways.

How do I use it?

1. Push the outer cover round with your thumb.
2. Push the dial round until you hear a 'click'.
3. Breathe out as far as is comfortable (without the device in your mouth).
4. Place lips tightly around mouthpiece and breath in quickly and deeply.
5. Remove your Accuhaler from your mouth and hold your breath for 10 seconds or as long as is comfortable and then breathe out slowly and calmly.

Repeat the above process as your prescription indicates. If you have an inhaler that contains a steroid you must rinse your mouth out with water to prevent developing a sore mouth, husky voice or oral thrush.

UHB is a no smoking Trust

To see all of our current patient information leaflets please visit
www.uhb.nhs.uk/patient-information-leaflets.htm

P [illegible] Authors: Sharon Rees and Dee Curry
Date: December 2014 Review date: December 2016

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API MICRONISATION

Micronisation

The objective is to reduce to the appropriate particle size the active ingredient to enable the right product performance. Micronized actives are used in respiratory products, ophthalmic ointments, tablets...

Evreux site is in charge of micronising the API for GSK manufacturing network. This stage requires a specific knowledge and a complex technology.

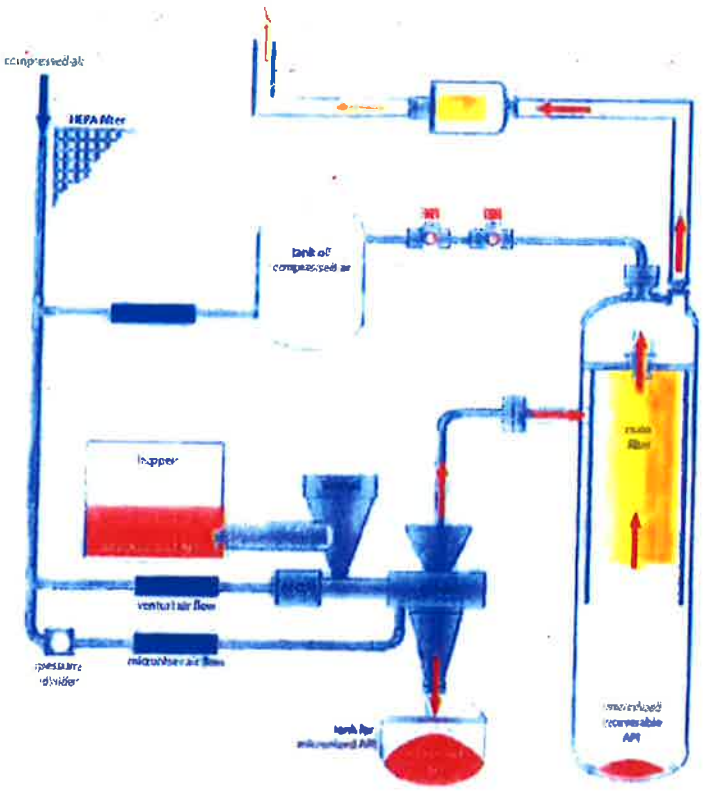
Equipements / Technologies:

- 4 micronisers of 8 inches technology
- Feeder: gravimetric system
- Nitrogen or air grind techno
- Compressed air with dew point – 70°c
- Respiratory free
- HVAC
- Capacity: from 3 to typically 10 kgs/hour
- Batch size: from 300 g to typically 7 kgs

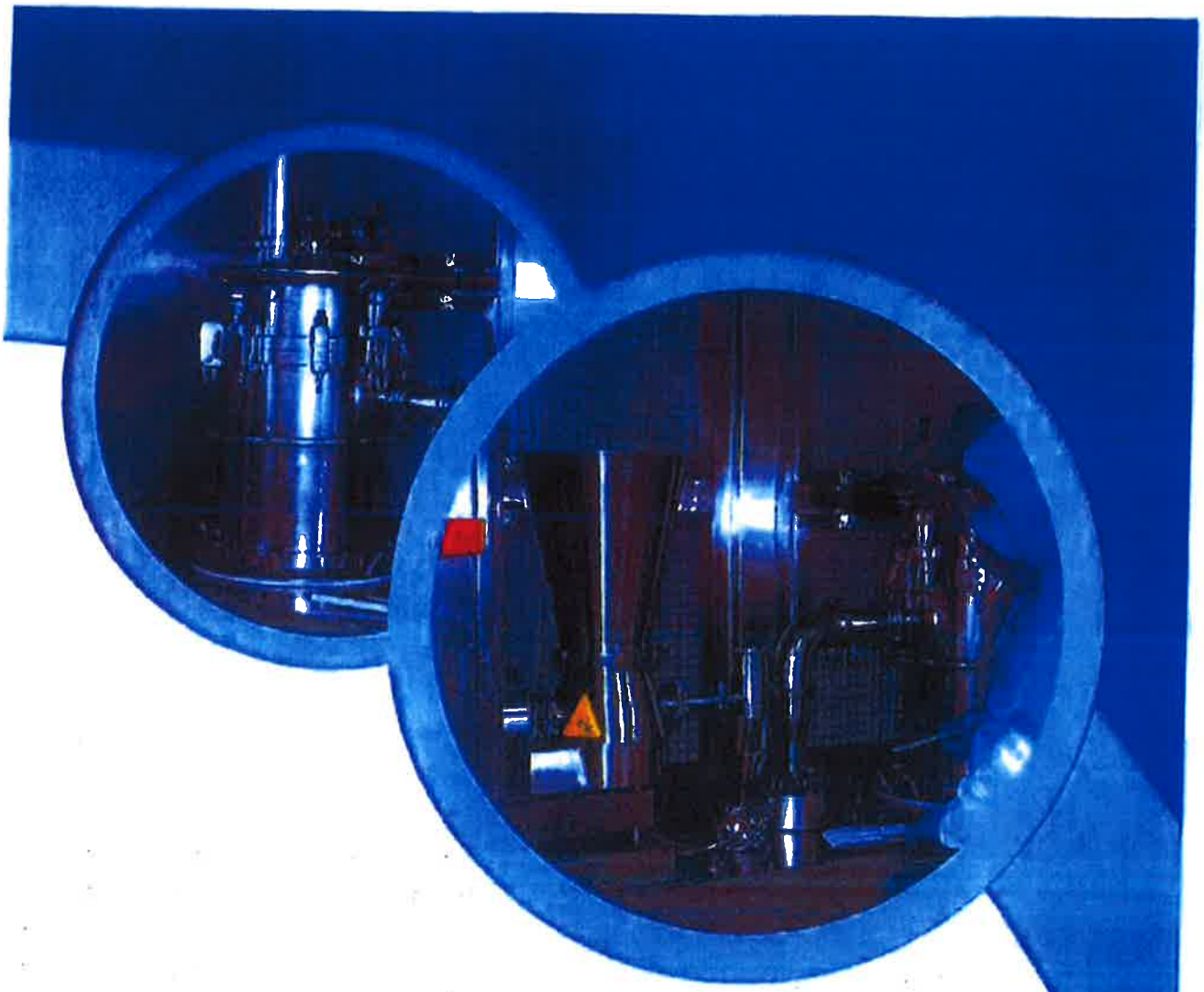
Process flow

Key Features:

- Particle Size Distribution: from ultra fine (<0.1 µm) to fine (100 µm) particles
- Real time data acquisition system

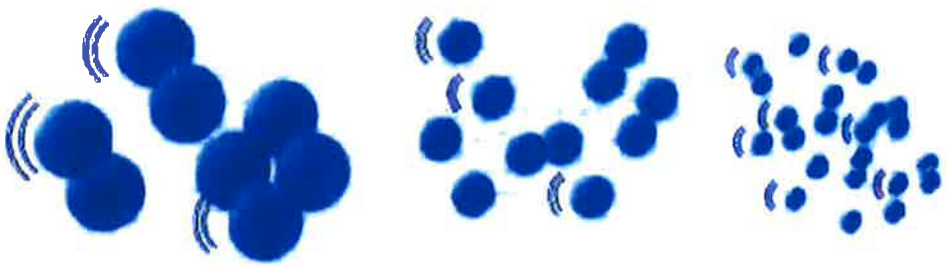


MICRONISATION



Overview

The active ingredient is introduced into a hopper and is fed to the venturi. The process air reaches a speed of Mach 2.5. At this speed, particles will collide with each other and their size will be reduced to meet required specifications. The micronised active ingredient is recovered in the vessel.



Aerosols PRODUCTS

Features

Aerosol specifications

A Metered Dose Inhaler is composed of 5 main components: active ingredient, propellant, can, valve and actuator. The combination of these components results in a product with high degrees of technology and technical complexity requiring a committed team of technical masters to produce.

Each year, about 80 million aerosol packs are produced for 120 customers around the world. Our main customers are the United Kingdom, France, Australia, the US and Japan.

Key Features:

- Aluminum can filled with a suspension or solution of API in a gas
- 60, 120 or 200 doses typically
- Colored actuator
- Dose counter available

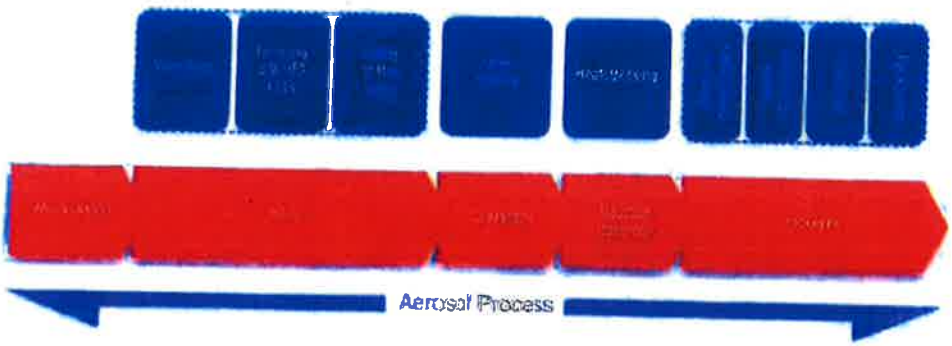
Main technical characteristics:

- Standard can design
- Recyclable components
- Color per API and darkness of color depending on strength
- Tamper evidence
- CFC Free - Environmentally friendly
- API full protection (no conservative)
- Constant pressure during all aerosol life
- Could be filled with different API
- Valve down use
- Easy to clean
- Decremental dose counter : feed back to patient
- Auto power pack
- No patient age constraints
- 3 Steps use: open, breathe, close
- Alternative to DPI/MDPI devices
- Cost competitive
- High level dose accuracy

AEROSOLS PRODUCTS

The active ingredient went previously through the micronisation process.

Production process



Aerosols PRODUCTS

Blending & filling

Filling operation

The micronized drug is weighed and blended with a defined amount of propellant HFA134a and transfered to a specific tank which then feeds this suspension to the filling line. First the valve is placed on the can. The can is purged with propellant to remove remaining air within the can and the valve is crimped on. Afterwards, the can is filled with the propellant and the suspension directly through the valve. Finally, the canister is weighed and printed with an identification code.

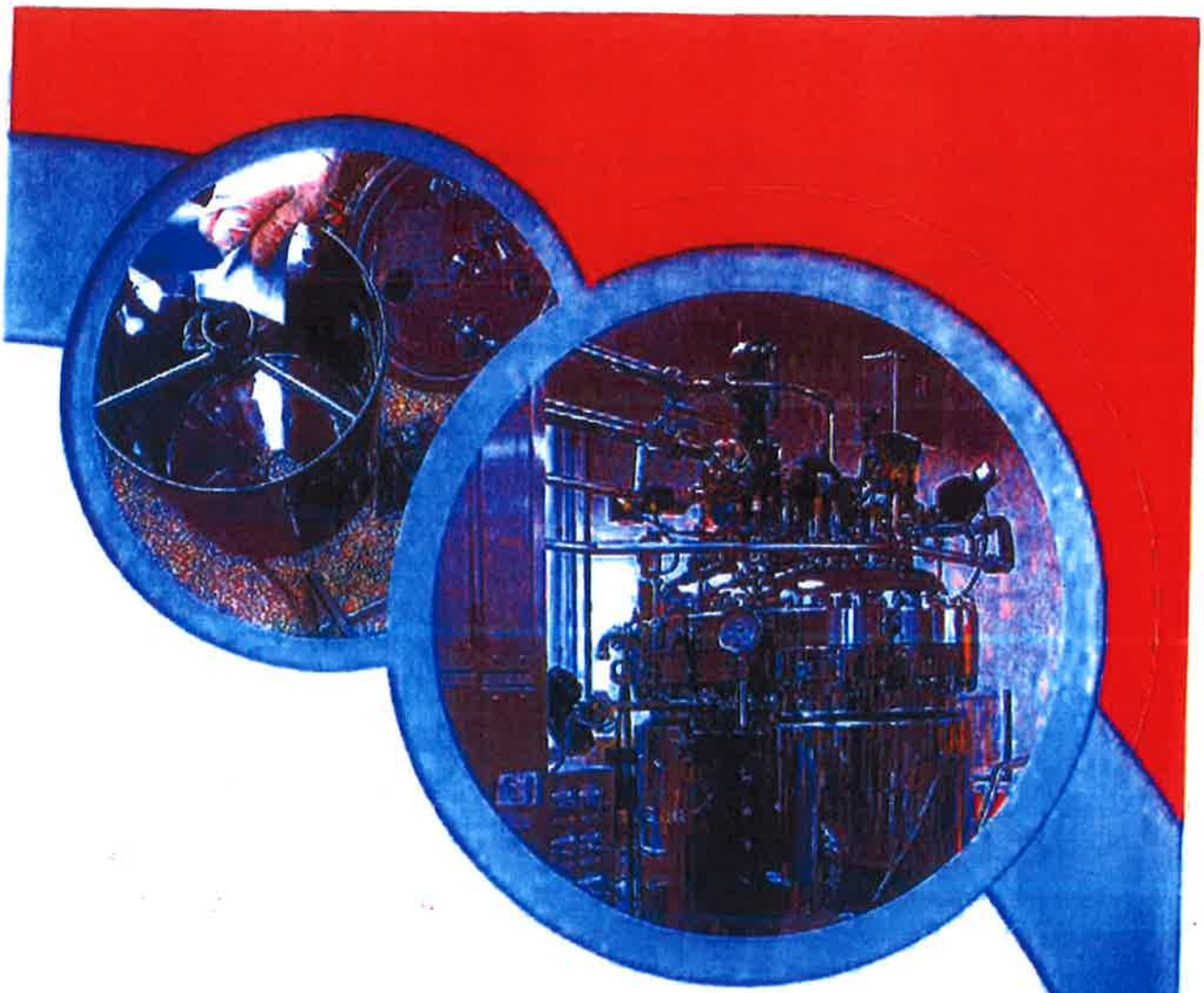
Key Features:

- 5 production HFA manufacturing lines
- 1 pilot line
- 1 line with double technology (solution or suspension)
- Dedicated dispensing room per line
- Dedicated pharmaceutical manufacturing facility
- ATEX (flam proof) environment
- Electronic Batch Record
- Air environment control
- Waste treatment
- Canisters are 100% check weighed

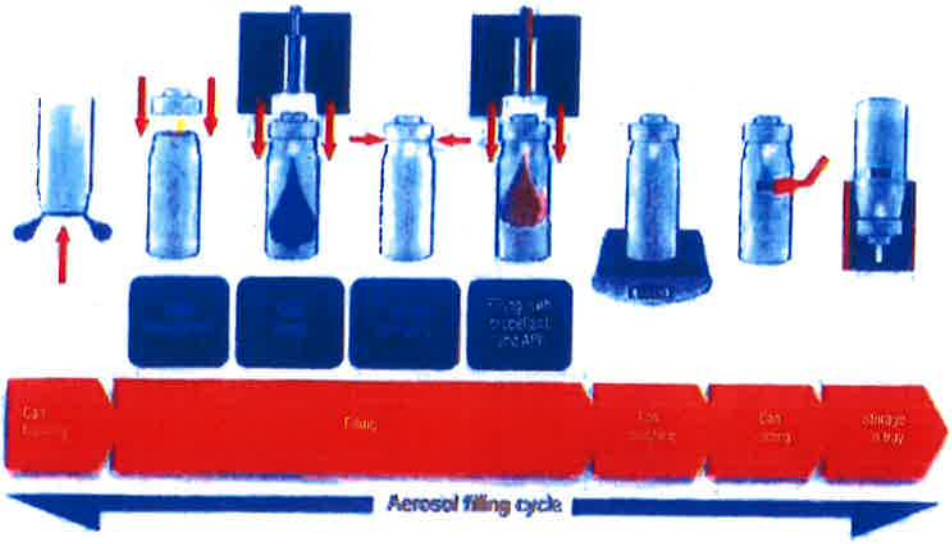
Equipements / Technologies:

- Drug Additionnal Volume capacity: 20 liters
- 400 L stainless steel vessel capacity
- Double jacket and heater/chiller system
- CIP (clean in place) water or ethanol
- 100 % filled weight checked
- Supervisory control and data acquisition system
- Coding station
- 1 pilot line: 45 cans/min and 20 L capacity
- Batch size: from 15 000 to 75 000 or from 90 kg to 405 kg
- Can of 5, 8 and 12.5 ml
- Can sizes 22 mm to 61 mm width and 55 mm to 165 mm height
- Valve sizes including 15 mm, 20 mm
- HFA 134a propellant

AEROSOLS PRODUCTS



Filling process



Aerosols PRODUCTS
Packaging

Packaging operation

8 packaging lines are dedicated to aerosols. After the quarantine period, each canister is identified, checkweighed and spray tested to ensure proper valve operation and to detect potential leakage.

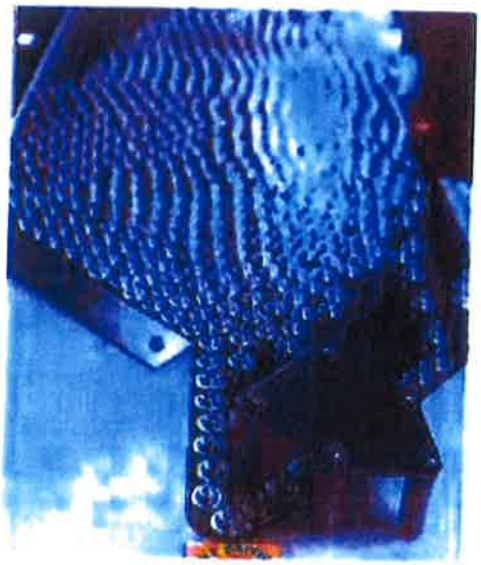
All the packaging components are controlled before use by identification code. The canister is labelled, coupled with an actuator, fitted with or without a dose counter and inserted into cartons with the patient leaflet.

Key Features:

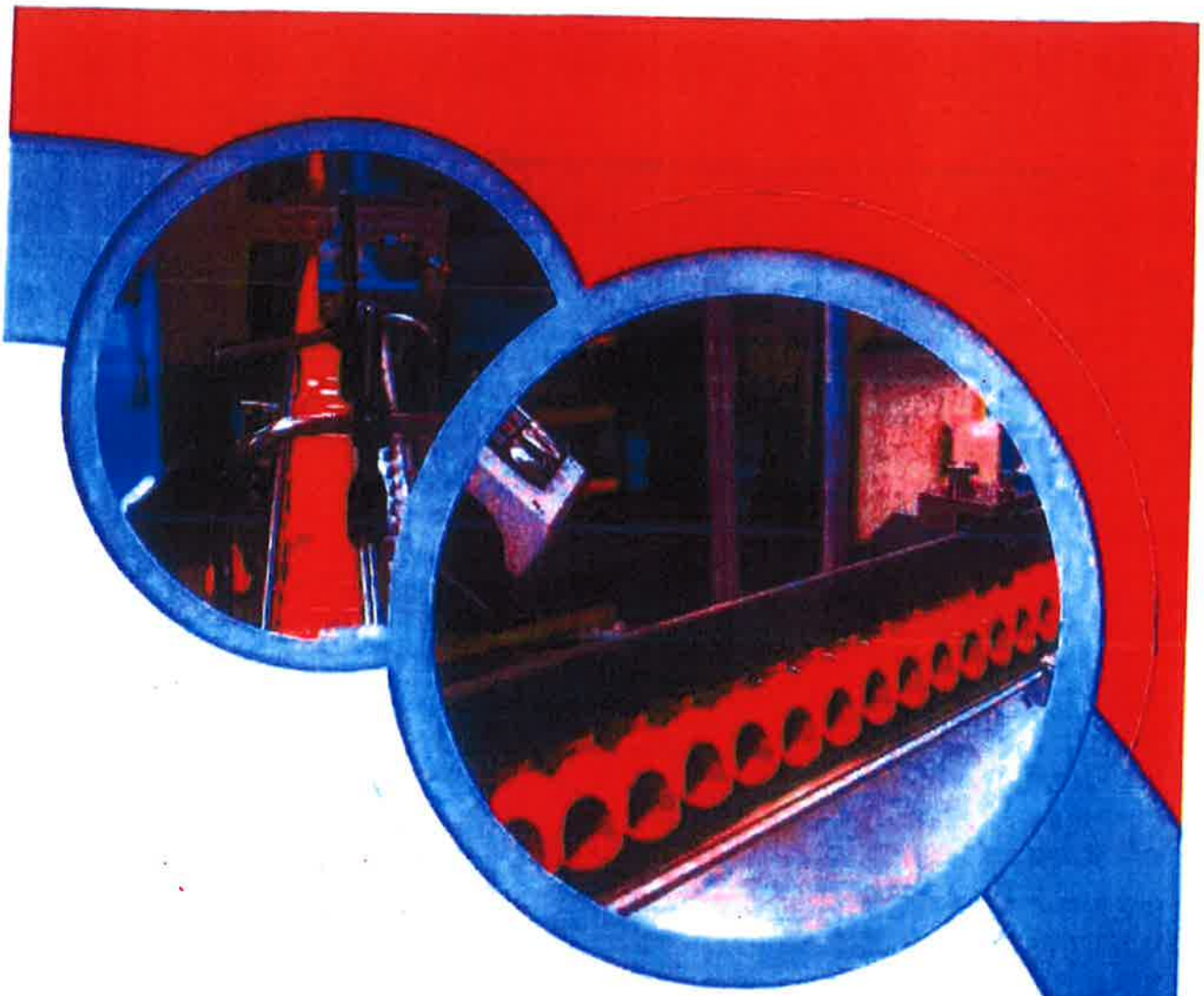
- **6 automatic packaging lines including 1 line with overwrap capacity**
- **2 manual packaging lines US/Japan/ Standard**
- **Assembling machine dedicated to Dose Counter**
- **Heat stress capacity**
- **Electronic Batch Record**
- **Automatic vision checking system**

Equipements / Technologies:

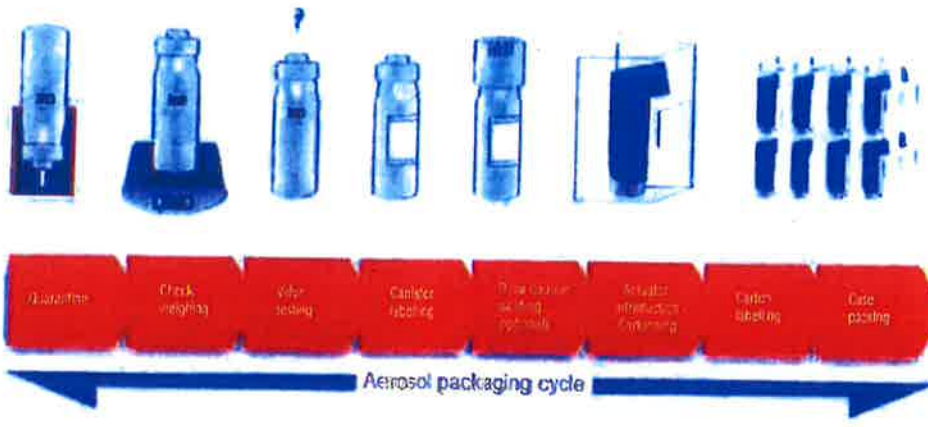
- Induction technology
- Laser or ink printer
- Check weighing, spray testing, labeling equipments
- Cartoner equipment
- Automatic check weighers
- Labellers
- Labeller case packer equipments
- Typical can size : 5 ml, 8 ml, 12.5 ml



AEROSOLS PRODUCTS



Packaging process



DPI PRODUCTS

Features

Rotadisks® and Diskus® specifications

Rotadisk® is an aluminium circular blister of 4 pockets. The associated device is the Diskhaler®, which is a multi-dose dry powder reusable device. At each use, the device pierces one pocket of the blister. The powder is released to be breathed by the patient.

