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| **Zacco ref** | **Date** |
|---|---|
| SPC483507NO00 | 14 January 2025 |
| **Your ref** | **Owner** |
| | Ascendis Pharma Bone Diseases A/S |
| **Case** | |
| SPC Application based on patent No. NO/EP3423103 | Yorvipath - palopegteriparatide |

Dear Sir/Madam

The following documents are attached to the SPC application for Yorvipath - palopegteriparatide:

1. Marketing Authorization no. EU/1/23/1766 for Yorvipath - palopegteriparatide granted by the Norwegian Medical Products Agency 2023-12-12.

2. Summary of the Product Characteristics related to Yorvipath where it is stated that palopegteriparatide is the active ingredient.

3. Decision date of the first MA for “Yorvipath - palopegteriparatide” within EEA, EU/1/23/1766; 2023-11-17.

4. Notification date of the first MA for Yorvipath within EEA, EU/1/23/1766; 2023-11-20.

5. WHO Drug Information extract (Vol. 37, No. 1, 2023) confirming the chemical name and structure of palopegteriparatide.

6. Memo Protection of the Product Palopegteriparatide by the basic patent EP 3 423 103 B1.

7. Copy of Power of Attorney filed in connection with the validation in Norway of the basic patent. No new Power of Attorney document should be needed.

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Designation of the product in the SPC application

The SPC application is directed to the product “palopegteriparatide”.

The Summary of Product Characteristics (SmPC) shows that palopegteriparatide is the active ingredient of the medicinal product Yorvipath (see Encl. 2, SmPC, point 2, “Qualitative and quantitative composition” and point 5.1 “Pharmacodynamic properties”, “Mechanism of action’”).

Description of the product and structure of “Palopegteriparatide”

The medicinal product "Yorvipath " is an orphan medicinal product for human use (see Encl. 3, English translation of the marketing authorisation, e.g., title and Article 1).

The Committee for Medicinal Products for Human Use of the EMA acknowledged that **“palopegteriparatide**” **is a new active substance** (see Encl. 3, English translation of the marketing authorisation, point (4)).

Yorvipath is a parathyroid hormone (PTH) replacement therapy indicated for the treatment of adults with chronic hypoparathyroidism (see Encl. 2, SmPC, point 4.1 “Therapeutic indications”).

Yorvipath contains palopegteriparatide as active ingredient as a solution for subcutaneous injection in a pre-filled pen. The doses of palopegteriparatide in the medicinal product Yorvipath are indicated in the SmPC under point 2 (see Encl. 2, SmPC, points 1 and 2, “Qualitative and quantitative composition” point 4.2 “Posology” and “Method of administration”).

Palopegteriparatide is a prodrug that consists of PTH(1-34), i.e. the N-terminal 34 amino acids of native human parathyroid hormone (PTH) that is transiently conjugated to a methoxypolyethylene glycol carrier (mPEG) via a proprietary TransCon linker. PTH(1-34), which corresponds to SEQ ID NO:51 in EP 3 423 103 B1, is conjugated to the TransCon Linker via the N-terminal amine functional group of PTH(1-34) (see Encl. 2, Annex I, SmPC, point 5.1 “Pharmacodynamic properties”, “Mechanism of action’”).

The structure of palopegteriparatide is described in the extract from the WHO Drug information, Vol. 37, No. 1, 2023 showing the International Nonproprietary Name (INN) entry for palopegteriparatide (see Encl. 5). Please note that this extract relates to the second correction of the INN entry for palopegteriparatide, which was first published as proposed INN in WHO Drug Information, Vol. 34, No. 4, 2020. A first correction was published as proposed INN in WHO Drug Information, Vol. 35, No. 4, 2021. The proposed INNs contained incorrect information and shall therefore not be included in the filing of this SPC application.

The INN shows that the sequence of **PTH(1-34)** in palopegteriparatide is as follows:

Sequence / Séquence / Secuencia

SVSEIQLMHN LGKHLNSMER VEWLRKKLQD VHNF 34

Furthermore, the INN shows that palopegteriparatide contains two mPEG chains and indicates that the average number of ethylene glycol units in each of the two mPEG side chains of Palopegteriparatide ranges from about 450-500.

Moreover, the INN shows that the PTH polypeptide is connected to the rest of the palopegteriparatide molecule via the N-terminal amine functional group provided by **the serine at position 1** of the PTH polypeptide.

Protection of the product “Palopegteriparatide” by the basic patent EP 3 423 103 B1 (Art. 3(a) of Regulation (EC) No. 469/2009)

The **Memo Protection of the Product Palopegteriparatide by the basic patent EP 3 423 103 B1** (see Encl. 6) explains in detail by which claims of the basic patent the product palopegteriparatide is protected in terms of Art. 3(a) of Regulation (EC) No. 469/200).

Thus, the requirement to submit information showing that the product is protected by the basic patent has been complied with.

First Marketing Authorisation for palopegteriparatide in Norway (Art. 3(b)(d) of Regulation (EC) No. 469/2009), in the European Union (EU) and in the European Economic Area (EEA))

The first marketing authorisation for the product “palopegteriparatide” in Norway pursuant to Art. 3(b)(d) of Regulation (EC) No. 469/2009 is the **Decision C(2023)8037** granting **marketing authorisation no. EU/1/23/1766** for the orphan medicinal product "Yorvipath" (see Encl. 3).

Please note that an earlier marketing authorisation has been granted by the European Commission on 10 June 2003 (see C(2003) 1884) for the medicinal product “Forsteo” with the active substance “teriparatide”.

However, said earlier marketing authorisation for the product “teriparatide” is not relevant for the grant of an SPC for the product “palopegteriparatide”, since **palopegteriparatide”**

**is a prodrug of "teriparatide"** and thus **a different active substance than** "**teriparatide**".

Importantly, as mentioned above, the Committee for Medicinal Products for Human Use of the EMA acknowledged that **"palopegteriparatide" is a new active substance** (see Encl. 3, English translation of the marketing authorisation, point (4)).

Moreover, this marketing authorisation is also the first marketing authorisation that has been granted in the EU and in the EEA. Ascendis Pharma has confirmed that no earlier marketing authorisation has been granted in Switzerland, Iceland or Norway.

The **date of notification of the marketing authorisation** relevant to the calculation of the duration of the SPC is **20 November 2023** (see Encl. 4; (Art. 13(1) of Regulation (EC) no. 469/2009, Seattle Genetics, Decision of the CJEU of 6 October 2015, C-71/15).

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It is believed that all information and documentation needed to examine the SPC application for Yorvipath - palopegteriparatide are hereby submitted and we look forward to hearing from you.

Yours faithfully
**Zacco Norway AS**

Rita Lillegraven