Diskus® is a multi-dose dry powder disposable device. Inside this discoid shape device comprising of 14 plastic moulded components, the inhaled dry powder is sealed in an aluminium blister, which is inserted into the Diskus®.

Typically, there are 28 or 60 doses in the blister. A dose counter indicates the remaining doses. The Diskus® device peels the base foil and the lid foil. The individual drug product is then released to be breathed by the patient.

Rotadisk® key Features:

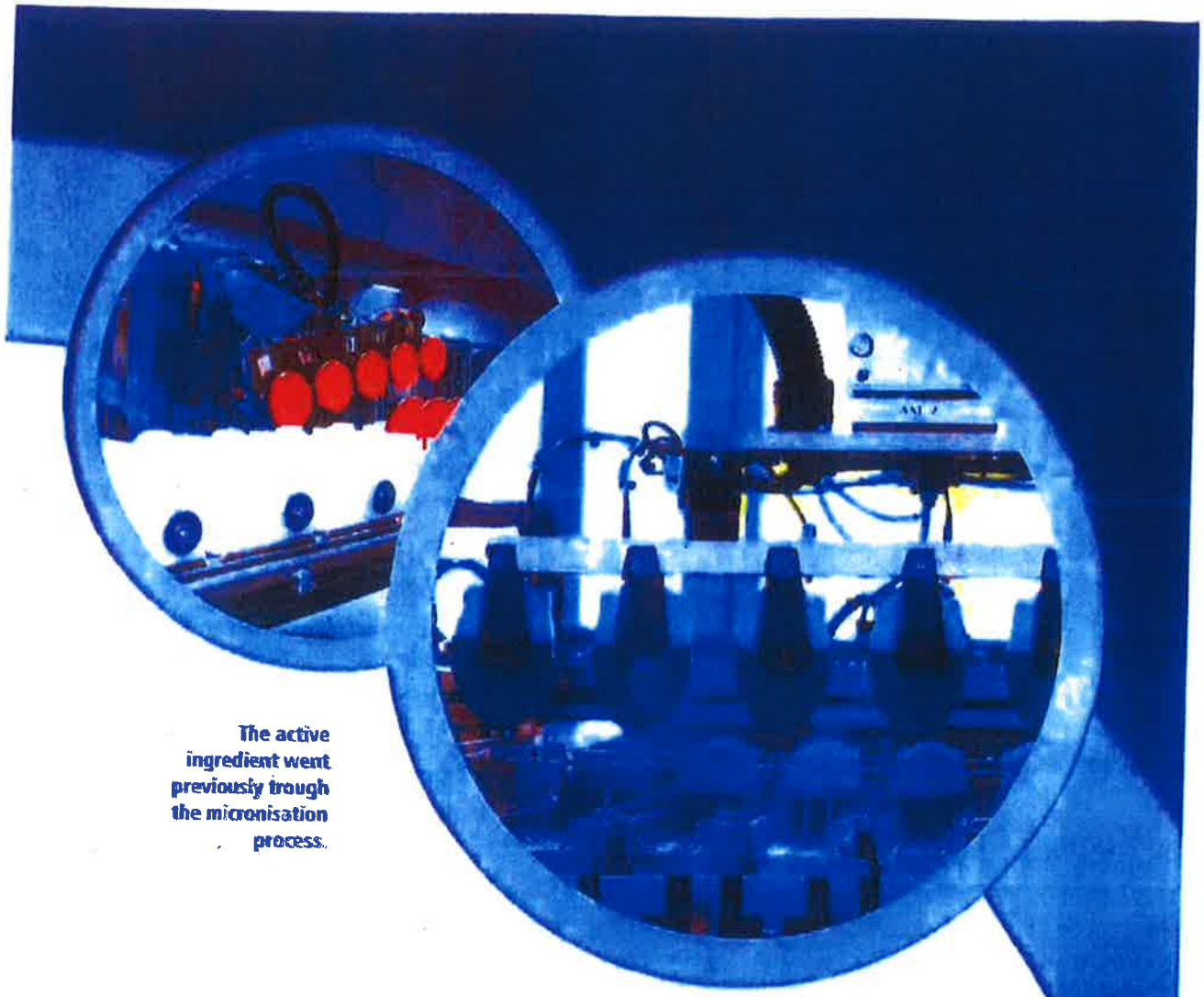
- The Rotadisk® is made of blister foil containing powder inside the 4 pockets.
- Reusable device with refill pack

Diskus® key Features:

- The Diskus® contains an aluminium strip
- Dose counter, high technology assembly process

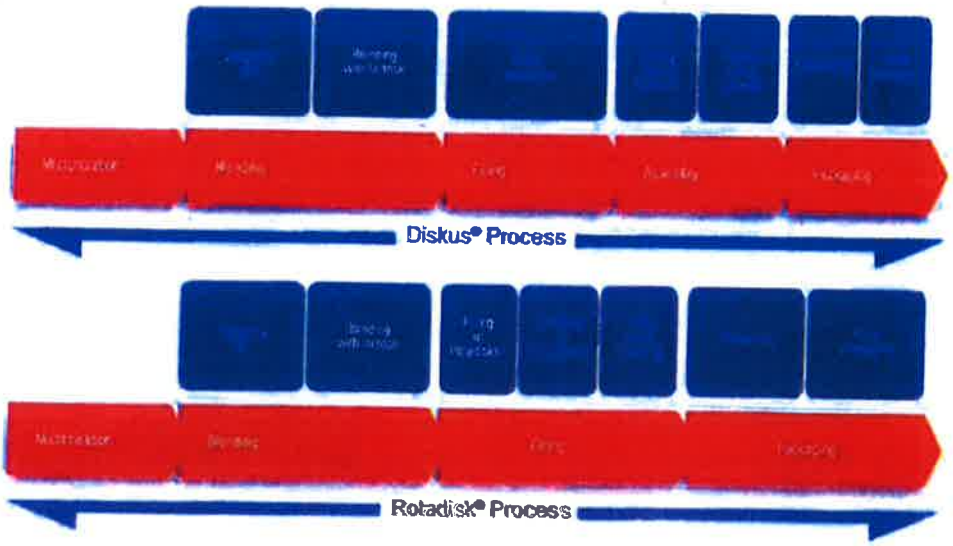
Commun main characteristics:

- Multi-dose device
- Easy & quick to use/learn/teach
- No coordination hand/breathe required (user independant)
- Compact, easy to carry
- Easy to grip
- Low force to operate
- Robust
- Distinctive image
- Tamper resistant and evident
- Color distinctive per API
- Discreet and safe
- Filled with blend of lactose and active



The active ingredient went previously trough the micronisation process.

Production process



DPI PRODUCTS

Blending & filling & packaging

Blending operation: Rotadisks® & Diskus®

Micronised API and excipient are blended together.

The blending step follows a very rigorous process : time, speed, temperature and humidity are strictly controlled. GSK has developed a specific know how to blend small quantity of API in a large amount of excipient (less than 1%).

Key Features:

- 6 blending areas
- Wastes treatment
- Electronic Batch Record
- Air environment control
- Dedicated pharmaceutical manufacturing facility

Equipments and Technologies:

- 4 low shear blenders:
  Speed: 250rpm / Energy: 18kW/m3
  Flat blad
- 2 high shear blenders:
  Speed: 470rpm - 600rpm
  Energy: 133kW/m3 / Double propeller
- 1 Sieve with batch size: from 12kg to 75kg
- Dedicated HVAC

Rotadisks® filling operation

The base foil is formed with pockets. Pockets are filled through a dosator with a very accurate low weigh of dry powder (typically 25mg). Each pockets are checked for the absence of powder by an automated vision system. The batch number and expiry date are embossed or printed on the lid foil.

Key Features:

1. 5 filling lines
2. Dosage accuracy: from 13 to 25 mg per pockets
3. Packaging in plastic tubes or in carton of 5 to 15 disks
4. 1 automatic high speed and accuracy checkweigher
5. Cold formed blister technic
6. Air environment control
7. Electronic Batch Record
8. Filling technic powder compaction
9. 100% checking vision system for powder absence and disk printing
10. 100% laser detection for micro crack

Equipments and Technologies:

- Filling lines with vision system
- Automatic coding equipment
- Automatic high speed checkweigher
  2 mg (speed = 60 cpm)

DPI PRODUCTS

The diskhaler® is loaded with a blister by the patient. No assembly step is requested before packaging activity.

Rotadisks® packaging operation

The Rotadisks® are inserted by group of 5 into tubes or grouped with a leaflet in small cartons. These are packed in larger cartons with a Diskhaler® device and a patient information leaflet. If required by market, the tube is overwrapped and an outsert is applied to the back of the box. The batch number and expiry date are printed on carton boxes.

Key Features:

- 3 automatic packaging lines
- 1 semi-automated packaging line, for pandemic preparation

Equipments and Technologies:

- Automatic packaging lines
- Flowwrap equipments
- Hybrid flexible printing systems (electronic cliche)
- Tamper evidence system by sticking equipment or labeling equipment
- Labellers
- Cartonners
- Tubing equipments

DPI PRODUCTS

Filling & assembly & packaging

Diskus® filling operation

The base foil is formed with pockets into a double strip with the appropriate number of blister pockets. Pockets are filled, by immersion, with a accurate low weigh of inhaled dry powder (typically 13 mg).

The drug is sealed into an individual pocket with a lid foil. Traceability is ensured by printing key information on every strip.

Key Features:

- 6 filling areas
- Waste treatment
- Electronic Batch Record
- Air environment control
- Dedicated pharmaceutical manufacturing facility
- 100% checking vision system for powder failure
- 100% laser detection for micro crack

Equipments and Technologies:

- Typical filed weight : 13 mg
- 4 lines dedicated to 60 Doses
- 2 lines dedicated to 28 and 60 Doses
- Automatic checkweigher on each line

Diskus® assembly operation

Assembly step consists in inserting the strip inside the device. All the different steps are fully automated on specific manufacturing lines. The filled strips are fed into the unit and cut and coiled to the appropriate length.

The machine places the cut coiled strip into the device sub assembly. The assembly station assembles the top onto the body base. The mouth piece and the cover are then assembled onto the device. 23 critical quality parameters are checked on all devices through a X-Ray checking system. Devices which do not meet specifications are automatically rejected.

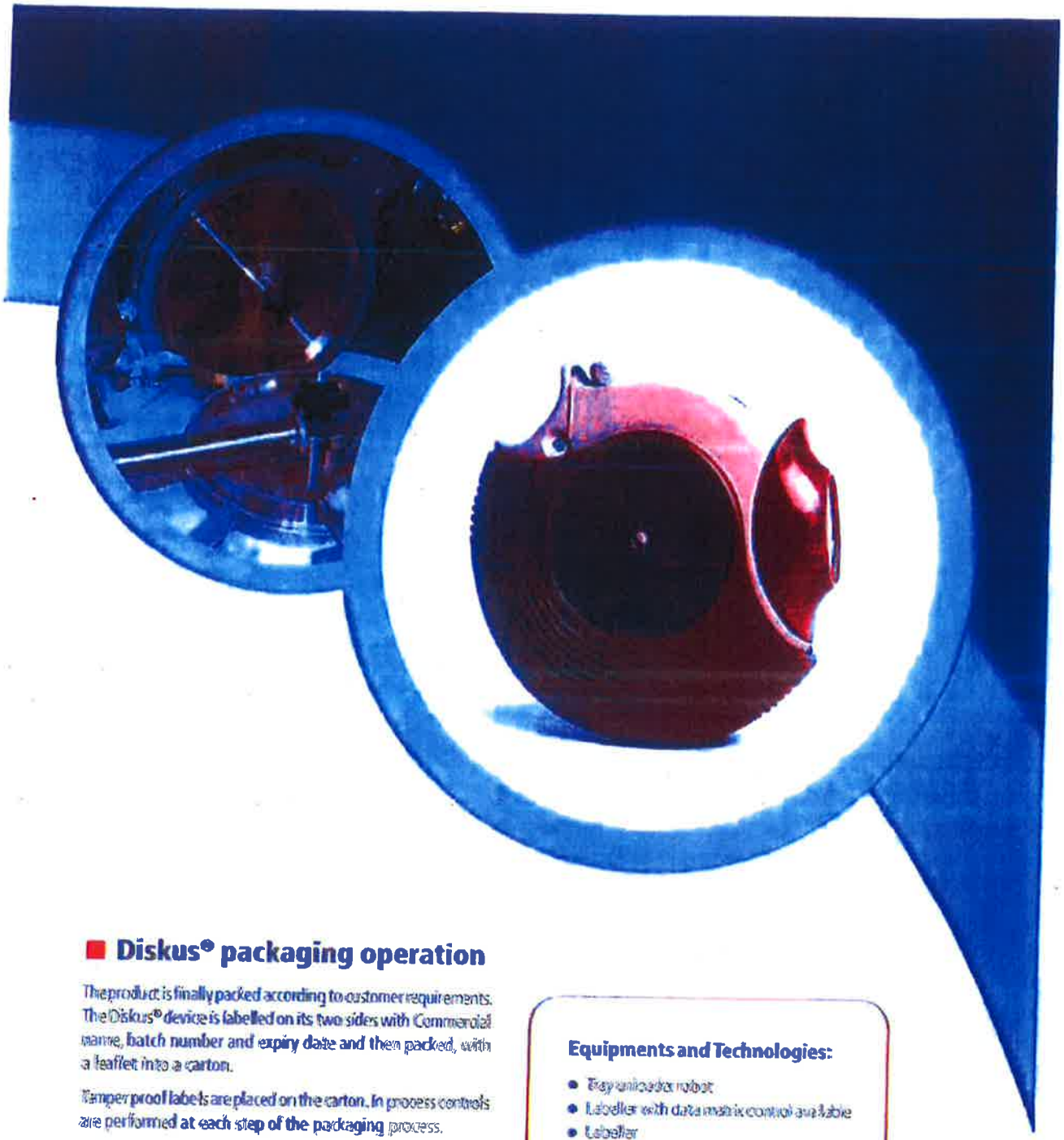
Key Features:

- 5 assembly lines (28 and 60 Doses)
- Automated X-Ray checking station (23 non destructive tests)
- 5 in process control indexing robots
- 4 palletizer automated lines
- Electronic Batch Record
- Waste treatment

Equipments and Technologies:

- Assembly lines in cells concept
- Roll cutting equipment

DPI PRODUCTS



Diskus® packaging operation

The product is finally packed according to customer requirements. The Diskus® device is labelled on its two sides with Commercial name, batch number and expiry date and then packed, with a leaflet into a carton.

Tamper proof labels are placed on the carton. In process controls are performed at each step of the packaging process.

Key Features:

- 5 packaging lines (including 2 for Japan)
- Pack of 1, 3 or 10 units
- Top loading packaging equipment
- 1 line equipped with overwrap equipment
- Electronic Batch Record

Equipments and Technologies:

- Tray unloader robot
- Labeller with data matrix control available
- Labeller
- Vision system
- Continuous process cartoner
- Packaging line
- Overwrap equipment
- Ultrasonic system for overwrap welding
- Laser printing
- Case packer
- Robot for pallet unloading

Development

pilot and industrialisation

Pilot and industrialisation

The pilot unit contains equipment, facilities and competencies for the development of inhaled drugs. It allows to carry out many different studies:

- small scale or exploratory batches
- formulation & process development
- clinical studies phase I to III
- commercial process development

Key Features:

- **500 m² of 9 GMS flexible and multi-purpose work zones**
- **Controlled environment (35/55% RH, < 15% RH) with a central weighing station, and a dedicated warehouse**
- **GMP qualified pilot plan, from lab development to large-scale.**
- **Mecanic grinder**
- **Microfluidiser (2 batch scales)**
- **Spray-dryer**

Equipments and Technologies:

- 500m² + 2,200m² Technical Plant Area
- Manufacturing and Packaging from a few grams up to 30 kg
- Full GMP conditions for exploratory to clinical
- Micronization
- Blending: rotary blenders, planetary blenders, high shear mixers
- Coating: perforated pan, fluid bed dryer, spray dryer
- Capsule Filling: laboratory scale, pilot scale
- Automated Dose Delivery (ADD)
- Automatic Sample Recovery System (ASRS)
- Andersen Cascade Shake Fire (ACSF)
- Tomography
- Particle sizing by laser diffraction

DEVELOPMENT

An industrialisation knowledge to meet your business challenges

The Evreux site is fully dedicated to respiratory products. The site has developped a recognized knowlekdge and a specific know-how around respiratory business: process, components and devices, technology.

Respiratory high skills are covering:

- Process expertise with a dedicated team managing process improvements, new product introduction and technical mastery.
- Device expertise with a dedicated team highly skilled in respiratory packaging components, devices and packaging.
- Equipment Expertise with a dedicated team in charge of maintenance, improvement of current equipments and introduction new technology.
- Qualification and validation team experienced in Pharmaceutical national and international references and guidelines.
- Regulatory registration expertise who can support registration of product from full filing to post approval changes.

Key Features:

- **Changes introduction, with an impact on existing products:**
  - **Primary (API)**
  - **Manufacturing process and new technologies**
- **Process improvement implementation**
- **Support to technical investigation**
- **Development of primary and secondary components**
- **Development and implementation of devices and packaging components**
- **Management of packaging components changes (specifications, suppliers' equipment,...)**
- **Management of data related to technical specifications of packaging components**
- **Knowledge Management**

Equipments and Technologies:

- Tomography
- Automatic data collection system on equipment
- High speed camera
- Statistical softwares
- Lean sigma tools
- Product data base

Development

pilot and industrialisation

Expertise in Tomography

2D X-ray image

Section issued from 3D volume

X. Ray Technology: Understanding the science

We identify all the quality critical parameters and design the optimum manufacturing processes and control these parameters. Working this way will allow us to launch products more quickly, operate our processes more effectively with higher yields, fewer batch refusal and ultimately, lower cost of goods.

The X.Ray objectives

- X-ray technologies can provide relevant and detailed information about our products in a way to:
- Improve our control and measurement on components and product at reception or during manufacturing process.
- Reduce the investigation time (ap. 30%) and the potential re-test in QC labs.
- Validate process component.
- Support new product development.

DEVELOPMENT

GSK EVREUX

BILAG 37

Sherwood Forest Hospitals NHS
NHS Foundation Trust

INFORMATION FOR PATIENTS

How to use an Accuhaler

This leaflet will inform you how to use an Accuhaler.

Always read the patient information leaflet which comes with this inhaled medication.

This is an Accuhaler device and comes in different colours indicating different medicines.

The benefit of using your inhaler correctly is that your asthma or chronic obstructive pulmonary disease (COPD) will be controlled more effectively.

Incorrect use of your inhaler may result in reduced control.

To use your Accuhaler device effectively follow this step by step guide:

1. Use only as prescribed.
2. Open the Accuhaler by holding the outer casing of the Accuhaler in one hand, while pushing the thumb grip away until a click is heard.
3. Hold the Accuhaler with the mouthpiece towards you and slide the lever away until it clicks. This makes the dose available for inhalation and moves the dose counter on.
4. Holding the Accuhaler level, breathe out gently away from the device, put the mouthpiece in the mouth and breathe in steadily and deeply.
5. Remove the Accuhaler from the mouth and hold your breath for about ten seconds.
6. For a second dose, repeat steps 1-5.
7. To close, slide the thumb grip back towards you as far as it will go until it clicks.

How to clean the Accuhaler

- To clean, wipe the mouthpiece of the Accuhaler with a dry tissue only
- Do not wash

How to store the Accuhaler

- Each dose of medicine is sealed in a separate blister in a foil strip within the device
- Only the primed dose is susceptible to damp
- Store away from extremes of temperature
- Store in a safe place away from small children

Replacement of the Accuhaler

- Accuhaler contains 60 doses
- Counts down from 60 – numbers in black
- Last five numbers in red
- Counter remains on 0 when empty and should be replaced
- Do not use after the expiry date.

Contact details

If you require any help, advice or support please contact:

Respiratory Specialist Nurse
Cardio-Respiratory Department (Clinic 4)
King's Treatment Centre
King's Mill Hospital
01623 622515 ext 6831, 3541 and 6324
Monday – Friday, 9am–5pm

Further sources of information

Our website: www.sfh-tr.nhs.uk

External websites may be referred to in specific cases. Any external websites are provided for your information and convenience. We cannot accept responsibility for the information found on them. Stating a web address does not imply we endorse a particular site. Neither does not stating a web address imply lack of endorsement.

Patient Advice and Liaison Service (PALS)

The PALS team is available to help with any of your comments, compliments or concerns and will ensure a prompt and efficient service. Contact details:

- King's Mill Hospital **01623 672222**
  (out of hours answer phone)
  Email: Pals.kmh@sfh-tr.nhs.uk

- Newark Hospital **01636 685692**
  (out of hours answer phone)
  Email: Pals.nwk@sfh-tr.nhs.uk

If you need this information in a different language or format, please contact PALS, as above.

Leaflet code: PIL3151
Created: Feb 2013/ Review Date: Feb 2015

Inhalation Devices and Propellants:

Key Recommendations[1]

- The inhalation device that best fits the needs of the individual patient should be chosen.
- Inhaled drug delivery is recommended over oral or parenteral delivery for adrenergic bronchodilators and glucocorticosteroids.
- With adequate teaching, adults and older children can use any of the commercially available hand-held inhalation devices. MDIs with spacers can be considered for all age groups, and specifically MDIs with valved spacer and face mask are advocated for young children and the elderly. Dry-powder inhalers can provide adequate drug delivery for most children by the time they reach age 5 years. (Note: ADVAIR® DISKUS® is indicated in children as young as 4 years of age.[2] Consult respective prescribing information for other products.)
- Patients' method of using their inhalation device must be reassessed and reinforced periodically.
- Health care professionals must teach correct inhaler technique when devices are prescribed and dispensed.

References: 1. Boulet LP, Becker A, Bérubé D, *et al.* Canadian asthma consensus report, 1999. *CMAJ* 1999;161(11 Suppl):S44-S50. 2. Product Monograph of ^*ADVAIR*®, GlaxoSmithKline Inc., October 2006.

^*ADVAIR*® (salmeterol xinafoate/fluticasone propionate) inhalation preparation is indicated for the maintenance treatment of asthma in patients with reversible obstructive airways disease where the use of a combination product is considered to be appropriate. *ADVAIR*® should not be used in patients whose asthma can be managed by occasional use of short-acting, inhaled β_2-agonists. *ADVAIR*® contains a long-acting β_2-agonist and should not be used as a rescue medication. To relieve acute asthmatic symptoms, a short-acting bronchodilator (e.g., salbutamol) should be used.

ADVAIR® DISKUS® inhalation preparation contains lactose (which contains milk protein) and is contraindicated in patients with IgE mediated allergic reactions to lactose or milk.

In adolescents and adults, the most common side effects are throat irritation (2%), hoarseness/dysphonia (2%), headache (2%), and candidiasis (2%) which can be reduced by rinsing and gargling with water after inhalation; and palpitations (1%). In children aged 4 to 11, the only adverse event with an incidence of >2% was candidiasis.

HPA-axis function and hematological status should be assessed periodically. Height should also be regularly monitored in children and adolescents receiving prolonged treatment with inhaled corticosteroids. Concomitant use of fluticasone propionate and ritonavir, an HIV protease inhibitor, has been shown to result in clinically significant systemic side effects and should be avoided unless the potential benefit to the patient outweighs the risk.

Interim results from a large U.S. study (Salmeterol Multicentre Asthma Research Trial - SMART) showed increased risks of asthma-related deaths and other serious respiratory-related outcomes in patients receiving salmeterol, (a component of *ADVAIR*®/*ADVAIR*® DISKUS®) vs. those on placebo, in addition to their usual asthma therapy. The study was prematurely terminated after enrollment of half the intended number of patients. Post-hoc analyses of the data suggest that the risks may be greater in African-American patients and in those patients who did not report using inhaled corticosteroids (ICS) at study entry. Since the study did not assess the ICS dosages actually used by the patients, and may be different from those in *ADVAIR*® products, it is not known whether the increased risks seen with salmeterol would also apply to *ADVAIR*®/*ADVAIR*® DISKUS®. The *ADVAIR*®/*ADVAIR*® DISKUS® dosage form prescribed should reflect the patient's optimal inhaled steroid requirement.

ADVAIR® is available in 2 dosage forms, *ADVAIR*® DISKUS® for patients 4 years and older and *ADVAIR*® MDI for patients 12 years and older.

ADVAIR®
salmeterol xinafoate / fluticasone propionate
Asthma Control.

Consult respective prescribing information before prescribing.

GlaxoSmithKline

88981

Respiratory Inhaler Quick Reference Guide

ADVAIR®
salmeterol xinafoate / fluticasone propionate

CONTROLLERS

Anti-Inflammatories

"FLOVENT" DISKUS" Inhalation Device (Fluticasone propionate)
Available in 50, 100, 250 & 500 mcg per inhalation
GlaxoSmithKline

"FLOVENT" HFA (Fluticasone propionate)
Available in 50, 125 & 250 mcg per inhalation
GlaxoSmithKline

"PULMICORT" TURBUHALER" (Budesonide)
Available in 100, 200 & 400 mcg per inhalation
AstraZeneca

"ALVESCO" (Ciclesonide)
Available in 100 & 200 mcg per inhalation
ALTANA Pharma AG

"QVAR" (Beclomethasone dipropionate)
Available in 50 & 100 mcg per inhalation
3M Pharmaceuticals

This is not a complete list of available agents.
Please consult the CPS for others.

Combination Medications

"ADVAIR" DISKUS" Inhalation Device (Salmeterol xinafoate/fluticasone propionate)
Available in 50/100, 50/250 & 50/500 mcg per inhalation
GlaxoSmithKline

"ADVAIR" MDI (Salmeterol xinafoate/fluticasone propionate)
Available in 25/125 & 25/250 mcg per inhalation
GlaxoSmithKline

"SYMBICORT" TURBUHALER"" (Budesonide/formoterol fumarate dihydrate)
Available in 100/6 & 200/6 mcg per inhalation
AstraZeneca

Long-Acting Bronchodilators

"SEREVENT" DISKUS" Inhalation Device (Salmeterol xinafoate)
50 mcg per inhalation
GlaxoSmithKline

"SPIRIVA" HandiHaler" Inhalation Device (tiotropium bromide monohydrate)
18 mcg per inhalation
Boehringer Ingelheim

"OXEZE" TURBUHALER"" (Formoterol fumarate dihydrate)
Available in 6 & 12 mcg per inhalation
AstraZeneca

RELIEVERS (Short-Acting Bronchodilators)

"VENTOLIN" HFA
(Salbutamol sulfate)
100 mcg per inhalation
GlaxoSmithKline

"VENTOLIN" DISKUS"
Inhalation Device
(Salbutamol sulfate)
200 mcg per inhalation
GlaxoSmithKline

"BRICANYL" TURBUHALER"
(Terbutaline sulfate)
0.5 mg per inhalation
AstraZeneca

"ATROVENT" HFA INHALATION AEROSOL
(Ipratropium bromide)
20 mcg per inhalation
Boehringer Ingelheim

"AIROMIR"™ INHALATION AEROSOL
(Salbutamol sulfate)
100 mcg per inhalation
3M Pharmaceuticals

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Respiratory Inhaler Identification Chart

This is not a complete list of available agents. Please consult the CPS for others.

WHICH INHALERS HAVE BEEN PRESCRIBED FOR YOU?

CONTROLLERS

Anti-Inflammatories

"FLOVENT" HFA
(Fluticasone propionate)
Available in 50, 125 & 250 mcg per dose
GlaxoSmithKline

"FLOVENT" DISKUS"
Inhalation Device
(Fluticasone propionate)
Available in 50, 100, 250 & 500 mcg per dose
GlaxoSmithKline

"PULMICORT" TURBUHALER"
(Budesonide)
Available in 100, 200 & 400 mcg per dose
AstraZeneca

"QVAR"
(Beclomethasone dipropionate)
Available in 50 & 100 mcg per dose
3M Pharmaceuticals

Long-Acting Bronchodilators

"SEREVENT"
(Salmeterol xinafoate)
25 mcg per dose
GlaxoSmithKline

"SEREVENT" DISKUS"
Inhalation Device
(Salmeterol xinafoate)
50 mcg per dose
GlaxoSmithKline

"OXEZE" TURBUHALER"
(Formoterol fumarate dihydrate)
Available in 6 & 12 mcg per dose
AstraZeneca

"SPIRIVA"
HandiHaler Inhalation Device
(tiotropium bromide monohydrate)
18 mcg/capsule
Boehringer Ingelheim

Combination Medications

Inhaled steroids and long-acting β_2-agonists.

"ADVAIR" MDI
(Salmeterol xinafoate/fluticasone propionate)
Available in 125 & 250 mcg per dose
2 puffs BID
GlaxoSmithKline

"ADVAIR" DISKUS"
Inhalation Device
(Salmeterol xinafoate/fluticasone propionate)
Available in 100, 250 & 500 mcg per dose
1 inhalation BID
GlaxoSmithKline

"SYMBICORT" TURBUHALER"
(Budesonide/formoterol fumarate dihydrate)
Available in 100 & 200 mcg per dose
AstraZeneca

- Controllers help prevent respiratory symptoms such as wheezing, coughing and shortness of breath.
- Take your controller medication exactly as your doctor told you.

RELIEVERS

Short-Acting Bronchodilators

"VENTOLIN" HFA
(Salbutamol sulfate)
100 mcg per dose
GlaxoSmithKline

"VENTOLIN" DISKUS" Inhalation Device
(Salbutamol sulfate)
200 mcg per dose
GlaxoSmithKline

"BRICANYL" TURBUHALER"
(Terbutaline sulfate)
0.5 mg per dose
AstraZeneca

"ATROVENT" HFA INHALATION AEROSOL
(Ipratropium bromide)
20 mcg per dose
Boehringer Ingelheim

"COMBIVENT" INHALATION AEROSOL
(Ipratropium bromide/salbutamol sulfate)
20 mcg per dose
Boehringer Ingelheim

"AIROMIR" INHALATION AEROSOL
(Salbutamol sulfate)
100 mcg per dose
3M Pharmaceuticals

- Relievers help relax the tight muscles around airways therefore opening them up and making it easier to breathe. These medications provide quick relief when an asthma attack occurs.
- Relievers should only be taken when needed unless your Doctor tells you otherwise. More than 4 times per week could mean your asthma is getting worse and you should be reassessed by your Doctor.

Asthma is a common lung disease that can affect your breathing. Asthma is a chronic inflammatory lung disease characterized by recurrent breathing problems. While there is no "cure" for asthma, proper medical care and treatment can help most asthma patients live normally.

Chronic Obstructive Pulmonary Disease (COPD) is a disease that causes the airways of the lungs to be inflamed and become "obstructed" or blocked. COPD includes two major breathing diseases: chronic bronchitis and emphysema. Unlike asthma, COPD gets worse over time. Medications cannot cure COPD but they can help relieve symptoms; but quitting smoking is the most effective way to prevent the progression of COPD.

Consult respective prescribing information before prescribing.

GlaxoSmithKline
www.asthmacanada.com

ASTHMA SOCIETY OF CANADA
www.asthmakids.ca
www.asthma.ca

THE LUNG ASSOCIATION
www.lung.ca

COMMUNITY ASTHMA CARE CENTRE

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Asthma Q&A

The more you know about asthma and its treatment, the more you'll be able to control your breathing difficulties. These are some frequently-asked questions.

Questions

Open All Close All

There are many different medicines available for asthma treatment and most involve taking asthma inhalers. Your healthcare professional will go through the possible treatments with you and together you will agree on the ones most suitable for you. Here's a brief description of some of the terms you may hear:

Relievers

A reliever medicine, usually delivered by a blue inhaler, provides rapid, but short-acting relief of chest tightness and wheezing by relaxing the narrowed airways (known as bronchoconstriction) to help ease wheezing and breathlessness.

The most commonly recommended relievers are drugs called short-acting beta-2 agonists. These work within a few minutes to make it easier for you to breathe. There are a number of different reliever inhalers that can be used and your healthcare professional will advise which is most suitable for you.

Carry your reliever with you in case you experience symptoms, but relievers shouldn't be needed very often. If you need them most days or are waking at night in need of yours, then your asthma is not well controlled and you should talk to your healthcare professional.

Preventers

People with asthma have inflammation of the lining of the air tubes. This inflammation causes irritation and narrowing of these tubes, which in turn causes wheezing, tight chest and cough. Preventer medicines are designed to reduce this inflammation, preventing symptoms and asthma attacks.

To achieve this protective effect, preventers must be taken regularly (usually morning and night), even when you're feeling well, as there will nearly always be persisting inflammation in the lungs that will cause problems if left untreated. Most people with asthma will be prescribed preventer medicines as they are a cornerstone of treatment. The most widely prescribed preventer medicines are inhaled steroids that usually come in brown, red, or orange inhalers.

Some preventers come in tablet form, like leukotriene receptor antagonists (LTRAs) and theophylline. Sometimes steroid tablets (e.g. prednisone) are required to treat badly controlled asthma.

Other medicines

If your asthma is not well controlled with your regular preventer, your healthcare professional may suggest using additional, or 'add-on', therapy like a long-acting bronchodilator to better control your asthma. There are also combined therapies which are both preventer and bronchodilator medication. Other types and formats of medicine are available to help your healthcare professional give you the most appropriate treatment specific to your needs.

Side effects

Many people worry about the side effects of asthma medication, particularly if they're taken over a long period of time. There has been a lot of research into the benefits and side effects of asthma medicines, and overall the benefits outweigh the risks for those who need them.

The steroids used in many preventer inhalers do not cause addiction, lose their effectiveness over time or cause weight gain. The majority of people with asthma only require low doses of inhaled steroids, which are unlikely to cause serious side-effects. Sometimes regular inhaled steroids can lead to ulcers or oral thrush, but this can usually be avoided with simple measures like rinsing your mouth after using your inhaler or using a spacer device.

As the dose of a treatment increases, so does the possible risk of side effects, but high doses are only rarely needed, becoming necessary if your asthma is not well controlled. Your healthcare professional will work with you to maintain good control and keep your medication at the lowest possible dose.

The patient information leaflet you receive with your asthma treatment has detailed information about side-effects. If you are concerned about particular side effects or think a treatment is causing a side effect, ask your healthcare professional for advice.

How can my job affect my asthma?

What type of asthma devices are available?

What happens to my asthma as I get older?

How does asthma change during pregnancy?

Does alcohol consumption affect asthma?

Glossary

Here is a brief definition of terms you might come across relating to asthma:

Acute asthma - A sudden worsening of asthma symptoms.

Allergen - Something that comes into contact with the body (either by being inhaled, eaten, or contacting the skin), producing an allergic response.

Allergic rhinitis - Inflammation in the nose causing congestion, sneezing, runny nose and itchy eyes due to an allergic response to allergens in the environment. It can be due to allergens that only occur at certain times of the year, like pollen (hay fever), or allergens that are present year round, like house dust. It's more common in people with asthma and can trigger asthma.

Anaphylaxis (anaphylactic attack) - A sudden, severe allergic response to an allergen that can be life-threatening without urgent treatment.

Asthma Control Test™ (ACT) - A short questionnaire to help patients assess their asthma control.

Bronchoconstriction/bronchospasm - The contraction of the muscles around the airways causing narrowing of the air tubes resulting in wheezing, breathlessness and chest tightness.

Bronchodilator - A medicine that helps open (dilate) the air tubes. Usually given in a blue inhaler.

Chronic - A term used to describe a long-lasting condition or disease.

Chronic obstructive pulmonary disease (COPD) - A disease of the lungs, usually caused by smoking in which the air tubes are permanently narrowed or blocked. It has some symptoms and treatments similar to asthma. However, in asthma, the effects on the air tubes are reversible with the right treatment.

Control - Good asthma control means no symptoms of wheezing, breathlessness, cough or chest tightness. This also includes no restrictions to activities or asthma attacks and an infrequent need to use rescue (usually blue) inhalers.

Dander - Animal hair and flakes of skin which can cause allergic reactions.

Diagnosis - The identification of an illness or health problem by its signs, symptoms and medical tests.

Dry powder inhaler - An inhaler delivering medication to the lungs in powder form rather than as an aerosol.

Exacerbation - An asthma attack.

Exercise-induced asthma - Asthma symptoms brought on by exercise.

Hay fever - A name for allergic rhinitis in response to pollens that usually occurs in the spring. It may be associated with poor asthma control.

Healthcare professional - A person qualified in a health profession, such as a doctor, nurse or pharmacist.

Inflammation - Inflammation occurs when the body's defence mechanisms react to injury, infection or allergens. Inflamed tissues (e.g. the lining of the air tubes in people with asthma) become red and swollen.

Inhaler - A device that delivers asthma medicines to the lungs. Inhalers for relief medication are usually blue and preventers are often brown, red, or orange.

Late-onset asthma - Asthma that begins in adulthood.

Leukotriene receptor antagonists (LTRA) - Medicines used to treat asthma in some people, in the form of a tablet as opposed to an inhaler. LTRA medicines are taken regularly and work by blocking one of the chemicals involved in producing air tube inflammation.

Long-acting beta agonist (LABA) - A bronchodilator that works over a longer period of time (around 12 hours) than the 'short-acting' beta agonists. Usually used regularly as an 'add-on' to treatment with inhaled steroids.

Lung function tests - 'Blowing' measurements made on medical devices that describe how well the lungs are working and whether the air tubes are constricted. A peak flow measurement is an example of a lung function test.

(Pressurised) Metered dose inhaler (MDI) - Inhalers that use pressurised gas to deliver asthma medicine as a fine spray (aerosol) to the lungs.

Occupational asthma - Asthma caused by allergens inhaled in the work environment.

Ozone - A gas present in the atmosphere that, when present in the lower atmosphere, is a pollutant and can trigger asthma. (In the upper atmosphere (the ozone layer) ozone is beneficial and protective against harmful radiation from the sun.)

Peak flow rate - A measure of how fast a person can blow air out of their lungs and is a measure of how narrowed the air tubes are. It is measured by a peak flow meter and regular recording of results can be useful in monitoring asthma.

Personal asthma action plan - A plan of what to do when your asthma changes, containing details of your medication, asthma triggers, how to notice if your asthma is getting worse and what to do if you have an asthma attack. Drawn up with your healthcare professional, it is essential in helping you keep control of your asthma.

Preventer - Medicine taken regularly to control asthma by stopping inflammation in the lungs and asthma symptoms from occurring. Usually given as regularly taken inhalers, preventer medicines are the most important in controlling asthma and allowing you to lead a full life.

Primary care - Care delivered by healthcare professionals in the community as the first point of contact for patients. Primary care includes general practitioners, practice nurses and pharmacists.

Puffer - A common name for an inhaler, usually one that delivers medication in a spray.

Referral - Being sent to see a specialist for advice and treatment.

Reliever - Relieves inhalers (usually blue), also known as rescue inhalers. These act quickly to relax the airways making it easier to breathe and relieving symptoms, but have no effect on the underlying inflammation. People with well-controlled asthma should rarely need a reliever inhaler.

Review - An asthma check-up when the medicines and personal asthma action plan are reviewed. You should have an asthma review once every year and more often if things are not fully controlled.

Rhinitis - Irritation and inflammation of internal areas of the nose (see allergic rhinitis). Short-acting beta agonist (SABA) is the type of medicine used in reliever inhalers and acts as a bronchodilator opening the

air tubes. These medicines start to work within a few minutes but do not affect the underlying inflammation in asthma and should rarely be needed in well controlled asthma.

Skin prick test - A test for allergies where a small amount of allergen is pricked into the skin to see if a reaction occurs.

Spirometry - Detailed blowing tests carried out to determine how well the lungs are functioning. They give more information on the state of the lungs and air tubes than peak flow meters.

Steroids - A group of chemicals produced by the body and also made synthetically as medication in either an inhaled or tablet form. In asthma, they are used to treat inflammation in the airways which causes symptoms.

Theophylline - A medicine used in some patients that works by relaxing the muscles around the air tubes and is usually given in the form of a tablet. It is important that the dose of theophylline is exactly right for the individual, so blood tests are used to check this.

Triggers - Factors which may irritate the airways and bring on asthma symptoms or asthma attacks.

Uncontrolled asthma - This is when asthma symptoms are not well controlled and if nothing is done could lead to a full blown asthma attack. Use the **Asthma Control Test** to help you decide how well your asthma is controlled

How Seretide Can Help

Learn how Seretide works for patients with asthma, relieving symptoms and treating the underlying cause.

References:
1. Bateman ED et al. *Am J Respir Crit Care Med* 2004;170:836-844 | 2. Bateman ED et al. *Allergy*. 2008;63:932-938.

For further product information on Seretide, view the Consumer Medicine Information (CMI) and Data Sheet at www.medsafe.govt.nz.

Seretide® (fluticasone propionate/salmeterol xinafoate, available as a 50/25, 125/25 or 250/25 micrograms per actuation inhaler, or as a 100/50 or 250/50 micrograms per actuation Accuhaler®) is a Prescription Medicine for the treatment of reversible obstructive airway disease (ROAD) including asthma, and for the treatment of chronic obstructive pulmonary disease (COPD). Seretide is a fully funded medicine. Seretide 250/25 micrograms inhaler is a private purchase medicine that you will need to pay for. Use strictly as directed. Seretide is not the relief of acute symptoms. Always carry your reliever inhaler. Do not discontinue Seretide abruptly. Tell your doctor if you are having any other medicines or herbal remedies, you have pulmonary tuberculosis (TB), a thyroid problem or a heart problem, or you are having treatment for high blood pressure. Side Effects may include: Headache, 'shaky' feeling, fast heart rate, soreness in the nose and throat. If symptoms continue or you have side effects, talk your doctor, pharmacist or health professional. For more information, see Seretide Consumer Medicine Information at www.medsafe.govt.nz. Normal doctor's office visit fees apply. Ask your doctor if Seretide is right for you.

Fitroid® in addition to the Seretide information above which also applies to Fitroid® (fluticasone propionate). Fitroid® is available in 50, 125 or 250 micrograms per actuation inhaler and 50, 100, or 250 micrograms per actuation Accuhaler. Fitroid® is a fully funded medicine.

Serevent® in addition to the Seretide information above which also applies to Serevent® (salmeterol). Serevent® is available in 25 micrograms per actuation inhaler and 50 micrograms per actuation Accuhaler. Serevent® is a fully funded medicine.

Ventolin® (salbutamol) is available as an inhaled blue and CFC-free inhaler, 100 micrograms per actuation. Ventolin® is a partially funded Prescription Medicine. You will need to pay a part charge for this medicine. It is a short-acting bronchodilator used for the relief of asthma symptoms. Use strictly as directed. Do not use Ventolin® if you are sensitive to any of the ingredients in the preparation. Tell your doctor if you feel that the medicine has become less effective or you are using more than usual, have hypertension, high blood pressure, cardiovascular disease, diabetes, are taking any other medicine or herbal remedy including those you buy from a supermarket, pharmacy or health food shop. Side Effects may include: Headache, nausea, shaky or tense feeling, fast or irregular heart beat, 'warm' feeling (caused by blood vessels expanding under the skin), mouth or nasal irritation, shortness of breath or wheezing. If symptoms continue or you have side effects, talk your doctor, pharmacist or health professional. Additional Consumer Medicine Information for Ventolin® is available at www.medsafe.govt.nz. Prices for Ventolin® may vary across pharmacies. Normal doctor's office visit fees apply. Ask your doctor if Ventolin® is right for you.

Seretide, Fitroid®, Serevent, Ventolin® and Accuhaler are registered trade marks of the GlaxoSmithKline group of companies. Marketed by GlaxoSmithKline NZ Limited, Auckland. Adverse events involving GlaxoSmithKline products should be reported to GSK Medical Information on 0800 808 500. TAPS HAB269-13MA.

Asthma Control Test™ is a trade mark of QualityMetric Incorporated. Asthma Control Test is distributed by GlaxoSmithKline NZ Ltd, Auckland.

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Library

Asthma medicines

There are many different medicines available for the treatment of asthma and most are taken as inhalers. Your healthcare professional will go through the possible treatments with you and together you will agree the ones most suitable for you. Here's a brief description of some of the terms you may hear.

Relievers

A reliever medicine, which is usually delivered by a blue inhaler, provides rapid, but short-acting relief of chest tightness and wheezing by relaxing the narrowed airways (known as bronchoconstriction) helping the symptoms of wheeziness and breathlessness.

The most commonly recommended relievers are drugs called short-acting beta-2 agonists. These work within a few minutes to make it easier for you to breathe. There are a number of different reliever inhalers which can be used. Your healthcare professional will advise which is most suitable for you.

Take your reliever with you in case you experience symptoms however relievers shouldn't be needed very often. If you need them most days or are ever waking at night needing them then your asthma is not well controlled and you should have your asthma reviewed by a health professional.

Preventers

People with asthma have inflammation of the lining of the air tubes. This inflammation causes irritation and narrowing of these tubes which in turn causes the symptoms of wheezing, tight chest and cough. Preventer medicines are designed to reduce this inflammation in the air tubes, prevent symptoms occurring and prevent asthma attacks.

To achieve this protective effect, they must be taken regularly (usually morning and night though sometimes just once a day), even when you are feeling well as there will nearly always be persisting inflammation in the lungs that will cause problems sooner or later if left untreated. Most people with asthma will be prescribed preventer medicines as they are a cornerstone of treatment. The most widely prescribed preventer medicines are inhaled steroids which usually come in brown, red, or orange inhalers.

Some preventers come in the form of tablets, such as those called leukotriene receptor antagonists (LTRAs), and theophylline. Sometimes steroid tablets (e.g. prednisolone) are required to treat badly controlled asthma.

Other medicines

If your asthma is not well controlled with your regular preventer, your healthcare professional may suggest using additional, or add-on, therapy such as a long-acting bronchodilator to help you get your control get back on track. There are also combined therapies which are both preventer and bronchodilator medication. Other types and formats of medicine are available to help your healthcare professional give you the most appropriate treatment for your needs.

Side effects

Many people are concerned about the side effects of asthma medication, particularly if it is taken over a long period of time. There has been a lot of research into the benefits and side effects of asthma medicines, and overall the benefit of using them has been shown to outweigh the risks from their use in those who need them.

The steroids used in many preventer inhalers at the doses most people use do not cause addiction, do not lose their effects over time or cause an increase in weight. The majority of people with asthma only require low doses of inhaled steroids which are unlikely to cause serious side-effects around the body. Sometimes regular inhaled steroids can have effects on the mouth and lead to mouth ulcers or oral thrush, but this can usually be avoided by simple measures such as rinsing the mouth after using the inhaler or by using a spacer device (/en/library/view/21).

As the dose of a treatment increases so does the possible risk of side effects however high doses are only rarely needed and only become necessary if your asthma is not well controlled. Your healthcare professional will work with you to maintain good control and keep your medication at the lowest possible dose.

The patient information leaflet you receive with your asthma treatment has detailed information about side-effects. If you are concerned about particular side effects or think that a treatment is causing a side effect speak to your healthcare professional for advice.

Back (https://myasthma.com/en/library)

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PJ

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Our concerns with Relvar Ellipta

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Wed, 19/02/2014 - 11:23 — journal corresp...

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Medicines

From Mr T. G. D. Capstick, MRPharmS, and others

We would like to alert pharmacists to the potential for inadvertent dosing errors that may occur when patients are prescribed the new Relvar Ellipta (fluticasone furoate/vilanterol) inhaler for asthma or chronic obstructive pulmonary disease.

Pharmacists should be alert to the fact that the licensed strengths of Relvar Ellipta (92µg/22µg and 184µg/22µg) are equivalent to medium to high doses of fluticasone propionate (500µg and 1,000µg, respectively). There is no low-dose inhaled corticosteroid version available and the 92µg/22µg strength, marketed as "low to mid dose of inhaled corticosteroid" is actually at the top of the dose-response curve in asthma. Consequently Relvar Ellipta is not appropriate for patients at Step 3 of the British Thoracic Society and Scottish Intercollegiate Guidelines Network asthma guidelines.

For many years, pharmacists and other healthcare professionals have been educating patients on when to use their inhalers for asthma and COPD, and frequently use simple terms such as "reliever" or "blue inhaler" to advise patients when to use their salbutamol or terbutaline, and terms such as "preventer" or "brown, red or purple inhaler" to advise patients when to use their inhaled corticosteroid inhaler.

We are concerned that the new Relvar Ellipta inhaler will be confusing for patients because it has a blue cover and the brand name sounds similar to "reliever". This could cause patients mistakenly to use Relvar Ellipta on an "as needed" basis rather than regularly just once a day.

When we have shown pictures of the new Relvar Ellipta inhaler to patients and healthcare professionals, almost all have thought that this looked like a reliever inhaler and that it should be used when necessary for symptomatic relief.

There are other brands and generic inhalers that do not conform to the usual expected colour coding convention of inhalers, and pharmacists should be aware of these when educating patients.

Toby Capstick

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Governance and Clinical Lead

The Queen Elizabeth Hospital King's Lynn NHS Foundation Trust

Suman Gupta

Lead Respiratory Pharmacist

Stockport NHS Foundation Trust

On behalf of the UK Clinical Pharmacy Association Respiratory Group

DECLARATION: In the past two years Mr Capstick has received payment for educational sessions to various healthcare professionals from GSK, Novartis, Teva, Pfizer and AstraZeneca. He has also received sponsorship from Teva to attend the European Respiratory Congress in 2014.

Hamzah Baig, respiratory medical director, GSK, responds: We would like to clarify the correct dosing and the patients who may benefit from Relvar Ellipta while addressing the other points raised. This new inhaled corticosteroid (ICS) and long-acting beta-2-agonist (LABA) combination treatment contains fluticasone furoate (FF) and vilanterol (VI), respectively. 92/22µg and 184/22µg are approved in asthma and 92/22µg in COPD patients.

FF/VI 92/22µg was granted a low-mid dose ICS licence, indicated for the regular treatment of asthma in patients ≥12 years not adequately controlled on ICS and as an "as needed" short-acting inhaled beta-2-agonist, where appropriate, and can be prescribed as such. The licence of "low-mid dose" FF/VI was granted on the basis of clinical trials that have demonstrated its effectiveness and safety in thousands of patients on low-mid ICS. FF/VI is generally well tolerated, similar to other ICS/LABAs (see summary of product characteristics). A dose of 92µg FF once daily is approximately equivalent to 250µg fluticasone propionate (FP) twice daily. The approved indication is consistent with BTS-SIGN guidance in asthma management when stepping up appropriate patients from Step 2 to Step 3.

Traditionally, ICS dose has been described according to equivalence to beclometasone dipropionate (BDP). However, the exact equivalence of FF to BDP is not known because this has not been studied. FP was used as a comparator and is relevant as the ICS component of Seretide which is the most widely used ICS/LABA in the UK, with extensive clinical safety data over 16 years. Equivalence of FP to BDP was demonstrated through bioequivalence studies whereas FF to FP equivalence was measured through improvement in lung function. Therefore, no comparison of FF to BDP can be determined.

BTS-SIGN guidance states that an absolute threshold of steroid dose for introduction of LABA add-on therapy in all patients cannot be defined and patients should be initiated on a dose suitable for disease severity, and regularly assessed for stepping down treatment where appropriate.

Relvar Ellipta is a dry powder inhaler (DPI), has a light grey body, a pale blue cap and stands up on flat surfaces. Patients and healthcare professionals were involved throughout the development of Relvar Ellipta, including shape and colour, which from the limited scope of colours should be globally accepted.

Many inhalers are metered dose inhalers (MDIs) and are distinct from DPIs in shape, operation and handling. In studies, Relvar Ellipta showed that at least 95 per cent of patients with asthma and COPD used Ellipta correctly first time after one demonstration and >99 per cent were still using it correctly at day 28.

The name "Relvar" was created to suit many languages throughout the world. This has gone through the rigorous European Medicines Agency Name Review Group approval process to review suitability and one name is authorised throughout all member states. GSK has fully complied with this strict guidance. To date, we have not observed any safety signals relating to the name or colour.

We believe that pharmacists are well placed to help support patients on the appropriate use of their medication. Further information for pharmacists is available at www.relvar.co.uk.

See also: European Medicines Agency to approach GSK after respiratory pharmacists raise concerns about Relvar Ellipta

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Comment: *

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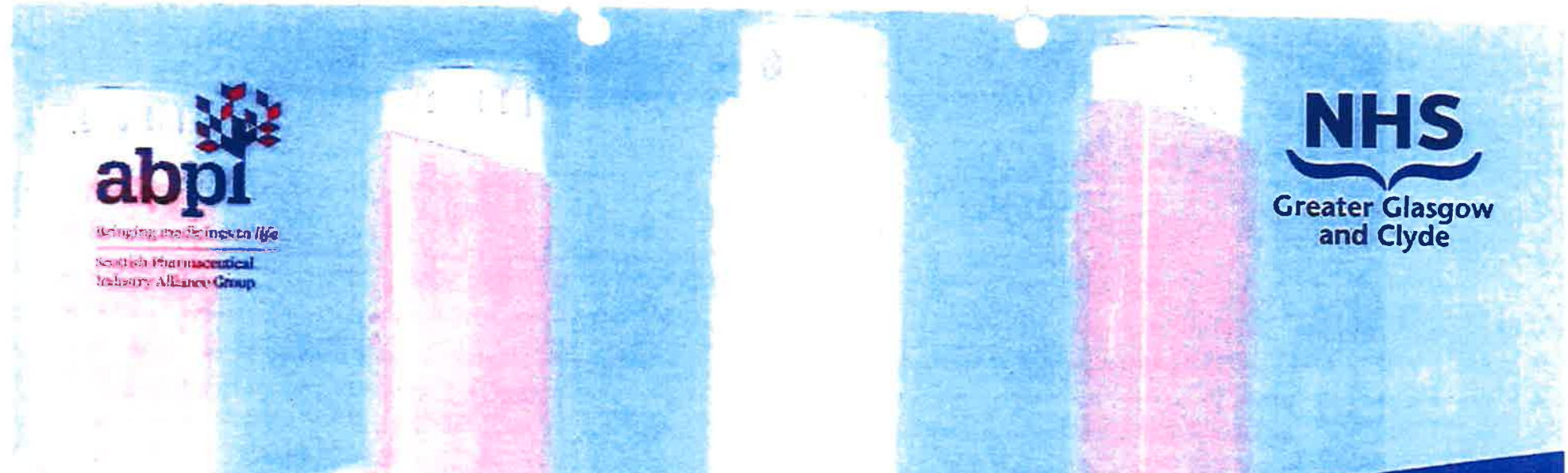
Security code

Please enter the characters below so that we can be sure this is a genuine submission.



abpi

Scottish Pharmaceutical Industry Alliance Group

NHS Greater Glasgow and Clyde

Respiratory Inhalers

Identification Guide

Version 2

This booklet has been produced by NHS Greater Glasgow and Clyde together with the following companies, Almirall, AstraZeneca, Boehringer Ingelheim Ltd, Chiesi, GSK, Napp and Novartis as a service to medicine.

Endorsed by NHSGGC Respiratory Managed Clinical Network, September 2013

Designed by Medical Illustration Services

230801

BILAG 43

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• Long-acting beta$_2$ agonist inhalers (LABAs)	Salmeterol Formoterol Indacaterol
• Short-acting muscarinic antagonists (SAMAs) • Long-acting muscarinic antagonists (LAMAs)	Ipratropium Tiotropium Aclidinium Glycopyrronium
• Corticosteroid inhalers	Beclometasone Fluticasone Budesonide
• Compound preparations	Seretide® Symbicort® Fostair® Flutiform®

Examples of High Cost Respiratory Inhaler Devices

Some inhaler devices are relatively more expensive than others. Examples of some of the higher cost devices are provided below. (Costs from eMIMS May 2013)

Seretide Accuhaler®

250 strength (60 doses) **£35**
500 strength (60 doses) **£40.92**

Seretide Evohaler®

125 strength (120 doses) **£35**
250 strength (120 doses) **£59.48**

Symbicort Turbohaler®

200/6 strength (120 doses) **£38**
400/12 strength (60 doses) **£38**

Spiriva®

cap pack with HandiHaler® device **£34.87**
30 cap refill **£33.50**

NB. For patients on Seretide® 500 micrograms twice daily, the 250 evohaler® is more expensive than the equivalent 500 accuhaler®

Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

Recommendations for Inhaler Supply

**** Important points to consider before issuing or prescribing inhalers ****

- Approximately £1.5 million□ was spent in 2012/13 on inhalers within NHSGGC Acute care. A lot of inhaler wastage occurs across NHSGGC Acute and most would be considered preventable.
- By adhering to the following recommendations, inhaler wastage could be minimised. Patient safety would also be improved by ensuring patients receive the correct inhaler, strength and device during hospital admission.
- Encourage the use of patient's own inhalers.
- Always ask patients if they have their own inhaler(s) before ordering or issuing a new inhaler. If patients have their own inhaler(s), check the expiry date and if it is the current inhaler prescribed by the GP. If they don't have their inhaler, ask if a relative or carer could bring it in at their earliest convenience.
- If a patient is transferred to another ward, ensure inhaler(s) are transferred with the patient. Similarly, if a patient has been transferred from another ward, always check if they have been issued with inhaler(s) prior to transfer.
- Always check what type of inhaler device and strength the patient uses before ordering or issuing a new one. If unsure, discuss with the doctor, clinical pharmacist, or respiratory nurse specialist.
- Ensure the correct device is clearly prescribed on the medicine prescription form (e.g. Accuhaler®, turbohaler®, evohaler®) prior to administration.
- Always check if a patient has an inhaler before documenting code '13' (patient self administration) on the medicine prescription form. Do not assume that patients have their own inhalers and they are using them as prescribed.
- When patients are started on inhalers for the first time, inhaler technique should be assessed. Seek advice from pharmacy or respiratory nurse specialist if unsure of the most suitable device.

**** Stop and think before ordering, issuing or prescribing inhalers ****

□(costs from Ascribe business objects acute database)

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Respiratory Inhaler Identification

There are many different inhaler devices available. Examples of the different types of inhaler devices are illustrated to aid identification. Please note however, that different strengths of inhalers may be slightly different colours than those shown. The manufacturer's packaging may also differ from time to time.The following images are for illustrative purposes only. If the patient does not have any of the inhaler devices illustrated, and you are unsure what device the patient normally uses, please speak to a pharmacist or respiratory nurse specialist for further advice.

This booklet is not intended to be a prescribing guide. Although dosage information is provided for some preparations, always refer to the BNF or manufacturer's Summary of Product Characteristics (SPC) for current dosage advice and further information.

The examples of the medicine prescription forms (kardexes) are for illustrative purposes only and do not reflect all doses available for each inhaler preparation.

The Asthma UK website has useful information on how to use spacers and different inhaler devices. Refer to the link below to access videos on inhaler technique:
http://www.asthma.org.uk/knowledge-bank-treatment-and-medicines-using-your-inhalers

Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

Bronchodilator – short-acting beta$_2$ agonist (blue/reliever) Inhalers (SABAs)

SALBUTAMOL

Salbutamol
***MDI** (aerosol)
(brands include
Ventolin evohaler®)

Strength: 100 micrograms/ metered inhalation

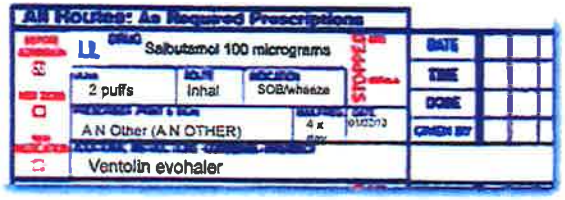
Salamol
Easi-Breathe®
(aerosol)

Strength: 100 micrograms/ metered inhalation

Airomir
Autohaler®
(aerosol)

Strength: 100 micrograms/ metered inhalation

Adult Dose
By aerosol inhalation
100-200 micrograms for persistent symptoms up to 4 times daily. Refer to manufacturer's dosing instructions or BNF for further advice



Example of medicine prescription form

(*MDI = metered-dose inhaler)

NB. Different strengths of inhalers may be slightly different colours to those illustrated.

Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

Bronchodilator – short-acting beta$_2$ agonist (blue/reliever) Inhalers (SABAs)

SALBUTAMOL

Pulvinal®
Salbutamol
(dry powder)

Strength: 200 micrograms/ metered inhalation^

Easyhaler®
Salbutamol
(dry powder)

Strengths: 100, 200 micrograms/ metered inhalation^

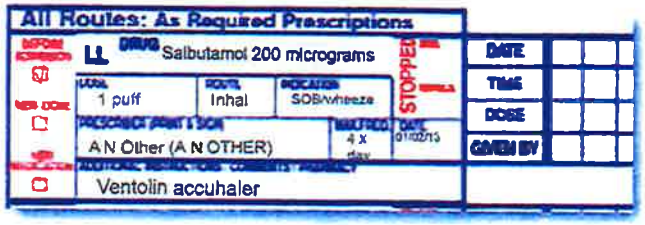
Asmasal Clickhaler®
(dry powder)

Strength: 95 micrograms/ metered inhalation^

Ventolin Accuhaler®
(dry powder)

Strength: 200 micrograms/ metered inhalation^

^Refer to manufacturer's dosing instructions or BNF for further advice.



Example of medicine prescription form

NB. Different strengths of inhalers may be slightly different colours to those illustrated.

Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

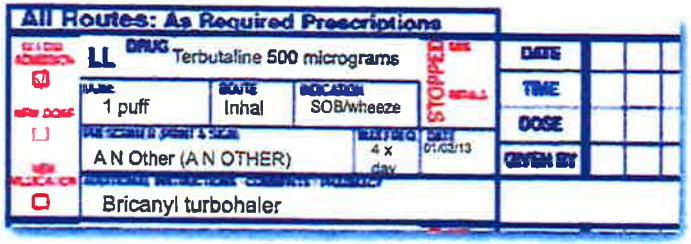
Bronchodilator – short-acting beta$_2$ agonist (blue/reliever) Inhalers (SABAs)

TERBUTALINE SULPHATE

Bricanyl Turbohaler®
(dry powder)

Strength: 500 micrograms/metered inhalation

Adult Dose
By inhalation of powder
500 micrograms for persistent symptoms up to 4 times daily. Refer to manufacturer's dosing instructions or BNF for further advice.


All Routes: As Required Prescriptions

DRUG Terbutaline 500 micrograms

STOPPED

1 puff | Inhal | SOB/wheeze

A N Other (A N OTHER) | 4 x day | 01/02/13

Bricanyl turbohaler

DATE | TIME | DOSE | GIVEN BY

Example of medicine prescription form

NB. Different strengths of inhalers may be slightly different colours to those illustrated.

Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

Long-acting beta$_2$ agonist Inhalers (LABAs)

SALMETEROL

Serevent Accuhaler®
(dry powder)

Strength: 50 micrograms/metered inhalation

Serevent Diskhaler®
(dry powder)

Strength: 50 micrograms/blister

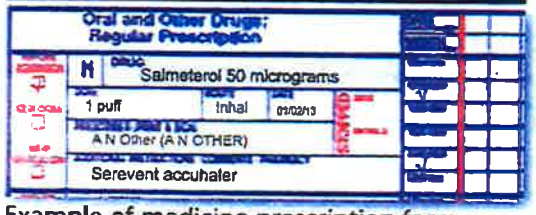
Serevent Evohaler®
MDI (aerosol)

Strength: 25 micrograms/ metered inhalation

Neovent®
MDI (aerosol)

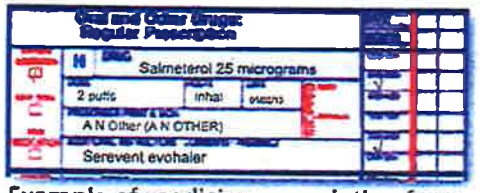
Strength: 25 micrograms/ metered inhalation

Adult Dose
By inhalation of dry powder
50 micrograms twice daily
up to 100 micrograms twice daily
Refer to manufacturer's dosing instructions or BNF for further advice.



Example of medicine prescription form

Adult Dose
By aerosol inhalation
50 micrograms twice daily up to 100 micrograms twice daily
Refer to manufacturer's dosing instructions or BNF for further advice.



Example of medicine prescription form

NB. Different strengths of inhalers may be slightly different colours to those illustrated.

Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

Long-acting beta$_2$ agonist Inhalers (LABAs)

FORMOTEROL FUMARATE

Oxis Turbohaler®
(dry powder)

Strengths^: 6, 12 micrograms/ metered inhalation

Easyhaler® Formoterol
(dry powder)

Strength: 12 micrograms/metered inhalation^

Atimos Modulite®
(aerosol)

Strength: 12 micrograms/metered inhalation^

^Refer to manufacturer's dosing instructions or BNF for further advice.

Example of medicine prescription form

NB. Different strengths of inhalers may be slightly different colours to those illustrated.

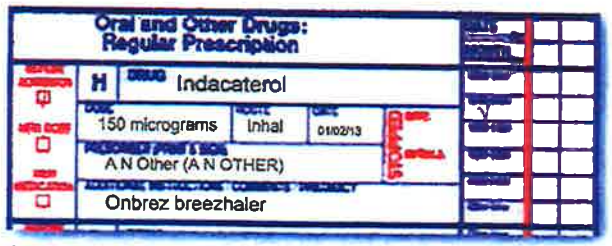
Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

Long-acting beta$_2$ agonist Inhalers (LABAs)

INDACATEROL

Onbrez Breezhaler®
(inhalation powder, hard capsule)
Strengths: 150, 300 micrograms/metered inhalation

Adult Dose:
By inhalation of dry powder
150 micrograms once daily increased to max. 300 micrograms once daily
Refer to manufacturer's dosing instructions or BNF for further advice



Example of medicine prescription form

NB. Different strengths of inhalers may be slightly different colours to those illustrated.

Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

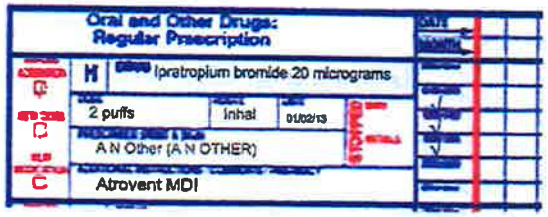
Antimuscarinic Bronchodilator Inhalers – short-acting muscarinic antagonists (SAMAs)

IPRATROPIUM BROMIDE

Atrovent®
MDI (aerosol)

Strength: 20 micrograms/metered inhalation

Adult Dose
By aerosol inhalation
20-40 micrograms 3-4 times daily. Refer to manufacturer's dosing instructions or BNF for further advice.



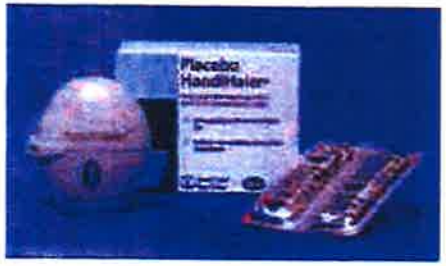
Example of medicine prescription form

NB. Different strengths of inhalers may be slightly different colours to those illustrated.

Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

Antimuscarinic Bronchodilator Inhalers – long-acting muscarinic antagonists (LAMAs)

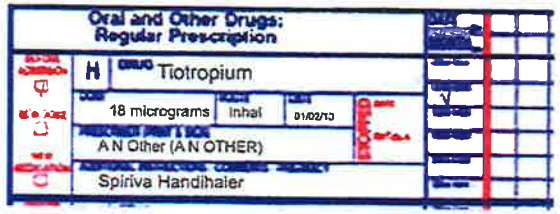
TIOTROPIUM



Spiriva®
(inhalation powder, hard capsule for use with HandiHaler® device)

Strength: 18 microgram cap

Adult Dose
By inhalation of powder
18 micrograms once daily.
Refer to manufacturer's dosing instructions or BNF for further advice.

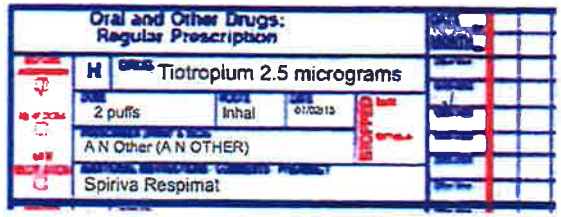


Example of medicine prescription form

Spiriva Respimat®
(solution for inhalation) Please note. Spiriva Respimat is currently non-formulary in NHSGGC.

Strength: 2.5 micrograms/ metered inhalation

Adult dose
By inhalation
5 micrograms (2 puffs) once daily. Refer to manufacturer's dosing instructions or BNF for further advice.



Example of medicine prescription form

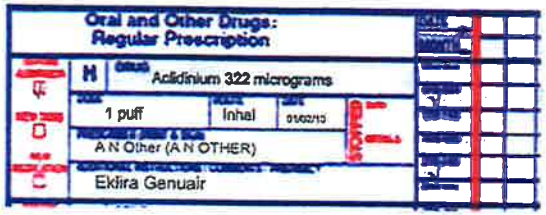
NB. Different strengths of inhalers may be slightly different colours to those illustrated.

Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

Antimuscarinic Bronchodilator Inhalers – long-acting muscarinic antagonists (LAMAs)

ACLIDINIUM BROMIDE

Adult Dose
By inhalation of dry powder
1 inhalation twice daily.
Refer to manufacturer's dosing instructions or BNF for further advice.



Example of medicine prescription form

Eklira Genuair®
(dry powder)

Strength: 400 micrograms/metered inhalation

Equivalence: each 400 micrograms metered inhalation of aclidinium bromide delivers 375 micrograms of aclidinium bromide which is equivalent to 322 micrograms of aclidinium.

NB. Different strengths of inhalers may be slightly different colours to those illustrated.

Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

Antimuscarinic Bronchodilator Inhalers – long-acting muscarinic antagonists (LAMAs)

GLYCOPYRRONIUM

Adult Dose
By inhalation of powder
50 micrograms
once daily. Refer to manufacturer's dosing instructions or BNF for further advice.

Example of medicine prescription form

Seebri Breezhaler®
(inhalation powder, hard capsule)

Strength: 50 micrograms cap

Equivalence: each 50 microgram capsule of glycopyrronium delivers 44 micrograms of glycopyrronium

NB. Different strengths of inhalers may be slightly different colours to those illustrated.

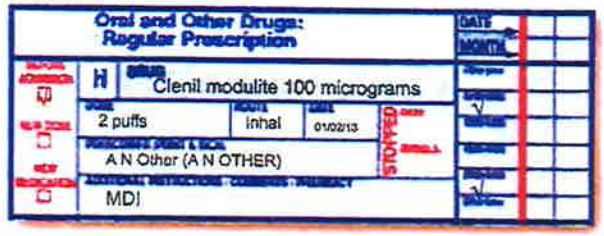
Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

Corticosteroid (brown/preventer) Inhalers

BECLOMETASONE DIPROPIONATE

** NOTE
BECLOMETASONE CFC-FREE AEROSOL INHALERS ARE NOT INTERCHANGEABLE AND MUST BE PRESCRIBED BY BRAND NAME **

Adult Dose
By aerosol inhalation
200-400 micrograms twice daily (up to 1mg twice daily)
Refer to manufacturer's dosing instructions or BNF for further advice



Example of medicine prescription form

Clenil Modulite®
(CFC-free) MDI (aerosol)

Strengths: 50, 100, 200, 250 micrograms/ metered inhalation

NB. Different strengths of inhalers may be slightly different colours to those illustrated.

Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

Corticosteroid (brown/preventer) Inhalers

BECLOMETASONE DIPROPIONATE

** NOTE:
BECLOMETASONE CFC-FREE AEROSOL INHALERS ARE NOT INTERCHANGEABLE AND MUST BE PRESCRIBED BY BRAND NAME **

Qvar®
(CFC-free) MDI (aerosol)

Strengths: 50, 100 micrograms/ metered inhalation

Qvar Autohaler®
(aerosol)

Strengths: 50, 100 micrograms/ metered inhalation

Qvar Easi-Breathe®
(aerosol)

Strengths: 50, 100 micrograms/ metered inhalation

Adult Dose
By aerosol inhalation
50-200 micrograms twice daily (up to 400 micrograms twice daily). Refer to manufacturer's dosing instructions or BNF for further advice.


Oral and Other Drugs: Regular Prescription
M
Qvar 100 micrograms
1 puff
Inhal
01/02/13
STOPPED
A N Other (A N OTHER)
MDI

Example of medicine prescription form

NB. Different strengths of inhalers may be slightly different colours to those illustrated.

Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

Corticosteroid (brown/preventer) Inhalers

BECLOMETASONE DIPROPIONATE

Pulvinal®
Beclometasone
(dry powder)

Strengths^: 100, 200, 400 micrograms/ metered inhalation

Easyhaler®
Beclometasone
(dry powder)

Strength^: 200 micrograms/ metered inhalation

Asmabec Clickhaler®
(dry powder)

Strengths^: 100, 250 micrograms/metered inhalation^

Example of medicine prescription form

^Refer to manufacturer's dosing instructions or BNF for further advice.

NB. Different strengths of inhalers may be slightly different colours to those illustrated.

Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

Corticosteroid (brown/preventer) Inhalers

FLUTICASONE PROPIONATE

Adult Dose
By aerosol inhalation
100-500 micrograms twice daily (up to 1mg twice daily)
Refer to manufacturer's dosing instructions or BNF for further advice.

Flixotide Evohaler®
MDI (aerosol)

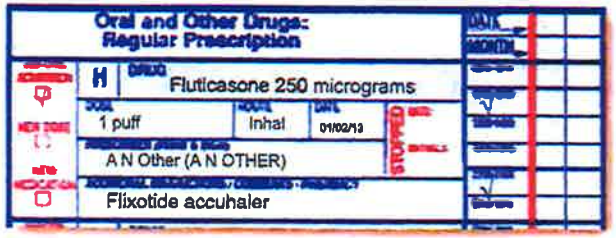
Strengths: 50, 125, 250 micrograms/metered inhalation

Example of medicine prescription form

Adult Dose
By inhalation of dry powder
100-500 micrograms twice daily (up to 1mg twice daily)
Refer to manufacturer's dosing instructions or BNF for further advice.

Flixotide Accuhaler®
(dry powder)

Strengths: 50, 100, 250, 500 micrograms/metered inhalation



Example of medicine prescription form

NB. Different strengths of inhalers may be slightly different colours to those illustrated.

Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

Corticosteroid (brown/preventer) Inhalers

BUDESONIDE

Pulmicort Turbohaler®
(dry powder)

Strengths^: 100, 200, 400 micrograms/metered inhalation

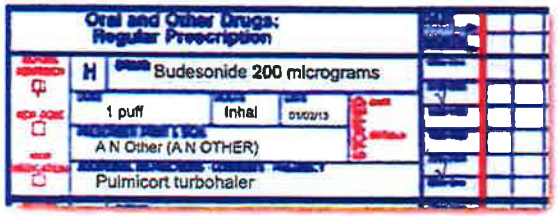
Easyhaler® budesonide
(dry powder)

Strengths^: 100, 200, 400 micrograms/ metered inhalation

Budelin novolizer®
(dry powder)

Strength: 200 micrograms/metered inhalation^

^Refer to manufacturer's dosing instructions or BNF for further advice.


Oral and Other Drugs: Regular Prescription
H Budesonide 200 micrograms
1 puff Inhal
A N Other (A N OTHER)
Pulmicort turbohaler

Example of medicine prescription form

NB. Different strengths of inhalers may be slightly different colours to those illustrated.

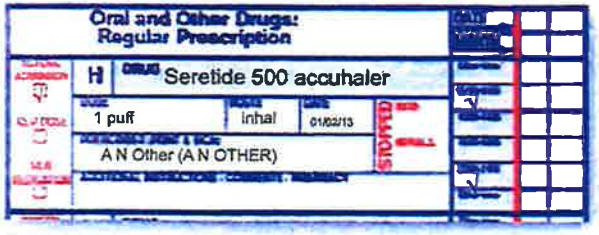
Produced by NHSCGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

Compound Preparations (Corticosteroid/ Long-acting beta$_2$ agonist)

FLUTICASONE/SALMETEROL

Seretide Accuhaler®
(dry powder)

Strengths^:
100 Accuhaler®
(fluticasone 100 micrograms/salmeterol 50micrograms)
250 Accuhaler®
(fluticasone 250 micrograms/salmeterol 50micrograms)
500 Accuhaler®
(fluticasone 500 micrograms/salmeterol 50micrograms)

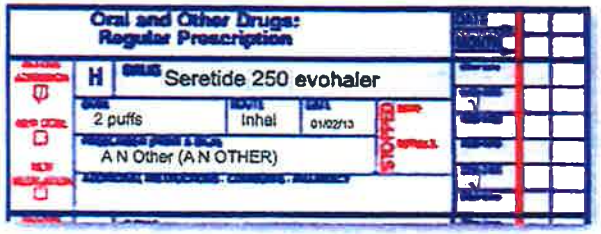


Example of medicine prescription form

^Refer to manufacturer's dosing instructions or BNF for further advice.

Seretide Evohaler®
MDI (aerosol)

Strengths^:
50 Evohaler®
(fluticasone 50 micrograms/salmeterol 25micrograms)
125 Evohaler®
(fluticasone 125 micrograms/salmeterol 25micrograms)
250 Evohaler®
(fluticasone 250 micrograms/salmeterol 25micrograms)



Example of medicine prescription form

NB. Different strengths of inhalers may be slightly different colours to those illustrated.

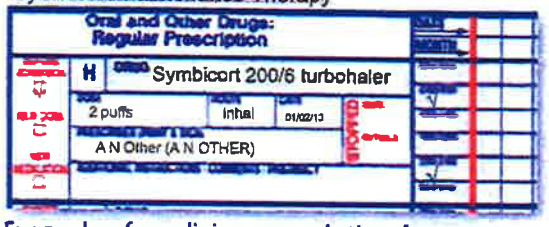
Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

Compound Preparations (Corticosteroid/ Long-acting beta$_2$ agonist)

BUDESONIDE/FORMOTEROL

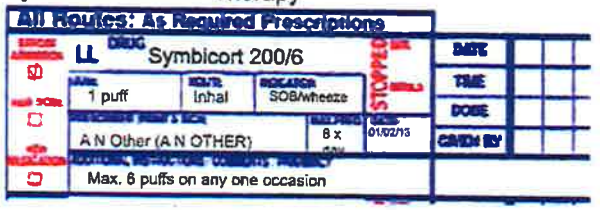
Symbicort Turbohaler®
(dry powder)

Symbicort Maintenance Therapy



Example of medicine prescription form

Symbicort Reliever Therapy



Example of medicine prescription form

Strengths^:
100/6 Turbohaler® (budesonide 100 micrograms/formoterol 6micrograms)
200/6 Turbohaler® (budesonide 200 micrograms/formoterol 6micrograms)
400/12 Turbohaler® (budesonide 400 micrograms/formoterol 12micrograms)

^Refer to manufacturer's dosing instructions or BNF for further advice.

NB. Different strengths of inhalers may be slightly different colours to those illustrated.

Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

Compound Preparations (Corticosteroid/ Long-acting beta$_2$ agonist)

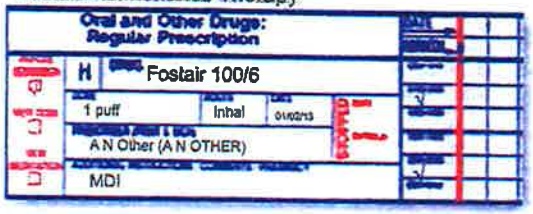
BECLOMETASONE/FORMOTEROL

Fostair®
(aerosol)

Strength: 100/6 (beclometasone 100 micrograms/ formoterol 6 micrograms)^

^Refer to manufacturer's dosing instructions or BNF for further advice.

Fostair Maintenance Therapy



Example of medicine prescription form

Fostair Reliever Therapy

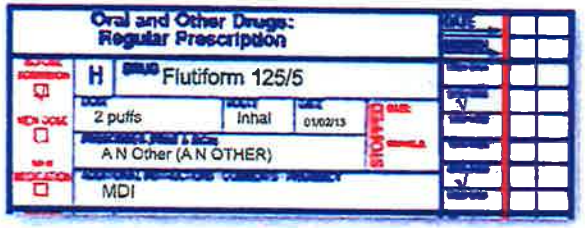
Example of medicine prescription form

NB. Different strengths of inhalers may be slightly different colours to those illustrated.

Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

Compound Preparations (Corticosteroid/ Long-acting beta$_2$ agonist)

FLUTICASONE/FORMOTEROL



Example of medicine prescription form

Flutiform®
(aerosol)

Strengths^: 50/5 (fluticasone 50 micrograms/formoterol 5 micrograms)
125/5 (fluticasone 125 micrograms/formoterol 5 micrograms)
250/10 (fluticasone 250 micrograms/formoterol 10 micrograms)

^Refer to manufacturer's dosing instructions or BNF for further advice.

NB. Different strengths of inhalers may be slightly different colours to those illustrated.

Spacer Devices

Some patients use spacer devices which remove the need for coordination between actuation of a pressurised metered-dose inhaler (MDI) and inhalation. Spacers reduce the velocity of the aerosol and subsequent impaction on the oropharynx and allow more time for evaporation of the propellant so that a larger proportion of the particles can be inhaled and deposited in the lungs.

Spacers should be cleaned once a month and replaced every 6 to 12 months. It is important to prescribe a spacer device that is compatible with the MDI. Spacer devices should **not** be regarded as interchangeable; patients should be advised not to switch between spacer devices.

1070

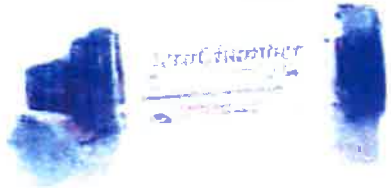
Volumatic®

- Large-volume device
- Compatible with all GlaxoSmithKline brand MDIs eg. Ventolin®, Serevent®, Flixotide®, Seretide® and also Clenil Modulite®
- Also available with paediatric facemask

Produced by NHSGGC Medicines Information, September 2013. Endorsed by Respiratory Managed Clinical Network.

Spacer Devices

AeroChamber® Plus



- Medium-volume device
- For use with all pressurised (aerosol) inhalers*
- Available as standard device (blue), child device (yellow), infant device (orange)
- Also available with facemask

Able Spacer®

- Small-volume device
- For use with all pressurised (aerosol) inhalers*
- Available with infant (small), child (medium) or adult (large) mask

A2A Spacer®

- For use with all pressurised (aerosol) inhalers*
- Available with small or medium mask

Optichamber®

- For use with all pressurised (aerosol) inhalers*
- Available with small, medium or large mask

Vortex Spacer®

- Medium-volume device
- For use with all pressurised (aerosol) inhalers*
- Available with infant, child or adult mask

Pocket Chamber®

- Small-volume device
- For use with all pressurised (aerosol) inhalers*
- Available with infant, small, medium or large mask

*Please check compatibility of all inhaler devices before prescribing.
Flutiform® has not been tested with all of the spacers listed on this page.

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Symbicort

Asthma treatments

There are four main types of inhaled asthma treatments (asthma inhalers).

Relievers

Relievers (usually blue) give rapid relief from asthma symptoms by relaxing your airways. Relievers work within 1-3 minutes and last for 3-4 hours.

Preventers

Preventers (usually brown or orange) reduce inflammation inside your airways to help prevent asthma symptoms from occurring in the first place.

Symptom Controllers

Symptom Controllers (usually green) also relax the airways but they last for longer (around 12 hours). They should always be taken with a Preventer.

Combination Inhalers

Combination inhalers (red or purple) contain a Preventer AND a Symptom Controller in one inhaler. They do two jobs by helping prevent asthma symptoms AND by relaxing the airways.

Symbicort SMART is a combination treatment. With Symbicort SMART you only need one inhaler because it combines two medicines - one that helps prevent asthma AND one that gives rapid relief when you need it, so you don't need a separate blue inhaler any more.

Symbicort SMART is the only asthma medication that can be used as both a preventer and a reliever.

If you have a question relating to an adverse event or product complaint for an AstraZeneca product, please contact us on +64 9 306 5673 or by email at Regulatory.NZ@astrazeneca.com

Symbicort® Turbuhaler® 100/6 & 200/6

Symbicort Turbuhaler used in Symbicort SMART (Symbicort Maintenance and Reliever Therapy) contains budesonide 100µg or 200µg per dose (preventer) and eformoterol 6µg (symptom controller). Symbicort SMART is indicated for the regular treatment of asthma where combination therapy is appropriate. Specific criteria apply for the use and funding of Symbicort. Not all patients are eligible for treatment with Symbicort. Ask your doctor if Symbicort is right for you. Use strictly as directed. Symbicort should not be initiated as emergency treatment for severe exacerbations or for patients with acutely worsening asthma symptoms. Do not use if you are allergic to budesonide or eformoterol. Tell your doctor if you have thyroid problems, heart problems, diabetes, problems with potassium levels, pregnancy, breast-feeding. Common side effects include mild irritation in the throat, coughing, hoarseness, thrush (fungal infection in mouth and throat), headache, trembling, fast or irregular heartbeat. Rarely, allergic reactions. Prescription Medicine. If symptoms continue or you experience side effects, see your healthcare professional. Your doctor's fee and a prescription fee will apply.

For full Consumer Medicine Information for Symbicort Turbuhaler see www.medsafe.govt.nz. Symbicort SMART and Turbuhaler are trademarks of AstraZeneca Group. AstraZeneca Limited, P299 Private Bag 92175, Auckland 1142, Telephone (09) 306 5660 Facsimile (09) 306 5651. TAPS NA 5723 APRIL 2012 essence AZ5730.

* Symbicort Maintenance And Reliever Therapy

1. Symbicort Turbuhaler Data Sheet 31 October 2011.
2. Jackson et al. J Allergy Clin Immunol 2010;125:1178-1187

Inhaled medicinal products - the Easyhaler® platform

The Easyhaler®, a device-metered dry powder inhaler developed and patented by Orion, is an environmentally friendly and efficient, yet easy to use inhaler for the treatment of respiratory illnesses such as asthma and chronic obstructive pulmonary disease (COPD). Orion aims to expand the product family of inhalable Easyhaler® drugs used for treating asthma and chronic obstructive pulmonary disease. Easyhaler products are available in more than 25 countries worldwide.

Currently four medicinal products are available in the patient-friendly Easyhaler® device.

Medicinal product	Active substance	Use
Budesonid Easyhaler®	Budesonide	Controller medication for asthma.
Beclomet Easyhaler®	Beclometasone	Controller medication for asthma.
Formoterol Easyhaler®	Formoterol	Controller medication for combination treatment of asthma and bronchodilator for maintenance treatment of COPD.
Buventol Easyhaler®	Salbutamol (albuterol)	Reliever medication for asthma and COPD; protector against bronchoconstrictors.

A dry powder inhaler delivers the active drug substance directly to the lower airways, where it exerts its intended effect. Only small amounts of active substance become available in the circulating blood, keeping any unintended harmful effects to a minimum. This guarantees a maximal benefit-to-risk ratio for inhaled treatments.

New medicinal products utilizing the Easyhaler technology platform are under development.

Orion is developing known active substances and their combinations for use in the Easyhaler and there are clinical studies on-going.

In addition, the Easyhaler platform can be used in the research and development of new molecular entities and proprietary products. In the future it is possible to develop dry powder formulations for inhalation of drugs used in the systemic treatment of illnesses outside the respiratory tract.

Orion has ongoing projects to broaden the range of the inhalable ***Easyhaler® drugs*** product family. Orion submitted an application for marketing authorisation for a combined ***budesonide-formoterol formulation*** in Europe in March, and the application is being processed. In this formulation, budesonide acts as an anti-inflammatory agent and formoterol acts as a long-acting bronchodilator.

In addition, Orion has another Easyhaler research programme in progress to develop a combined ***fluticasone-salmeterol formulation*** for European markets. In this formulation fluticasone acts as an anti-inflammatory agent and salmeterol acts as a long-acting bronchodilator.

Updated Oct 30th 2013

Orion Corporation, Orionintie 1A, 02200 Espoo, PO Box 65, FI-02101 Espoo, Finland
Phone +358 104261

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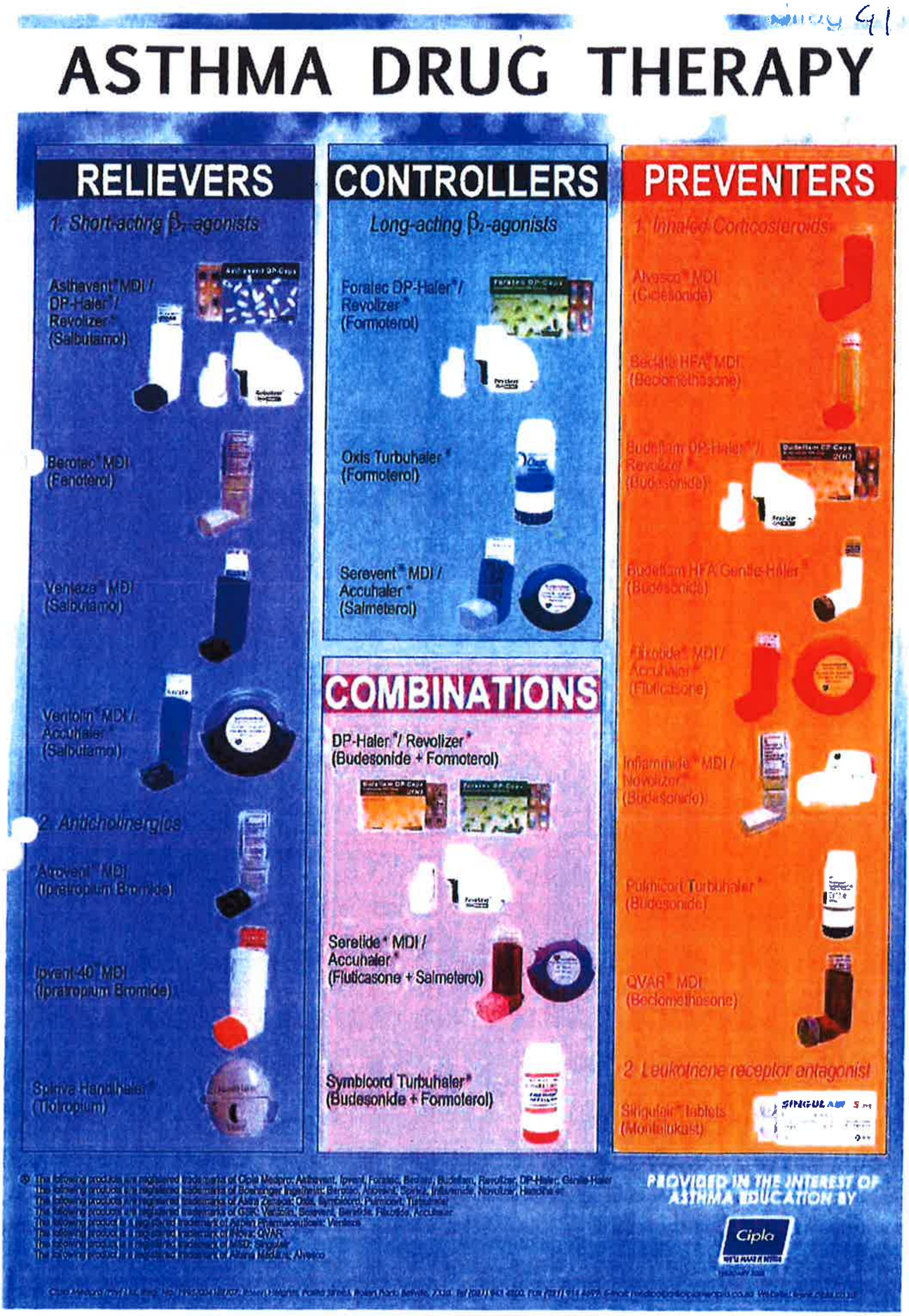
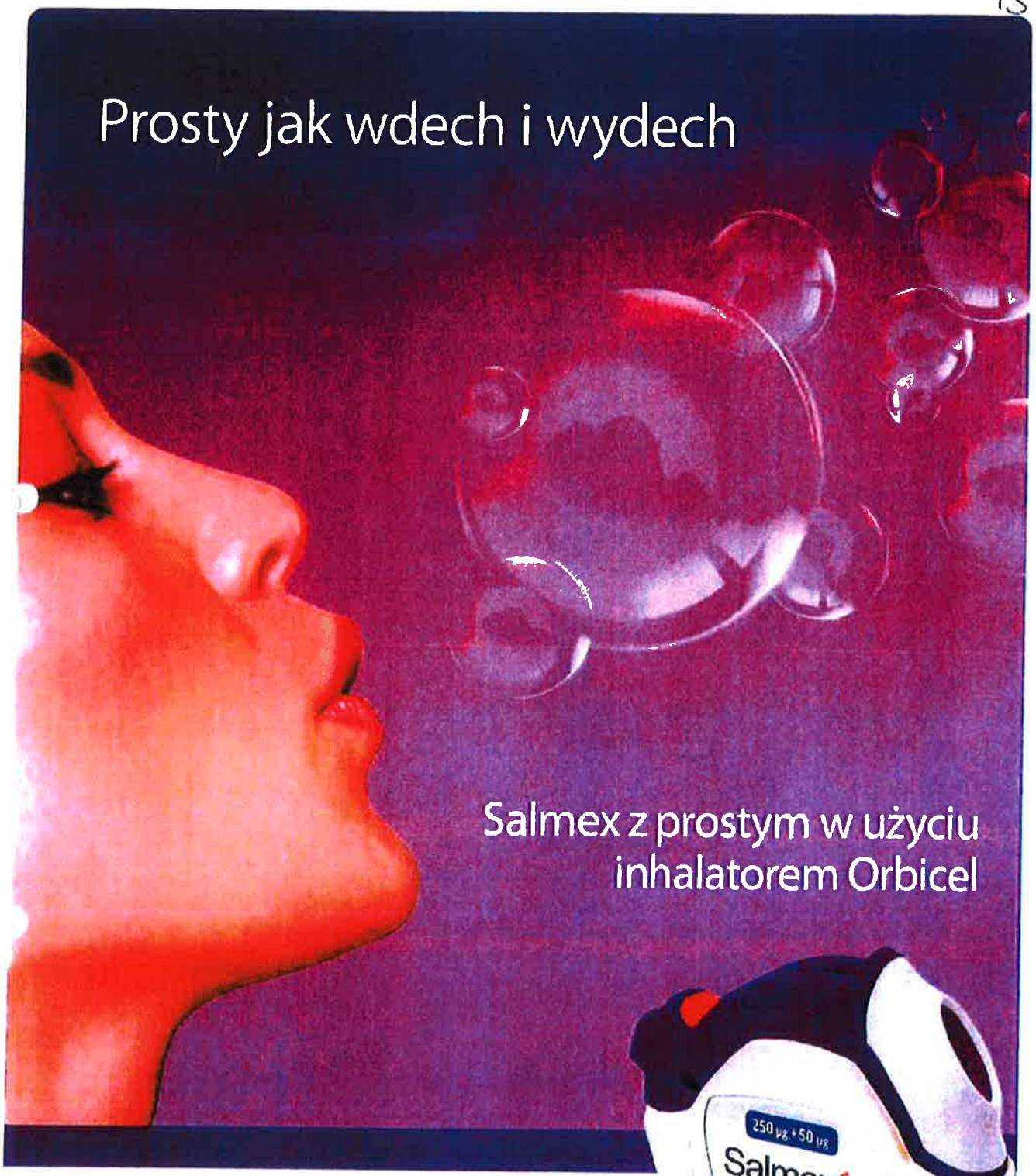


ASTHMA DRUG THERAPY
RELIEVERS
1. Short-acting β2-agonists
Asthavent® MDI / DP-Haler® / Revolizer® (Salbutamol)
Berotec® MDI (Fenoterol)
Venteze® MDI (Salbutamol)
Ventolin® MDI / Accuhaler® (Salbutamol)
2. Anticholinergics
Atrovent® MDI (Ipratropium Bromide)
Ipvent-40® MDI (Ipratropium Bromide)
Spiriva Handihaler® (Tiotropium)
CONTROLLERS
Long-acting β2-agonists
Foratec DP-Haler® / Revolizer® (Formoterol)
Oxis Turbuhaler® (Formoterol)
Serevent® MDI / Accuhaler® (Salmeterol)
COMBINATIONS
DP-Haler® / Revolizer® (Budesonide + Formoterol)
Seretide® MDI / Accuhaler® (Fluticasone + Salmeterol)
Symbicord Turbuhaler® (Budesonide + Formoterol)
PREVENTERS
1. Inhaled Corticosteroids
Alvesco® MDI (Ciclesonide)
Beclate HFA® MDI (Beclomethasone)
Budeflam DP-Haler® / Revolizer® (Budesonide)
Budeflam HFA Gentle-Haler® (Budesonide)
Flixotide® MDI / Accuhaler® (Fluticasone)
Inflammide® MDI / Novolizer® (Budesonide)
Pulmicort Turbuhaler® (Budesonide)
QVAR® MDI (Beclomethasone)
2. Leukotriene receptor antagonist
Singulair® tablets (Montelukast)
PROVIDED IN THE INTEREST OF ASTHMA EDUCATION BY
Cipla

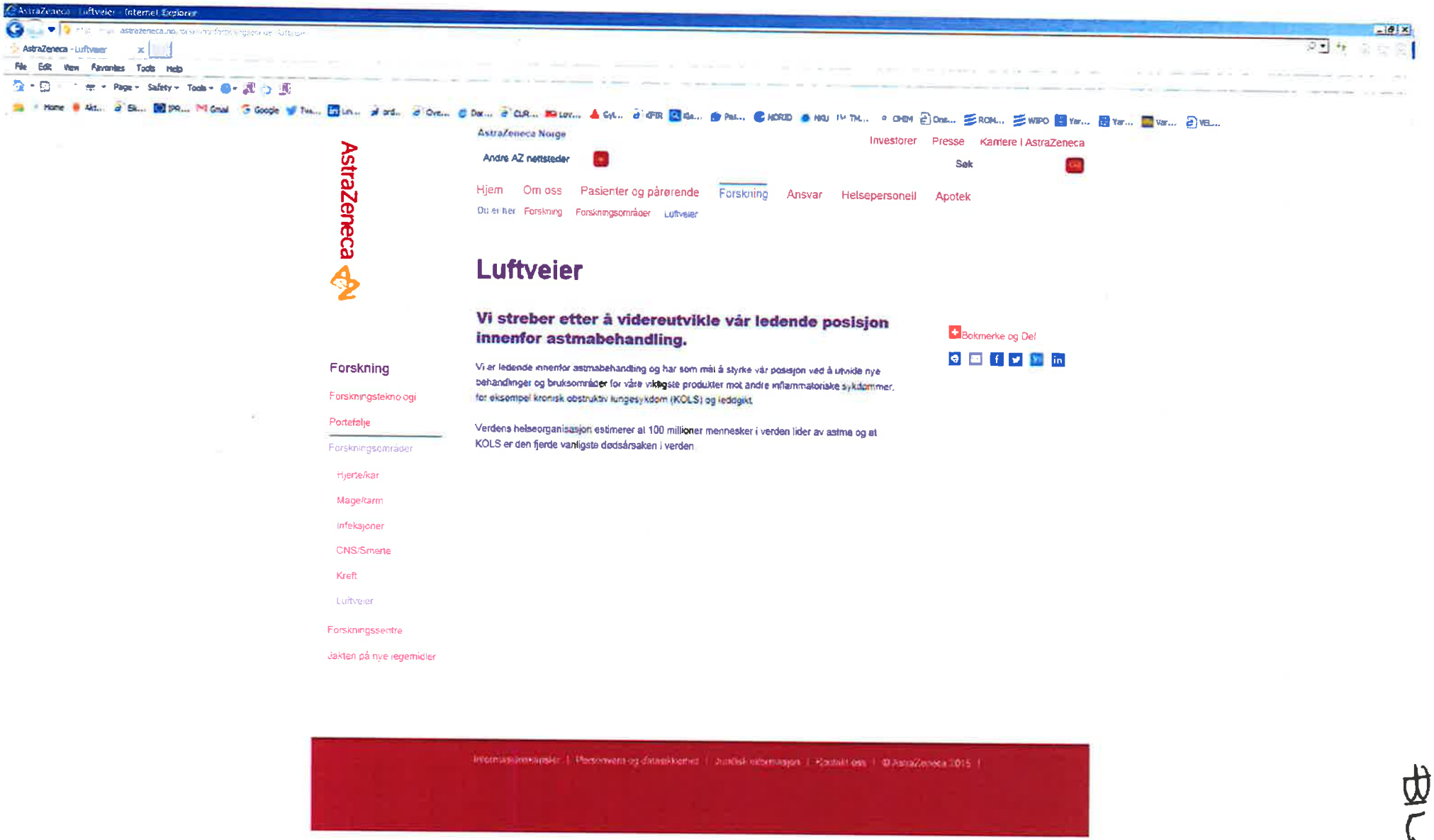


Salmex to pierwszy lek stosowany w terapii astmy oskrzelowej i POChP, który posiada instrukcję użycia umieszczoną bezpośrednio na inhalatorze. Dzięki prostym piktogramom obrazującym **cztery kroki obsługi** inhalatora, teraz Twój pacjent będzie dokładnie wiedział, jak z niego korzystać.

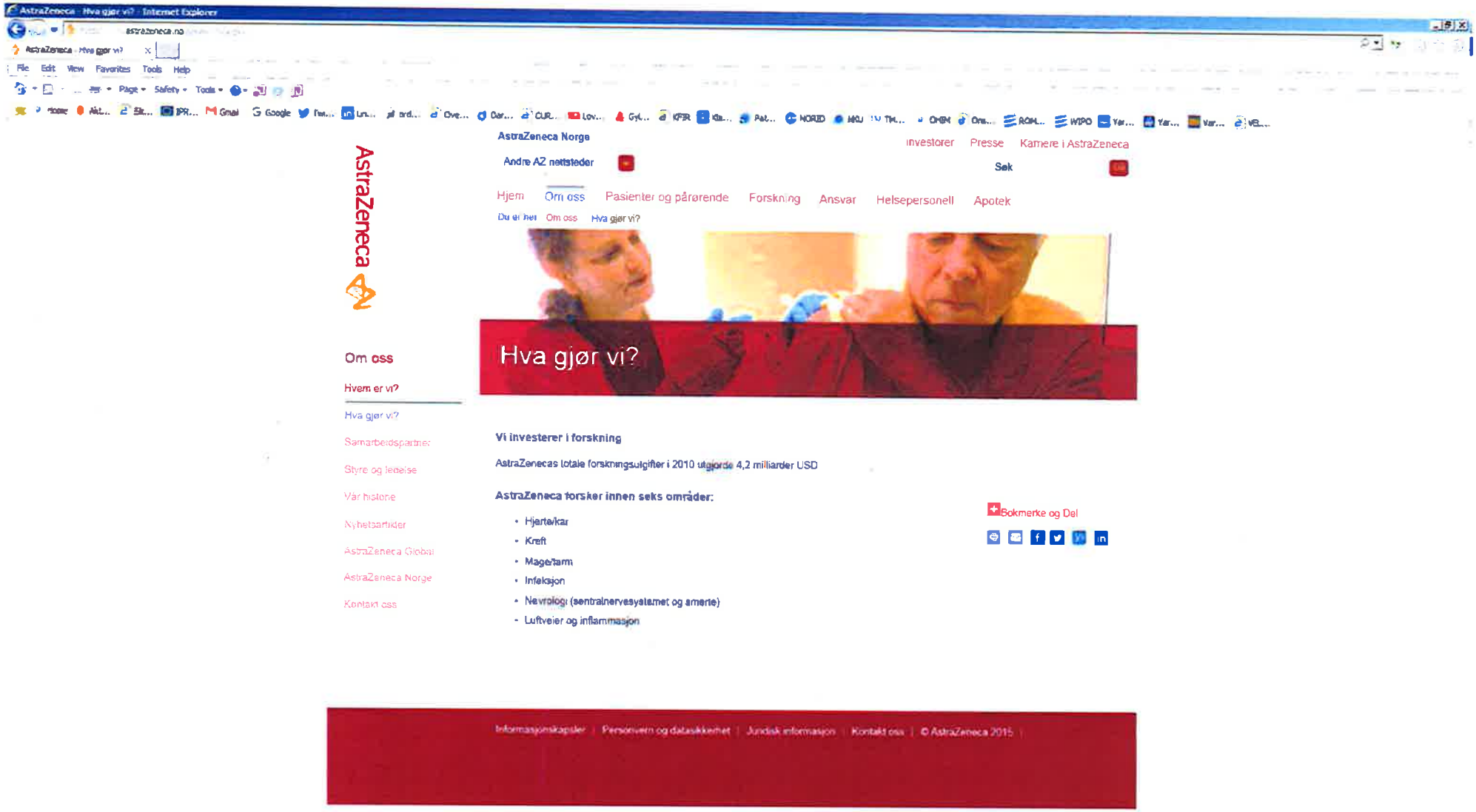
Salmex

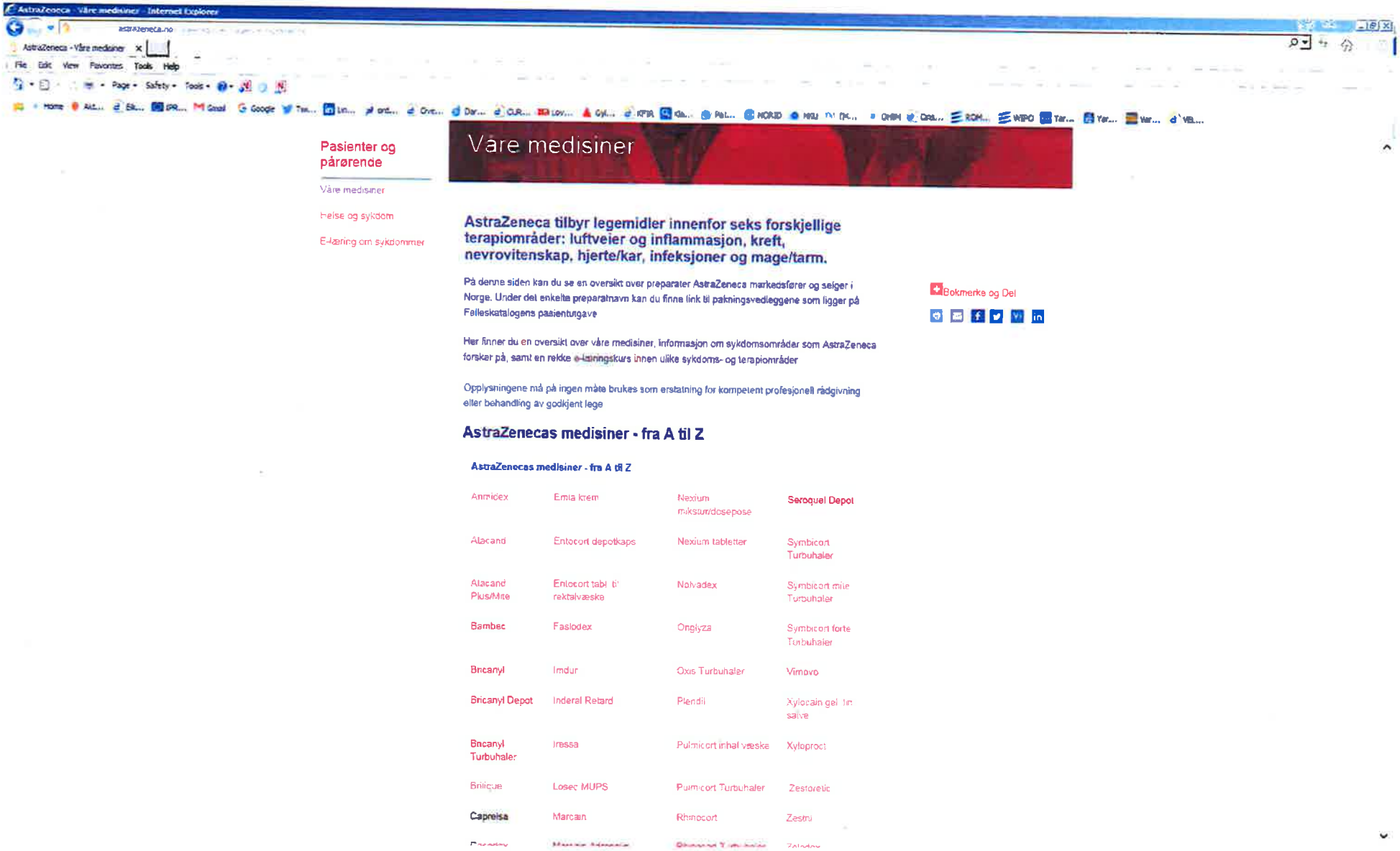
www.celonpharma.com

CELON PHARMA


AstraZeneca - Luftveier - Internet Explorer
AstraZeneca - Luftveier
File Edit View Favorites Tools Help
AstraZeneca Norge
Andre AZ nettsteder
Investorer
Presse
Karriere i AstraZeneca
Søk
Hjem
Om oss
Pasienter og pårørende
Forskning
Ansvar
Helsepersonell
Apotek
Du er her Forskning Forskningsområder Luftveier
AstraZeneca
Luftveier
Vi streber etter å videreutvikle vår ledende posisjon innenfor astmabehandling.
Vi er ledende innenfor astmabehandling og har som mål å styrke vår posisjon ved å utvikle nye behandlinger og bruksområder for våre viktigste produkter mot andre inflammatoriske sykdommer, for eksempel kronisk obstruktiv lungesykdom (KOLS) og leddgikt.
Verdens helseorganisasjon estimerer at 100 millioner mennesker i verden lider av astma og at KOLS er den fjerde vanligste dødsårsaken i verden.
Bokmerke og Del
Forskning
Forskningsteknologi
Portefølje
Forskningsområder
Hjerte/kar
Mage/tarm
Infeksjoner
CNS/Smerte
Kreft
Luftveier
Forskningssentre
Jakten på nye legemidler

09


AstraZeneca Norge
Andre AZ nettsteder
Investorer
Presse
Kamere i AstraZeneca
Søk
Hjem
Om oss
Pasienter og pårørende
Forskning
Ansvar
Helsepersonell
Apotek
Du er her: Om oss Hva gjør vi?
Om oss
Hvem er vi?
Hva gjør vi?
Samarbeidspartner
Styre og ledelse
Vår historie
Nyhetsarkiver
AstraZeneca Global
AstraZeneca Norge
Kontakt oss
Hva gjør vi?
Vi investerer i forskning
AstraZenecas totale forskningsutgifter i 2010 utgjorde 4,2 milliarder USD
AstraZeneca forsker innen seks områder:
Hjerte/kar
Kreft
Mage/tarm
Infeksjon
Nevrologi (sentralnervesystemet og smerte)
Luftveier og inflammasjon
Bokmerke og Del
Informasjonskapsler | Personvern og datasikkerhet | Juridisk informasjon | Kontakt oss | © AstraZeneca 2015


AstraZeneca - Våre medisiner - Internet Explorer
AstraZeneca - Våre medisiner
File Edit View Favorites Tools Help
Pasienter og pårørende
Våre medisiner
Helse og sykdom
E-læring om sykdommer
Våre medisiner
AstraZeneca tilbyr legemidler innenfor seks forskjellige terapiområder: luftveier og inflammasjon, kreft, nevrovitenskap, hjerte/kar, infeksjoner og mage/tarm.
På denne siden kan du se en oversikt over preparater AstraZeneca markedsfører og selger i Norge. Under det enkelte preparatnavn kan du finne link til pakningsvedleggene som ligger på Felleskatalogens pasientutgave
Her finner du en oversikt over våre medisiner, informasjon om sykdomsområder som AstraZeneca forsker på, samt en rekke e-læringskurs innen ulike sykdoms- og terapiområder
Opplysningene må på ingen måte brukes som erstatning for kompetent profesjonell rådgivning eller behandling av godkjent lege
Bokmerke og Del
AstraZenecas medisiner - fra A til Z
AstraZenecas medisiner - fra A til Z
Anmidex
Emla krem
Nexium mikstur/dosepose
Seroquel Depot
Atacand
Entocort depotkaps
Nexium tabletter
Symbicort Turbuhaler
Atacand Plus/Mite
Entocort tabl til rektalvæske
Nolvadex
Symbicort mite Turbuhaler
Bambec
Faslodex
Onglyza
Symbicort forte Turbuhaler
Bricanyl
Imdur
Oxis Turbuhaler
Vimovo
Bricanyl Depot
Inderal Retard
Plendil
Xylocain gel 1in salve
Bricanyl Turbuhaler
Iressa
Pulmicort inhal væske
Xyloproct
Brilique
Losec MUPS
Pulmicort Turbuhaler
Zestoretic
Capreisa
Marcain
Rhinocort
Zestril

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Statement of Dr. Anne Niedermann,
Institut für Demoskopie Allensbach

I, the undersigned, Dr. Anne Niedermann, Director of Research for Legal Evidence at the Institut für Demoskopie Allensbach, Germany, hereby declare as follows:

a. I am regularly asked by courts and private entities in several European countries to render expert opinions about fact-finding issues on the basis of surveys in connection with trademark disputes.

b. Along with a brief filed on August 19th, 2015, GLAXO SMITH KLINE introduced another survey conducted in Norway by GFK HEALTHCARE DIVISION in collaboration with the fieldwork provider, RESPONS ANALYSE AS (= Exhibit 16, entitled "272.201.10008 – Inhaler: Colour Association Survey – Norway", accompanied by an English translation of a statement by Mr. Morten Engan, the responsible researcher at RESPONS (= Exhibit 17. According to GSK's brief of 19 August, p. 4, this third GSK survey focuses on the perception of the colour shade PANTONE 2587C, which is one of the two colours featured in the GSK SERETIDE inhaler. The fieldwork took place between January and March 2015 (according to the statement by Mr. Engan = Exhibit 17, p. 3). I would like to point out that even though the data for the survey according to Exhibit 16 was established back in January-March of 2015, the translation of which was only brought to my attention on August 25th, 2015.

c. Furthermore, two statements, one by Prof. Lars Erling Olsen (= Exhibit 19) and one by Dr. Almut Pflüger (= Exhibit 18) pertain to this survey.

d. I was asked by the company SANDOZ to submit a statement on the probative value of the aforementioned third GSK survey in the pertaining case from my professional viewpoint as a social scientist specialised in survey research for legal evidence, including surveys on trade mark issues at both the national and the European level. The Allensbach Institute will charge SANDOZ for my work on this matter in accordance with the Institute's regular fee schedule but I render this statement in an independent, scientific and neutral manner on the basis of the attachments cited above.

I examined the RESPONS survey in the light of general scientific criteria as well as any applicable specific guidelines and rules developed by case law that should be adhered to for a survey to qualify as neutral, unbiased evidence with probative value.

With the third survey, GSK seeks to support a finding *of "distinctiveness of the colour purple, namely pantone 2587C"* (cf. brief of August 19th, 2015, p. 5). At the same time GSK refrains from deriving any conclusions from the survey with regard to the issue of a "mark with reputation".

My overall conclusion with regard to the method employed is the same as with the two former GSK-surveys (Exhibit 113 and 116): Also the survey submitted in the form of Exhibit 16 does not prove acquired distinctiveness in Norway.

My main reasons for coming to this conclusion are as follows:

In reaction to my criticism in my first statement on the first two surveys from Norway (= Exhibit 113 and 114 in the writ of 28 October 2014), the third GSK-survey omits several grave mistakes in the sampling and recruiting process that were detrimental to the probative value of both the first and second survey of 2014 (= Exhibit 113 and 114). It is correct to select professional respondents without any restrictions as to the number of inhalers sold or the frequency of prescribing them. Based on the available information, I will not raise objections as to the recruiting process here. I will also not attack the sample size, although the sample size of n = 145 among pharmacists and 150 among doctors is at a low end.

Nevertheless, implementing some lessons learned from earlier surveys, omitting some mistakes in sampling and analysis and making minor changes to the wording and order of questions still does not render the new approach a useful survey overall. Even the third GSK survey far from delivering a proper survey on distinctiveness. The persisting problems are not so much rooted within the technical execution by the fieldwork company RESPONS (sampling, recruiting etc.) but concern the covering of the whole relevant public as well as, most importantly, the test object and questionnaire wording.

1. Relevant public not covered entirely

A central criticism is that the third GSK survey (Exhibit 16) - in contrast to the two surveys before - completely lacks results for patients, even though GSK included this group in the first surveys as being just as relevant as the other two groups (doctors and pharmacists).

The problem of not being able to find enough respondents in Norway among patients that did not already take part in the two GSK surveys of 2014, is not inherent in the survey method as such. If GSK had commissioned an unbiased sampling approach from the very start and had refrained from conducting two surveys with biased method back in 2014 (= Exhibit 113 and 116), they would not

now have to deal with a shortage of respondents among patients in the new survey from Exhibit 16.

There is a basic requirement that must be fulfilled before a survey on the legal concept of distinctiveness can be afforded any probative value: the survey must have been conducted among the entire relevant public (which in this particular case also includes patients). In INTA's international review of rules for surveys that are submitted for legal evidence, the rule that the survey has to include "*all actual / prospective purchasers*" is included in INTA's list of recommended best practices.[1] In OHIM's Manual of Trade Mark Practice on surveys in the context of CTMs, the rule reads as follows: "*The criteria for the selection of the interviewed public must be assessed carefully. The sample must be indicative of the entire relevant public and, accordingly, must be selected randomly.*" (OHIM Manual, Part B, at 2.12.8.4). The respective rule is also emphasised in Norwegian sources, cf. LASSEN/STENVIK, Kjennetegnsrett, 2011, 244; VIKEN, Markedsundersøkelser som bevis i varemerke- og markedsføringsrett, 2012, 70; cf. also Swedish sources: NORDELL, Varumärkesrättens skyddsobjekt om ordkännetecknets mening och referens, 2004,197.

The definition of what groups of people altogether constitute a relevant public is basically a legal definition and is not part of the general rule illustrated above. The definition must be found in each case individually and may differ substantially from cast to case. Obviously, in the two surveys of 2014 (= Exhibit 113 and 114), GSK held the patients as relevant as doctors and pharmacists. If one regards patients are being part of the relevant public in the specific case at hand, one has to conclude that this third GSK survey (= Exhibit 16) violates the basic rule for survey evidence, namely that the survey has to cover the entire public. Because the third GSK survey does not give any results for patients (users), despite GSK regarded them a relevant group in the case at hand, the survey can be discounted as one-sided. It shows only one side of the coin, the perspective of professionals.

2. Test object

The test object as well as the question wording of the third GSK survey of 2015 (= Exhibit 16) are in large parts nearly the same as in the first one (= Exhibit 113), for

[1] INTA, Report on best practices in conducting surveys in trademark matters, 2013, para. I/C (http://www.inta.org/Advocacy/Pages/Reports.aspx).

which we know that the questions were drafted by GSK themselves. Not surprisingly, therefore, the third GSK survey does repeat severe mistakes, already highlighted by me in Exhibit 67 to the Defendant's brief of 9 December 2014 in relation to the test object and question wording, which are both at the core of the probative value of any survey - with the result that this third survey also does not constitute valid proof of the distinctiveness of the GSK SERETIDE appearance.

Moreover, the third survey does not reflect the fact that the GSK SERETIDE inhaler features a combination of two shades of colour on a three-dimensional shape: As in the previous GSK-survey (= Exhibit 113), the test object, a colour card, displays only one single colour shade whilst the question wording throughout the survey also does not pertain either to the issue of a combination of two shades of purple on the GSK SERETIDE inhaler, or, respectively, to the combination of two shades of purple plus the shape.

As in Exhibit 113 and throughout Exhibit 16 before it, the question wording does not even focus on the specific shade of purple claimed, as the question wording throughout the entire survey leads respondents to think unspecifically about the colour purple in general. We cannot know for sure whether each respondent was actually thinking about the particular colour shade at issue when answering or whether he/she perhaps had some other shade of purple in mind.

3. Test approach and questionnaire wording

The general test approach and the questionnaire wording employed by the GSK/RESPONS survey of 2015 (Exhibit 16) remain, once more, unclear. Neither the title of Exhibit 16 ("Colour association survey"), nor the accompanying statement of Mr. Morten Engan (Exhibit 17), the researcher at RESPONS responsible for conducting the fieldwork, identifies properly the legal concept the study was designed to measure. What Mr. Engan describes on p. 1 as the assignment: "*... to determine ... whether the (purple colour 'pantone 2587C ... has a clear recognition value with regard to inhalers...*" does not grasp the legal concept of acquired distinctiveness. Mr. Engan does not mention any specific personal experience in designing surveys for legal evidence either, rather he seems to be qualified as a general market researcher. This fact taken together with the further fact that he did not state that he himself developed the test approach as well as the questionnaire wording independently from GSK, and the fact that the wording of the core questions is basically the same as before in Exhibit 113—where we already know

that it was drafted directly by GSK—it becomes clear that the approach of the new survey in Norway was also not developed independently from GSK. This is confirmed by Dr. Pflüger's statement on the third GSK/RESPONS (Exhibit 18) on p.1: GSK themselves and the law firm Stephenson Harwood LLP wrote the questions, instead of the responsible survey researchers at GFK or RESPONS.

Prof. Olsen also does not name the legal concept that was researched by Exhibit 16. His description of the research topic as being "*to determine the association and perceived connection between the colour purple and GSK/Seretide*" (Bilag 19, p. 1) is not matching the legal concept of source distinctiveness for which GSK claims the results of the survey. Prof. Olsen defines furthermore the test object as being the basic "*colour purple*". This is imprecise. The colour purple per se includes many different shades. The legally relevant test object would rather be "a specific purple colour shade". "*Perceived connection*" is also unclear. What specific connection is GSK's survey all about?

Obviously, 3 out of 8 questions posed in connection with the test object (Q2, Q4 and Q8) are meant to establish a so-called "3-step test", a standard test for distinctiveness.[2] As for the Nordic countries, Sweden has established the same approach of a 3-step test, cf. PBR 05-080 (Kexchoclad). In the present case, the test has been incorrectly executed.

> The questionnaire includes more test questions than just the three core questions required for a normally straightforward and compact 3-step-test. There is one biasing introductory question, Q1, and there are more questions mixed in between the core questions (specifically Q3 and Q5). These additional questions are not neutral but diminish the validity of the intended test, since the core questions Q2, Q4 and Q7 are adversely affected by the additional prior questions. The additional questions induce socalled framing effects. It is important that the respondents of a survey on distinctiveness keep strictly concentrated only on the sign to be tested and come to the abstract decision whether the sign is from only one single source or not (that would be Q4 here) before they think about the market in general or about names of companies. Instead, in the present survey, their focus was redirected and they were led to think more broadly as early as Q1 and, again, by Q3 and Q5 just before the respective core questions Q2, Q4 and Q7.
>
> In light of this, Dr. Pflüger's conclusion regarding Q1 on p. 4 of her statement (Exhibit 18): "*Such extremely high correct attributions ... at the beginning of an interview are a first indication ... that there is a link between the colour shown in connection with inhalers and the company*" is on the one hand very true: It perfectly describes the

[2] E.g. on CTM-level R 1810/2008-4 – 3D mark shape of a suitcase / *RIMOWA III*, para. 35; R 355/2007-4 - Colour mark Orange and Grey / *Stihl*, para. 41 et seqq.; R 1/2005-4 – Red tool case / *Hilti*, para. 34 et seq.; T-164/03 [2005] - Monbébé, para. 80 et seqq.

market leader effect induced by Q1—which is not to be confused with source distinctiveness. On the other hand Dr. Pflüger's conclusion is definitely incorrect, as Q1 does not capture attributions (as Q4 should) but mere associations without any source exclusiveness. In Q1, respondents merely state what comes to mind when they see the card and hear the product category "*inhalers*" without any focus that could possibly be interpreted as measuring source distinctiveness.

In this very case, the share of awareness in Q2, which at first sight appears high, is easily explained by the frame of the prior question, Q1, which invites answers in line with the market leader effect: as soon as you think about the category inhalers (instead of sticking strictly to a focus on the sign to be tested), respondents are likely to remember and name market leaders, of which, of course, they are aware.

- It is important not to insert any questions in between the three core questions of a 3-step-test, especially not general questions, in order to avoid a market leader effect. In this case, a market leader of the product category inhaler in Norway is the one who claims distinctiveness (GSK). It is imperative, that market leaders take steps to prevent the probable market leader effect when conducting surveys on distinctiveness. That effect is when respondents name a particular trade mark or company (here: GSK or SERETIDE) just because the name of a market leader or its product comes to their mind in the form of a loose mental association when they think about the product category (inhalers) and not because the individual respondent actually connects the very sign in question (the colour shade) exclusively with the company or product of a market leader. In the third GSK survey, there were less questions in between the core questions than in the survey according to Exhibit 113, yet the questions Q1, Q3 and Q7 before the respective core questions still invited the market leader effect and, most probably, hyped the results in favour of GSK.

- The most severe mistake of the first GSK-survey (Exhibit 113) is repeated: again, the core question (in Exhibit 16 Q4) has far too imprecise wording.

  The need for precision in the question wording was pointed out in the Norwegian case (Supreme Court) Rt. 1979, 1117 (Cash & Carry). Imprecise questions lead to the conclusion that the survey has low probative value.

  In the present case, the report in English (= Exhibit 16) suggests that a certain share of interviewees selected the statement that reads: "*Inhalers of this colour originate from **one** (accentuation by AN) specific company*". In fact, the actual wording of the statement that was read out to the respondents was according to the questionnnaire (Exhibit 17, Question 4 on p. 6): "*Etter min oppfating, så kommer inhalatorer med denne fargen fra **et** spesifikt selskap*". Translated correctly into English, this would be "*In my opinion, inhalers with this colour come from **a** (accentuation by AN) specific company*". So, by choosing this statement respondents merely confirm the easy-to-agree-on obvious fact that each inhaler on the market naturally must have been manufactured by some company. The statement in the original Norwegian version does not convey source distinctiveness properly, as the necessary reiterated and

exclusive attribution to origin from only one single commercial source, which would be indicative of the distinctive character of a trade mark, is not captured. The wording of Q4 is unable to measure the core of the legal concept of source distinctiveness as exclusive attribution.

In light of this, it is misleading to the reader to describe in the report (Exhibit 16), e.g. in Summary B (table 6) and Summaries, as analysis of the group of respondents with "*awareness and indication of Only (sic!, accentuation by AN) one company*". "Only" is exactly the word, namely the necessary focus on source exclusivity, that is missing from the actual wording of the relevant statement in the core question Q4.

Dr. Pflüger is correct in mentioning that I follow the same basic approach that GSK is aiming for with Q4 (p. 4, fn. 4). However, the important difference in approach to the present GSK surveys (Exhibit 113 and 16) is that ALLENSBACH surveys use proper core questions that definitely capture source exclusivity.

Prof. Olsen seems to be of the opinion that the "*associations*" measured here instead of distinctiveness were helpful to clarify the legal concept to be proven. However, "*associations*" are irrelevant when it comes to source distinctiveness. Associations are a much more superficial type of mental connection than what is actually to be proven here: exclusive attribution in the sense of indication of origin to only one commercial source. Therefore, contrary to what Prof. Olsen highlighted on page 3 of Exhibit 19, the results on spontaneous associations as triggered by Q1 are of little evidential weight compared to results on source attribution (that would be the interrelated analysis of Q2, Q4 and Q7, see section 4 below). As far as Prof. Olsen is of the opinion that the associations measured would even prove a transfer of opinion to other products, this is not a relevant remark in the context of distinctiveness: Only if all doubts on the existence of original and/or acquired distinctiveness of a sign were removed, one could start to look at the degree of awareness of the test object, and only then associations come into play. But if, as is the case here, the discussion is still about the basics, the distinctiveness, it is not possible to turn already to the next step, the reputation or "well known status" of a trade mark that definitely has acquired distinctiveness.

- Ultimately, the third GSK survey submitted as Exhibit 16 includes no control group that could measure the strength of the aforementioned market leader effect in order to clean (subtract) it from the data. At least an unknown quantity of the responses that mention GSK or SERETIDE as the brand name or manufacturer in Q7 can partly be explained independently of the colour: be it because of a market leader effect (which is in the end a top-of-mind effect). The GCEU recognised this frequent deficit in surveys on acquired distinctiveness in which the market leader is involved in the decision "BIC".[3] In the present case, responses that name GSK or SERETIDE in Q7 may represent nothing more than a reflection of brand market share. The brand comes to mind the moment

[3] GCEU, T-262/04 [2005] – Bic, para. 84 et seqq.

respondents are told the category of product, namely inhalers in general, or they were just guessing. Therefore the GSK/GFK survey fails to establish true causality. It is not able to determine what share of responses that mention "GSK" and/or "SERETIDE" were actually caused by the shade of purple in question. For establishing true causality, a control group test is imperative and 'state of the art' in surveys for legal evidence when a market leader is involved, e.g. in the U.S. Control groups are also listed by INTA as recommended "best practice".[4]

In Prof. Olsen opinion a control group was not necessary. Clearly, providing the standard answering category "*don't know*" does not prevent guessing effects. And it is not a logically valid point to argue that the answers to Q4 (if the object "is from a specific company") would show that there is no adverse effect. This very question, Q4, might be inflated by the market leader effect and only a control group design can measure the exact share of guessing of a market leader effect. The control group is always set up to re-check exactly the core questions. Here that would be a check on Q4 as well as on Q2 and Q7. The opportunity to simply guess a market leader occurs inevitably in any study on a product that belongs to the market leaders from the very first survey question on, as already the mere mentioning of the product category or service category (here: "*inhalers*") triggers the undesirable effect of guessing a market leader within that product category, not necessarily the test object itself (here: the colour shade). The opportunity to guess is inevitably introduced by the necessity of naming the product category in the survey.

If survey results are challenged because of a market leader effect as in the present case, this is basically a challenge of the underlying causal proposition in cases such as this one where the owner of the sign is one of the market leaders: Is the test object actually the reason for the answers of the respondents or the product category itself and what exact share of the answers ground in general guessing? Acquired distinctiveness is only definitely proven if the extend of a probable market leader effect is determined by means of control group design and the percentage share of respondents that nevertheless name the respective brand or company even when seeing a completely different and non-confusable test object (here it would be another colour shade far from the colour violet) is subtracted from the survey results that relate to the colour shade in question.

- The problem that the GSK/RESPONS test approach does not properly reflect distinctiveness and that the answers are most likely mixed with loose associations to a market leader is confirmed by Q5 "*Why do you say that?*". If there were actual distinctiveness because of the colour shade (causality!), the answers to this question would accordingly clearly centre on the very colour shade tested as being the reason for the previous answer ("*from one specific company*") in

[4] Seidman Diamond, Reference guide on survey evidence, in: Federal Judicial Center: Reference manual for scientific evidence, Third ed., Washington (2011), 359-424, p. 397 et seqq.; INTA, Report on best practices in conducting surveys in trademark matters, 2013, para. I/C (http://www.inta.org/Advocacy/Pages/Reports.aspx).

Q4. Unfortunately, no results of Q5 are disclosed for the decisive group (respondents who (a) know the colour or are undecided if they know it, (b) attribute it at the same time to only one company, (c) name at the same time in Q7—not in Q1!—GSK or SERETIDE and (d) whose reasons in response to Q5 at the same time pertain to the specific colour shade). However, from the basic count provided for Q5 in table 7 one can at least obtain a rough picture: the percentage shares among all pharmacists and GPs that pertain to the very colour shade tested are definitely well below 50 percent: the result of a simple addition of the relevant answers[5]—ignoring for once the necessity of a net value count—is only 3 percent of all pharmacists and only 14 percent of all doctors.

4. Data analysis

There is a basic problem in connection with the data analysis by GFK/RESPONS in Exhibit 16. I recognise the effort of RESPONS to provide interrelated counts like I had postulated in my first statement on the GSK survey of 2014 (Exhibit 113). Nevertheless, the interrelated counts that provide summaries are all incorrect (tables 6, 10, 11, 12 and 13)[6]. They all integrate results pertaining to Q1 into the analysis and these are irrelevant in the 3-step test. Q1 captures associations of names that come to mind, not exclusive source attribution. Mere associations, however, are definitely irrelevant in an analysis of a 3-step-test. A proper analysis should have combined only Q2, Q4 and Q7. Especially the end result that is to be derived from table 6/Summary B is incorrectly established for this reason.

Dr. Pflüger glosses over this problem in the analysis several times in her statement: firstly by giving the diagrams on the right side of p. 3 that cite the values 84 percent and 65 percent from table 6/Summary B a title which suggests these were actually denoting the share of respondents that were "*Aware and indicating origin of one specific company Q4*". This is not the true picture because association results from the irrelevant Q1 were mixed into this analysis, as is revealed by the text above the matching table 6 of Exhibit 16 and an easy-to-miss hint in the left side of the diagram in Exhibit 18: Q1 is listed among the questions that were part of the analysis.

[5] "*GSK uses that colour/Seretide uses that colour*": 2 percent among GPs; "*I have only seen it on one type of inhaler/manufacturer*" 3 percent among pharmacists and 4 among GPs, "*generic manufacturers tend to use the original colour*" 2 percent among GPs; "*I think it is a patented colour/only Seretide GSK uses this colour/have not seen it on anything other than Seretide*" 3 percent among GPs; "*Would be confusing if other company used this colour*", 1 percent among GPs.

[6] The tables 11, 12 and 13 are irrelevant for the end result as they incorporate follow-up questions after Q4 which do not belong to the standard 3-step test (Q6, Q7).

Similarly imprecise is Dr. Pflüger's sentence on p. 5 suggesting that tables 8 and 9 infer that 56 percent of pharmacists name "...*GSK / GLAXO SMITH KLINE to be 'the one company'* " (on p. 5). Also into this analysis, results from Q1 were mixed in inappropriately which have nothing to do with attributing to only one company (cf. text above tables 8 and 9 of Exhibit 16).

The imprecision reoccurs when Dr. Pflüger cites on p. 6 and p. 8 of Exhibit 18 the figures from table 10/Summary C of Exhibit 16 that seems to specify the share of those who name a wrong manufacturer. In that case also, results from the irrelevant Q1 were mixed into the analysis.

To mix in association results from Q1 in any of the analyses might perhaps have been an attempt to heal the defective wording of Q4 as the wording does not capture exclusive source attribution. However, this is logically incorrect as Q1 does not presuppose exclusive attribution.

It is nevertheless informative to take a look at the results in table 6/Summary B:

To make an exception and include Q1 for once into the analysis, as no other values were disclosed, the 84 percent of all Pharmacists and 65 percent of all GPs is my starting point for a proper analysis. From Table 10/Summary C we know that 10 percent of the pharmacists and 6 percent of the GPs named the wrong company as the source. German case law always subtracts these shares from the share of respondents who know the sign in question and attribute it correctly to only one single source, based on EuGH, Slg. 2002, I-5475 Rn 65 = GRUR 2002, 804 – Philips (cf. BGH, GRUR 2007, 1066 Rn. 36 = WRP 2007, WRP Jahr 20071466 – Kinderzeit; BPatG, Beschl. v. 8. 3. 2013 – 33 W (pat) 33/12 = Vorlage zum EuGH zur Verkehrsdurchsetzung abstrakter Farbmarken – Sparkassen-Rot, para 3a) Allgemeine Grundsätze zur Ermittlung des Durchsetzungsgrades), even if social scientists have challenged the established practice (cf. NIEDERMANN GRUR 2006, 367, 371).[7] In the present case, in accordance with established practice, the actual end result based on the inflated analysis in table 6 would be for Pharmacists: 84 percent minus 10 percent = 74 percent, and the end result for GPs would be: 65 percent minus 6 percent = 59 percent. The Norwegian Court is free to use the deduction or to dismiss it.

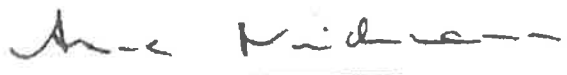
If one takes into account the other problems of this survey explained above in sections 1 to 3, it is overall very unlikely that a proper survey (with a straightforward

[7] The German Federal Court of Justice, Dr. Pflüger and myself all agree that, in the context of measuring distinctiveness, it is <u>not</u> necessary that respondents were able actively to specify the correct name of the brand owner or the brand.

3-question-only test, with a valid core question that actually grasps exclusive attribution—even if one did not subtract the share of those respondents who attributed the sign to the wrong manufacturer as is prevailing OHIM practice—with a control group for determining and subtracting the market leader effect (as required by OHIM) would arrive at least among GPs (and, most likely also among the patients for whom we did not receive any new data by GSK) in shares clearly below 50 percent, thus failing the threshold national legislations throughout Europe apply to the 3-step-test and failing the requirement that sufficient distinctiveness must be present not only in some, but in every single relevant group. One cannot offset one group against the other or create an average value. This means that a higher degree of acceptance in one of the relevant groups cannot compensate for an inadequate degree in another relevant group.

I confirm that the above statement is truthful and my own.

Allensbach, 31 August 2015



Institut für Demoskopie Allensbach
Dr. Anne Niedermann

BILAGA 50

JUDGEMENT

(office translation)

Court of Mid-Netherlands

Department Civil Law

Place of court session Lelystad

Judgement in P.I. of 30 December 2015 (early)

In the case between

1. Glaxo Group Limited
2. GlaxoSmithKline

claimants,

lawyers, Mrs. A.M.E. Verschuur, Mr. J.M. Boelens and Mr. A.H. Stoffels, Amsterdam, against

1. Sandoz B.V.
2. Sandoz N.V.

defendants,

lawyers, Mr. O.F.A.W. van Haperen, Mrs Th.Y Adam – van Straaten and Mrs. H.A.J. Pors, Rotterdam.

Claimants shall be jointly referred to as "GSK" and defendants jointly as "Sandoz".

1. The procedure

1.1. The course of the procedure follows from:
- The writ of summons dated 20 November 2015 with 69 exhibits;
- The statement in reply with 44 exhibits;
- The deed of deposit dated 7 December 2015 of Sandoz;
- The deed of deposit dated 9 December 2015 of GSK;
- The court hearing;
- The pleading notes of GSK;
- The pleading notes of Sandoz.

1.2. Judgement was rendered accordingly.

2. The facts

2.1 The GSK group is a worldwide pharmaceutical company as a result of a merger between Glaxo Wellcome and SmithKline Beecam in 2001. The GSK group develops, produces and sells prescription drugs, vaccines and OTC medicines. Glaxo Netherlands is the holder of several market authorizations for the distribution of prescription medicines and is the licensor in the Netherlands of the trademarks owned by Glaxo Group.

2.2 Sandoz Netherlands and Sandoz Belgium belong to the Novartis Group. Sandoz mainly focusses on the trade in generic medicines.

2.3 Both GSK and Sandoz are active in the field of breathing medication, more specifically in the field of asthma and COPD. The medicines within this market are divided, more or less in "relievers" and "preventers". Relievers are destined to quickly relief acute breathing difficulties and are active for a limited period. They are only used in the event a patient has immediate breathing difficulties. Preventers are used daily and for a longer period in time used to control the symptoms relating to asthma and COPD and to avoid immediate attacks.

2.4 GSK has applied for a patent on 7 September 1990 for medicines which contain the (combination) Salmeterol and Fluticason. The patent is registered on 13 October 1994 and publicized on 4 January 1995. Since 1999 GSK markets the Seretide-inhalers. Seretide falls within the category preventers and contains a combination of an anti-inflammatory agent (fluticasonpropionaat) and a long-acting ß2-agonist (salmeterol). The inhaler, the packaging as well as the promotion material contain the color purple .

On the Belgium market the medicine is offered in the following package.

2.5 The patent owned by GSK for this medicine (Seretide) is, after the obtained ABC-certificate (lapsed on 8 September 2013). Once a patent is lapsed, the previously patented medicine (hereafter: branded medicine), may also be marketed by third parties (generic medicine).

2.6 Sandoz has, after the lapse of the patent of GSK, developed the generic medicine Airflusal, which is offered in an inhaler named Forspiro. Sandoz Belgium has obtained a market authorization for this medicine for the Belgium market on 16 October 2014. The medicine has not been marketed on the Belgium market yet. On 14 Augustus 2015 Sandoz Netherlands has obtained a market authorization for the Dutch market.

2.7 Airflusal Forspiro is marketed by Sandoz Nederland since 1 October 2015. This medicine is presented as follows:

The color purple which Sandoz uses on the Airflusal Forspiro and (partly) on the package and promotional / information material contains the color Pantone 2573 C:

2.8 Both Seretide as well as Airflusal are prescription medicine.

2.9 GSK has applied for an accelerated trademark application on 30 June 2015 for the following color mark with the BOIP (Benelux Trademark Office):

The trademark is registered on 2 July 2015 under number 0977861 for pharmaceutical preparations and inhalers for asthma and or COPD in class 5 and 10 and contains the description CFE.29.1.5 (violet) and the PMS-code Violet 2587 C (hereafter the color mark).

2.10 GSK is also the owner of a community trademark registration (CTM) under number 3890126, which trademark was applied for on 16 June 2004 and has been registered on 19 December 2008 for inhalers in class 10. It concerns a combination color mark, consisting of two tones, with a description: "The trade mark consists of the colour dark purple (Pantone code 2587C) applied to a significant proportion of an inhaler, and the colour light purple (Pantone code 2567C) applied to the remainder of the inhaler".

2.11 The product Airflusal Forspiro in the color purple has been subject of various legal proceedings in Germany, Denmark, Norway, Ireland, Portugal and Korea between the GSK Group and the Novartis Group.

2.12 In Norway GSK has obtained an interim injunction proceedings and has started a proceedings on the merits against Sandoz based on slavish imitation and unfair practices. Both the P.I. judge as well as the judge on the merits have refused to award GSK its claims. In Germany GSK has won in first instance in the P.I. proceedings but Sandoz has filed appeal against these proceedings after which GSK has finally decided to revoke these proceedings. In Canada the filed color mark of GSK (which is similar to the community trademark) has been revoked after several parties, including Sandoz, had filed a revocation proceeding relating thereto.

2.13 In Denmark and Ireland GSK has summoned based on (presumed) infringement of the CTM by Sandoz (see point 2.10 above). Both the Danish court as well as the Irish court (in interim injunction proceedings) have denied the claims of GSK. At this moment in time proceedings on the merits are pending in Ireland between these parties, but no judgement has been rendered yet. In Canada, the registered color mark of GSK (similar to the CTM) has been declared void after parties, including Sandoz, filed revocation proceedings relating thereto.

2.14 On the color mark which is described above under point 2.9, which is subject of these proceedings, no judgement has been rendered yet. However, Sandoz has started several proceedings on the merits in order to obtain a revocation for the registered trademark, among which the currently pending proceedings before the court of The Hague and Brussels.

3. The conflict

3.1. GSK has demanded by judgement:

1. to order Sandoz BV and Sandoz NV with immediately affect after serving the judgement in the Benelux, to cease and desist from infringement on the trademark rights of Glaxo Group Limited, more especially but expressly not limited to cease and desist from every use as outlined in this writ of summons (particularly in paragraph 66) as well as the corresponding exhibits, as well as the use as specified in art. 2:20 paragraph 2 BTIP;
2. to order Sandoz BV with immediate effect after serving this judgement to cease and desist from (other) unlawful acts against Glaxo Group Limited and GlaxoSmithKline B.V., more especially but expressly not limited to cease and desist from every use as outlined in this writ of summons (particularly in no. 66) and the corresponding exhibits;
3. to order Sandoz BV and Sandoz NV within six weeks after serving this writ to provide to Mr. Dr. AME Verschuur, attorney from Glaxo Group Limited and GlaxoSmithKline BV, a written statement containing all information that is known to Sandoz BV and Sandoz NV with respect to the origin and distribution channels of the AirFluSal Products, (including, but expressly not limited to, the names and addresses of the relevant (legal) entity's), as well as the net profit (being the revenue from which exclusively the taxes

and direct variable costs are deducted) made in the Benelux as well as the exact manner how this met profit has been calculated as well as the total amount of AirFluSal Products that are still in stock with Sandoz B.V. and Sandoz NV, specified for the type of product; which statement must be provided by means of an audit report from an accountant, which is made taking into account COS 4400 (Control and Other Standards) by an independent chartered accountant chosen by Sandoz BV and Sandoz N.V. KPMG, PwC, EY or Deloitte, and must be accompanied with documentation from which the precision and completeness of those information appears;

4. to order Sandoz BV and Sandoz NV within two weeks after serving these judgment to send a signed letter on its own letterhead by register mail, without any (oral or written) accompanying text, to all its purchasers of the AirFluSal products in the Benelux, with exclusively the following text:

"The preliminary injunction Judge of the Court of The Hague has recently sentenced us to inform you about the following.

Recently we have offered and sold AirFluSal products which are infringing the purple trademark of GlaxoSmithKline. The preliminary injunction Judge has ordered that the products offered and delivered by us infringe the trademark rights of GlaxoSmithKline, as well as are otherwise unlawful towards GlaxoSmithKline.

By order of the preliminary injunction Judge we have taken the particular products immediately from our range of products and will no longer supply these in the future.

We request you to kindly but urgently immediately return to us the AirFluSal products that have been delivered to you. Of course we will reimburse you for the full purchasing amount as well as any transparent costs.

A copy of the judgment is enclosed to this letter.

Yours sincerely,

Sandoz"

Each letter always needs to be accompanied of an attachment which is a copy of the full text of the judgement,

Copy of each letter being send simultaneously, as well as proof that these letters have been sent, to Mr. Dr. AME Verschuur, attorney of Glaxo Group Limited and GlaxoSmithKline BV;

5. To allow the claimed under 1 t/m 4 on paying of an immediately and forceable penalty, to be paid by the relevant plaintiff(s), of
   (i) EUR 10,000 (in words: ten thousand euros) for each time that the plaintiff(s) does not (fully and/or timely) comply/complies with one or more of the convictions to which it is sentenced, in this respect that this penalty is owed as much time as need if (subject of) the convictions are not (fully and/or timely) complied with, and, cumulative, per day at a relevant non-compliance persists, whereby each part of a day is counted as a full day;

   or to choice of Glaxo Group Limited and GlaxoSmithKline B.V. and whether or not in combination,

(ii) EUR 500 (in words: five hundred euro) for each product with which the relevant plaintiff(s) does not (fully and or timely) comply/complies with one or more of the convictions against her, in this respect that the penalty will be owed as much time as if (subjects of) the relevant convictions are not (fully and timely complied) with;

6. to order the plaintiffs individually, or at least in equal parts,

(a) in so far the currents claim relates to the infringement of intellectual property rights, to reimburse to Glaxo Group Limited and GlaxoSmithKline BV the reasonable and proportional litigation costs as well as other costs with respect to the current litigation based on art. 1019h DCCP;

(b) in so far the current dispute relates to otherwise unlawful acts, to reimburse to Glaxo Group Limited and Glaxo Smith Kline BV because fixed based on the liquidation rate; and

(c) in the usual subsequent costs;

7. to set the reasonable term to initiate a claim on the merit, as outlined in art. 1019i CCP, on six months after this judgement has been served;

3.2. To substantiate its claim GSK has broad forward the following arguments. GSK has marketed the medicine Seretide since 1999 on the Benelux market in the color purple and also on the packaging and the marketing- and information material the color purple is frequently used. The color purple was not used up until that moment in time on the market for inhalers and was therefore unique. The color purple used by GSK has distinctive character ab initio but has at least obtained distinctive character by its use. For that reason the BOIP has agreed to register the color mark. Sandoz infringes this trademark acc. to article 2.20 paragraph 1 sub a) to d) BTIP with the medicine Airflusal Forspiro. This medicine contains the same combination of active ingredients as Seretide and is also offered on the market by Sandoz in the color purple (pantone 2573 C). Sandoz ALSO acts unlawful against GSK. There is unnecessary confusion due to the similarities (6:162 Civil Code). Also the use of the color purple by Sandoz constitutes a misleading statement (6:194 Civil Code) and Sandoz hereby acts unfairly in the course of trade (6:193b Civil Code).

3.3. Sandoz puts forward its defense arguments. Primarily Sandoz argues that the color mark of GSK is void because it lacks any distinctive character and the color mark consists solely of a sign that can serve to indicate the characteristics of the goods and is also a sign which has become customary in the bona fide course of trade. Sandoz has, based on these arguments, filed revocation proceedings both in the Netherlands and Belgium. Further, Sandoz argues that the registration of the color Pantone 2587C as a color mark constitutes an act of unfair competition because GSK is a dominant player on the market and does not obtain any efficiency advantage by the registration of the color mark. Further, Sandoz claims that GSK has obtained the registration for the color mark by misleading the BOIP. Sandoz also argues that the registration of the color mark infringes the fundamental rights of Sandoz. Finally, Sandoz denies to infringe rights to the color mark registration of GSK, or that she acts unlawful against GSK, or is acting unfairly in the course of trade. Unless and insofar the claims of GSK are allowed, Sandoz requests to do so under the condition that GSK sets up a considerable security.

3.4. Insofar relevant the statements of parties will be discussed hereunder.

4. The assessment

Competence

4.1. Insofar the claims of GSK are based on the Benelux trademark law the following is relevant. In a judgement of the Appeal Court of The Hague (ref. to document number) it is ruled that the rules of jurisdiction of the EEX regulation 44/2001 (hereafter: EEX I-Reg.), insofar the regulation is applicable in material, formal and temporal regards, prevails over article 4.6 BTIP. There is no reason to assume that

such is differently with the applicability of the EEX treaty 1215/2012 (hereafter: EEX II-Reg.). Based upon the aforementioned judgement of the Court of Appeal, the PI judge is entitled to consider these claims in interim injunction proceedings on the basis of article 4 para. 1 EEX II-Reg. in conjunction with (jo.) article 8 paragraph 1 EEX II-Reg. jo. article 99 Civil Proceeding Code now that one of the defendants, Sandoz Netherlands, is located in the Netherlands and the claims against Sandoz Netherlands and Sandoz Belgium are so closely related that it is against a fair administration of justice to not rule on these simultaneously. Insofar the claims of GSK against Sandoz Netherlands are based on unfair practices/ unlawful acts, it is law that the PI judge is competent on the basis of article 4 paragraph 1 EEX II-Reg. jo. article 99 civil procedures code.

4.2. It can be left aside if the jurisdiction needs to be established on the basis of national or Benelux law now that, on the basis of article 99 Civil Proceedings Code as well as on the basis of article 4.6 para. 1 BTIP, the PI judge is relative competent because Sandoz Netherlands has its seat in the district of Mid-Netherlands (thus: Lelystad).

4.3. The competence of the court is also not argued by Sandoz.

Trademark infringement

4.4. According to GSK, Sandoz is (by the use of its color purple) infringing the color mark of GSK which GSK uses on its medicine Seretide, with its medicine Airflusal Forspiro, the package and the marketing material.

4.5. The most far stretching defense of Sandoz concerns the argument that the registration of the color mark is void. Sandoz has already filed revocation proceedings against this color mark registration in the Netherlands with the Court of The Hague and in Belgium with the Court of Brussels. In relation thereto Sandoz invokes, among others, the grounds for revocation as included in article 2.28 para. 1 sub b, c and d BTIP. According to Sandoz, the color mark Pantone 2587C lacks any distinctive character, can serve as a characteristic/indication of the goods and the sign has become customary in the bona fide course of trade.

4.6. As Sandoz has filed proceedings concerning the revocation of the color mark with the Court of The Hague and Brussels, the PI judge shall first and foremost have to asses if there is a serious, real chance that the judge on the merits will award the revocation claim.

4.7. On the grounds of article 2.28 paragraph 1 sub b to d BVIE, anyone with an interest may invoke the revocation of a trademark in case the trademark lacks any distinctive character (b), consists solely of a sign that can serve in the course of trade as an indication of the sort, capacity, amount, destination, value, place of origin of the goods or the time of production of the goods (c), or have become customary in the normal language or in the bona fide course of trade (d). These grounds for revocation can however not succeed in the event it can be established that a trademark has obtained distinctive character due to the use thereof (article 2.28 para. 2 BTIP).

4.8. The PI judge concludes as follows. According to established case law the distinctive character of a trademark entails that a trademark for which the registration is obtained can identify the goods and services as originating from a specific company and thus that these goods or services are distinguished from other companies.

4.9. This distinctive character - either intrinsic (ab initio) or by use - must be judged for the goods and services for which it is registered based upon the probable perception of the relevant public, which is the normally informed and reasonably circumspect and attentive average consumer for the relevant category of goods and services. In the issue at hand, it concerns medicines for asthma/COPD, which can only be

obtained by (doctors) recipe. The relevant public for prescription medicines consist both of end users as well as professionals within the healthcare sector, which are the doctors prescribing the medicines and the pharmacists selling the prescription medicines (*reference made*: Travistan judgement ECJ).

4.10. For the assessment of the distinctive character of a specific color as a trademark the general Interest should be taken into account which means the availability of colors cannot be unjustifiably limited for other market parties which offer the same goods or services as those for which the registration was sought. The bigger the numbers of goods and services of the type for which a color trademark is applied, the sooner this comes into conflict with the system of unfair competition. In that respect it should also be taken into account that the consumer is not used to perceive colors as an indication of origin (*reference made*: Oberbank judgement ECJ). Only in case a color mark – before it was used –significantly differs from the norm which is customary in the relevant sector and therefore can fulfill the essential function of indication of origin, it can have distinctive character.

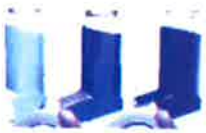
4.11. That the color mark of GSK has distinctive character ab initio, as argued by GSK, has, to the assessment of the PI judge, become insufficiently likely. Parties do not disagree that in the market of medicines for asthma/COPD, colors are often used by pharmaceutical companies on (the inhalers of) its medicines. The use of different colors is therefore a customary practice in the market. Although it is a fact that the color purple, at the moment of the market introduction of Seretide by GSK, was not used, it has been insufficiently motivated/claimed by GSK that the color purple was so characteristic in a market in which the use of colors became more and more customary, that it therefore could fulfill its essential function of indication of origin. Also in the letter of GSK to the BOIP of 29 June 2014 in which it requests to register the color mark, GSK hardly argues why the color mark applied for has obtained ab initio distinctive character (exhibit 25, writ of summons).

4.12. Further, Sandoz has argued that the use of color in the relevant market can serve to indicate the purpose of the good. GSK has denied this and states that in the relevant market no formal color coding system is applicable to indicate the purpose of the goods. However, with this GSK does not acknowledge, according to the PI judge, that on the basis of article 2.28 para. 1 sub c) BTIP, it is not necessary that the color purple of the color mark of GSK is [actually] used on the basis of a formal color code system. Even more so, it is not necessary to establish that the color mark is, at this moment in time, already used to indicated the purpose and the characteristics of the medicine. The word 'can' indicates that for this article to be applicable it is not necessary that the color mark refers to the purpose of the good at the time of the application of the trademark but that it is sufficient that the color mark can serve to indicate the purpose/characteristic of the goods. In the assessment of the PI judge the latter is sufficiently likely.

4.13. The PI judge assesses in relation thereto that the color blue is often used for reliever medication (in short: bronchodilators). For example this has become evident from the overview submitted by GSK (exhibit 12, writ of summons), in which GSK has included an overview per medicine in which color it is brought on the market. GSK has also acknowledged that for her product Relvar, a combination product falling into the category preventers, which was initially brought on the market in the color blue, it was changed to yellow after requests thereto from the market. In her information leaflet, GSK indicates that the change to the color yellow was done to prevent confusion with reliever medication. With that GSK endorses that reliever medication are featured in the color blue. Further, Sandoz has filed information leaflets from various hospitals in which reference is made to the "blue puff" to indicate reliever medicines (exhibit 16 – 18, statement in reply) and to the "red/brown puff" to indicate anti-inflammatory agents. From that it can be concluded that colors can serve to indicate the type of medicine.

4.14. Also GSK uses various colors to indicate the difference in type of medication and/or dose. For example, she has acknowledged during the oral hearing that the various tones of purple, from light to

dark, for its aerosol medicines of Seretide are available and relate to differences in dose. The higher the dose, the darker the color purple.



This means that GSK uses different tones of color to indicate the characteristics of the goods, namely the dose. Apart from that, GSK offers its Diskus-inhalers in various colors which indicates per color which medicine the Diskus contains (blue for short acting bronchodilators; orange for anti-inflammatory agents; green for long working bronchodilators; purple for the combination medicine).

The colors blue, orange, green and purple are thus used by GSK to indicate the purpose (type) of its medicine and to distinguish these medicines from one another.

4.15. The PI judge, as indicated above, concludes that it has become sufficiently apparent that the color purple of the color mark can serve in the course of trade to indicate the purpose of the medicine or the dose thereof, and the color purple of the color mark does not have distinctive character ab initio, which leads to the assessment of the question whether the color purple (Pantone 2587 C) of GSK has obtained distinctive character by use. Sandoz has argued against this with a motivation. The PI judge concludes as follows. In order to establish if a trademark has obtained distinctive character by use, all factors should be taken into account from which the conclusion can be drawn that the trademark is suitable to distinguish the relevant goods from a specific company and thus to distinguish these from other companies (*reference made*: Chiemsee judgement ECJ). Facts that can be taken into account are the period of time the trademark was used, the market share of the trademark, the intensity and geographical use of the trademark, the amounts of advertising/marketing costs of the company for the trademark and the percentage of the relevant users that can identify the goods as coming from a specific company on the basis of that trademark. It has to be established that the relevant consumer or at least a significant part thereof, identifies the goods as originating of a specific company on the basis of the use of that sign and therefore in relation to the nature and effect of the sign by which the relevant goods can be distinguished from other companies (*reference made*: Philips/Remington judgement ECJ). A market research can substantiate this.

4.16. As argued above under point 4.9, the relevant consumer in relation to prescription medicine consists from both the end user as well as professionals in the healthcare sector, doctors who prescribe the medicines and pharmacists who sell the medicines.

4.17. GSK has, in order to substantiate its claim that the color mark has acquired distinctiveness by use within the relevant public, referred to the extensive length of use of the color purple on its Seretide products, its market share of the Seretide products and (the intensity of) its marketing of the Seretide product. The PI judge however concludes that the color mark has always been used in combination with

the trademark Seretide and the name of GSK as the producer. Also the color mark on the Seretide Diskus has always been used in combination with another tone of purple. The aerosol Seretide furthermore is marketed in three different colors of purple (light purple, purple and dark purple; for each dose a color) in combination with a lighter color of purple for the mouthpiece. Also on the package of the Seretide Diskus and the aerosol various tones of purple are used (from light purple to dark purple). Therefore GSK presents its Seretide product in different shades of purple, among which the color Pantone 2587 C. Although a sign (the color purple Pantone 2587 C) does not necessarily has to be used individually to acquire distinctiveness as a trademark, as unrightfully claimed by Sandoz, these circumstances do raise the question if the relevant public has perceived the color purple (Pantone 2587 C) as a trademark and also in what extent the marketing and the market share of the Seretide products, which contain various tones of purple, substantiate the claimed acquired distinctiveness by use of the color purple (Pantone 2587 C) by GSK. GSK has insufficiently explained and made this clear due to which within the scope of these PI proceedings no correct and concrete judgement can be made of the influence of the indicated circumstances in relation to the claimed acquired distinctiveness by use of the color purple (Pantone 2587 C). Further, GSK refers for the substantiation of her claim that the color mark has acquired distinctiveness by use amongst the relevant public, to a market survey conducted in 2015. From this, according to GSK, it appears that a very high percentage of pharmacists and doctors recognize the color purple as an indication of origin. According to Sandoz this acquired distinctiveness of the color mark cannot be concluded from the market survey because it was not carried out amongst the entire relevant public (solely general practitioners and pharmacists, not specialists and patients) and also no survey was conducted in the entire Benelux area (Luxembourg was not included). Also the line of questioning in the market survey does not meet the requirement of the so-called 'three step test' as established in relevant case law and also there was no correction relating to the market leader effect of GSK which was the case given the fact that, as the owner of the patent, GSK was the only company entitled to market these specific medicines. Both parties have submitted experts opinion to substantiate their standpoints which, depending on the party by whom they were instructed, have indicated that the market survey was performed inadequately or correctly. In the scope of this PI it goes too far to discuss the market survey and the various criticisms and asses the market survey in full. Further, the PI judge thinks it likely that the judge on the merits, concerning the complications which arise with the assessment of the question if a color mark has acquired distinctive character by use, shall order its (own) expert opinion. For that, the scope of a PI is too limited.

4.18 Based on the above, and also in view of the observation under points 4.11 until 4.14 that the use of colors is standard practice with asthma and COPD medication, that the color blue is often used for reliever medication and that GSK itself also uses other colors to distinguish the function of its medication, in the assessment of the PI judge it seems for the time being not plausible that the color mark has acquired distinctive character.

4.19 Furthermore, the PI judge has assessed that the trademark registration by the BOIP has taken place on the basis of the information of GSK exclusively (exhibit 25, writ of summons). As Sandoz has rightfully noted, GSK did not consider the various legal procedures, which have taken place in Europe already about the use of the color purple. GSK has also not informed the BOIP about the use of colors by itself and by other medicine manufacturers as distinction of the type of medicine. Also, it is sufficiently likely that the BOIP in allowing the color mark registration, considering the explanation of the Belgium attorney of Sandoz during the oral hearing, has not taken into account the third party observations that where filed by Sandoz. The conclusion is therefore justified that with the application of the trademark, the BOIP has not been able to make an assessment based on all the specific circumstances of the case.

4.20 Based on this position, the PI judge is of the opinion that there is a serious, not to be neglected chance that the judge on the merits will allow the claim for invalidity of the trademark. This means that the claims of GSK in so far based on trademark infringement will be dismissed.

Slavish imitation

4.21 GSK is of the opinion that the product Airflusal Forspiro is a slavish imitation of the color purple (Pantone 2587 C) as used on its product Seretide and that Sandoz Nederland therefore acts unlawfully against it. Sandoz contests this with reasoning.

4.22 The Supreme Court has ruled that imitation of a product that is not (longer) protected by an absolute right of intellectual property is in principal free, unless confusion with the public can be expected because of the imitation and the imitating competitor fails to do anything reasonably possible and necessarily to prevent that by the similarity of both products the risk of confusion arises, without doing detriment to the validity or usability of its product. A need to standardization with the purchasers of the products may under circumstances be a justification for the imitation of a product that is confusing (HR 20 November 2009, ECLI:NL:HR:2009:B19666, Lego). For a successful appeal on slavish imitation it is necessary that the imitated product has a certain distinctive character, or in other words, has its own place on the market (HR 21 December 1956, NJ1960/414, drukasbakken). For the assessment of the risk of confusion, the basic principle is to take into account the overall impression that is decisive for each product as well as the consideration thereof by a barely attentive purchasing public that usually does not see both products side by side. The situation on the Dutch market is decisive for the claim (HR 7 June 1991, NJ 1992/392, Rummikub).

4.23 With its statement that the risk of confusion of the product Airflusal Forspiro should be assessed compared to the color purple (Pantone 2587 C), GSK fails to recognize that the risk of confusion must be assessed based on the total impression of both products at stake. In the assessment of the PI judge the total impression is, amongst others, decided by the shape of both products. The Diskus of GSK is characterized by its round shape, whilst the Airflusal Forspiro is more egg-shaped. Also the color combination is different; the Diskus consists of two colors purple (points 2.4 and 2.10 above), of which the color mark is predominant. The Forspiro consists of one tone of purple (Pantone 2573 C) in combination with white. Besides, both products have a sticker that deviates in shape and on which in clear letters the name of the product and the name of the manufacturer is indicated. Also the name of the products differ, as well as the way in which both inhalers function. It has not become evident that Sandoz has tried to imitate the Diskus of GSK. For example, Sandoz has been granted an award for the innovative character of the product Forspiro. Finally, also the packages in which both products are sold, distinguish from each other as regards to the shape (points.2.4 and 2.7 above). With the Seretide product, the color change of the color purple (from dark to light) is from the right to the left and is surrounded by an edge in a different color (red, green or purple depending on the dosage), which color comes back in the indication of the dosage on the package. Besides the dosage, the rest of the text on the package is in black. With Airflusal the color purple goes (from dark to light) from the top to the bottom and the name of the product, as well as the dosage, is mentioned in purple (from light to dark). The corresponding aspects, the use of a purple color and the fact that both products are indicated for asthma and/or COPD medication do not compensate the differences between the products. In the assessment of the PI judge, Sandoz has complied with its obligation to do anything reasonably possible and needed to prevent that the risk of confusion may arise. It is likely that the public, even though less attentive, will notify these differences. Also when it is assumed that Seretide has gained its own place on the market, which is disputed by Sandoz, the claim of GSK must be dismissed, because for the moment it is not likely that Sandoz has slavishly imitated GSK's product.

Misleading information

4.24 According to GSK the use of Sandoz Nederland of the color purple is misleading information within the meaning of article 6:194 DCC, because this unlawfully suggests a commercial connection with GSK and besides, it is unlawfully suggested that Airflusal Forspiro is equivalent to Seretide as regards to quality, indication and function.

4.25 One of the questions that must be answered in this regard, is whether the use of a color is covered by the concept of "information" within the meaning of article 6:194 DCC. According to Sandoz this is not the case and the PI judge agrees to that. Through the sole use of a color, in fact no information of any fact is being undertaken.[1] No misleading information in the sense of the before mentioned article has taken place.

4.26. Finally, GSK argues that Sandoz commits unfair commercial practices within the meaning of articles 6:193b and 6:193c DCC. According to GSK Sandoz Nederland uses an important character of the product of a competitor within the meaning of article 6:193c, para. 1 sub b DCC, as a consequence of which the average consumer is misled of may be misled. Furthermore, according to GSK confusion is caused with regard to the products, trademarks and distinguishing characters of a competitor, within the meaning of article 6:193c, para. 2 sub a DCC.

4.27. Sandoz has argued that GSK is not entitled to invoke these articles because, on the one hand the activities of Sandoz are not directly aimed at consumers because of the prohibition on public advertising included in article 85 Medicines Act and on the other hand because the consumer does not take the purchasing decision. According to Sandoz, the prescribing doctor is the one that takes the purchasing decision for the patient, as the doctor is the one that prescribes a certain medicine, after which it is the pharmacist who orders the medicine with Sandoz and to whom Sandoz delivers the medicine.

4.28. The PI judge concludes as follows. Articles 6:193a-j DCC exclusively pertain to business-to-consumer (hereinafter: B2C) communication. Besides, in Dutch law there is no explicit possibility that competitors may invoke the concerning articles towards each other. The foregoing articles, however, implement Directive 2005/29/EC (hereinafter: Directive) and in that Directive it is explicitly indicated that (also) competitors must be protected against unfair B2C commercial practices. Since it has not appeared from the legislative history that the national legislator has made an explicit choice to deviate from the Directive on this point, an explanation in accordance with the Directive is the starting point (reference HR 17 January 2014, IEPT20140117 (Ryanair/PR Aviation)). Considering what is included in the Directive, according to the PI judge it must be accepted that GSK can invoke the articles 6:193a-j DCC.

4.29. Based on the foregoing, a merchant acts unlawfully towards a consumer if he performs an act that is unfair, as result whereof the average consumer takes or can take a decision about a purchase which he otherwise would not have taken. In the current situation the medicines can only be obtained with a recipe and for which public advertising is forbidden based on article 85 Medicines Act. Whilst there is no direct advertising aimed at the consumer, it can be admitted to GSK that the patient, being the consumer, is ultimately the one using the product and the one receiving the package and potentially also information leaflets. The fact that advertising aimed directly at the consumer is not allowed, therefore does not mean that the aforementioned articles cannot be applied. Also through packaging and information leaflets, information is given to the consumer and also that information can potentially be misleading.

[1] Compare to: Court 's-Hertogenbosch 8 September 1997, NJ1998/431(Shampony)

4.30. However, in this case there is the particular situation that with prescription only medicines it is not the patient/consumer that takes the ultimate decision about the product, but it is the doctor and/or pharmacist. Although the patient can indicate its preference to the doctor and/or pharmacist, also in that even it is the doctor and/or pharmacist who decides which product will be provided to the patient and it is not the patient himself. The doctor and/or pharmacist are however not considered a consumer in the meaning of the forgoing articles, as a consequence whereof the claims of GSK fail. Besides, based on the arguments as described in point 4.23 above, there can be no question of misleading or confusion.

4.31. The claims of GSK will therefore be dismissed.

Costs of the proceedings

4.32. GSK will be ordered to pay the costs of the proceedings, being the party which is ruled against. Sandoz requests compensation by GSK of € 120.000,00 as costs of the proceedings further to article 1019h Civil Proceedings Code. With regard to the amount of the costs of the proceedings, parties have reached an agreement. The PI judge does not see any reason to deviate from that. The court fees are considered to be included in this amount.

4.33. The PI judge furthermore estimates, as also indicated by the parties, that the claims with a foundation in intellectual property, are 72,5% of the procedure. Therefore, 72,5% of the requested costs will be allowed, being € 87.000,00.

4.34. The claims, that do not have any foundation in intellectual property, are 27,5% of the legal proceedings. Normally, these costs would amount to € 816,00 on the basis of the regular court-approved costs. As the claims without any foundation in intellectual property are 27,5% of the legal proceedings, also 27,5% of these costs, therefore € 224,40, will be imposed on GSK.

4.35. The costs on the part of Sandoz are therefore in total estimated at € 87.224,40 for counsel's fixed fee.

5. The decision of the judgement

The PI judge

5.1. dismisses the claims,

5.2. orders GSK to pay the costs of the proceedings, until today estimated at € 87.224,40 on the part of Sandoz,

5.3. declares the judgement provisionally and forcible with regard to the order to pay costs.

This judgement is rendered by Mr. J.A. Schuman and was announced in public on 30 December 2015.