



(12) Translation of
European patent specification

(11) NO/EP 2780338 B1

NORWAY

(19) NO
(51) Int Cl.
C07D 401/12 (2006.01)
A61K 31/506 (2006.01)
A61K 31/53 (2006.01)
A61P 35/00 (2006.01)
C07D 491/04 (2006.01)

Norwegian Industrial Property Office

(21) Translation Published 2017.03.20

(80) Date of The European Patent Office Publication of the Granted Patent 2016.11.09

(86) European Application Nr. 12798087.8

(86) European Filing Date 2012.11.14

(87) The European Application's Publication Date 2014.09.24

(30) Priority 2011.11.14, US, 201161559312 P

(84) Designated Contracting States:
AL AT BE BG CH CY CZ DE DK EE ES FI FR GB
GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO
PL PT RO RS SE SI SK SM TR
Designated Extension States:
BA ME

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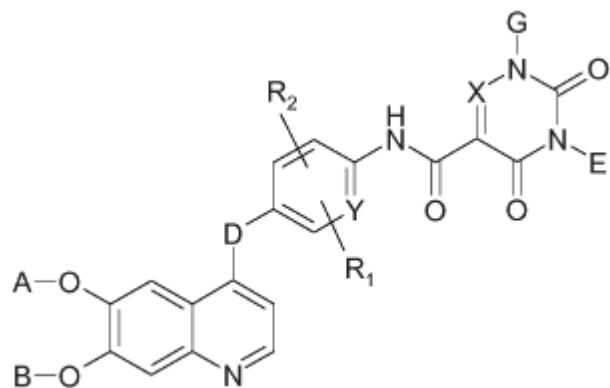
(54) Title **URACIL DERIVATIVES AS AXL AND C-MET KINASE INHIBITORS**

(56) References Cited:
WO-A1-2009/127417
WO-A1-2012/028332

Enclosed is a translation of the patent claims in Norwegian. Please note that as per the Norwegian Patents Acts, section 66i the patent will receive protection in Norway only as far as there is agreement between the translation and the language of the application/patent granted at the EPO. In matters concerning the validity of the patent, language of the application/patent granted at the EPO will be used as the basis for the decision. The patent documents published by the EPO are available through Espacenet (<http://worldwide.espacenet.com>) or via the search engine on our website here: <https://search.patentstyret.no/>

Patentkrav

1. Forbindelse med formel III,

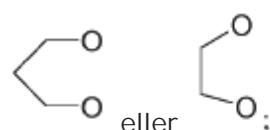


Formel III

5 hvor:

A og B uavhengig av hverandre er H, alkyl, alkoxysalkyl, cykloalkyl, cykloalkoksyalkyl, heterocyklylalkyl, heterocyklylalkoksyalkyl, arylalkyl eller arylalkoksyalkyl, eller A og B sammen med oksygenatomene som de er bundet til, danner

10



D er O, S, NH eller C=O;

E er H, alkyl, substituert alkyl, alkenyl, substituert alkenyl, alkynyl, substituert alkynyl, cykloalkyl, aryl, substituert aryl, heteroaryl, heterocyklyl, substituert heteroaryl eller heteroarylalkyl, hvor heteroarylgruppen i heteroarylalkyl kan være substituert eller usubstituert;

15

G er H, aryl, substituert aryl, heteroaryl, substituert heteroaryl, heterocyklyl, alkyl eller cykloalkyl, cykloalkylalkyl, alkenyl eller alkynyl, hvor alkylet, alkenylet eller cykloalkylet kan være substituert med én, to eller tre grupper valgt fra gruppen bestående av alkanoyl, cykloalkyl, alkenyl, alkynyl, halogen, hydroksyl, alkoxys, 20 alkoxyskarbonyl, heterocyklyl, aryl, substituert aryl, aryloksy, arylalkoxys, amino,

alkylamino, dialkylamino, hvor alkylgruppene i dialkylamino kan være like eller forskjellige, heteroaryl, karboksyl, okso, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl, hvor alkylgruppene i dialkylcarbamoyl kan være like eller forskjellige, og heterocyklylkarbonyl;

5 X er C-R₄ eller N, hvor R₄ er H eller alkyl;

Y er N, CH eller C, hvor C kan være substituert med en gruppe R₁ eller R₂; og

R₁ og R₂ uavhengig av hverandre er H, alkyl, halogen, alkoxsy, trihalogenalkyl, amino, alkylamino, dialkylamino, hvor alkylgruppene på dialkylamino kan være like eller forskjellige; eller

10 et farmasøytisk akseptabelt salt derav.

2. Forbindelse ifølge krav 1, hvor A og B uavhengig av hverandre er alkyl, heterocyklylalkyl eller heterocyklylalkoksyalkyl.

3. Forbindelse ifølge krav 1, hvor A og B uavhengig av hverandre er alkyl.

4. Forbindelse ifølge krav 1, hvor D er O, S eller NH.

15 5. Forbindelse ifølge krav 1, hvor D er O.

6. Forbindelse ifølge krav 1, hvor R₁ og R₂ uavhengig av hverandre er halogen, alkoxsy, alkyl eller H.

7. Forbindelse ifølge krav 1, hvor R₁ og R₂ uavhengig av hverandre er halogen eller alkoxsy.

20 8. Forbindelse ifølge krav 1, hvor R₁ og R₂ uavhengig av hverandre er metoksy eller fluor.

9. Forbindelse ifølge krav 1, hvor X er N eller CH.

10. Forbindelse ifølge krav 1, hvor X er CH.

11. Forbindelse ifølge krav 1, hvor G er alkyl, hvor alkylet kan være substituert med én, to eller tre grupper valgt fra gruppen bestående av alkanoyl, cykloalkyl, alkenyl, alkynyl, halogen, hydroksyl, alkoxsy, alkoxsykarbonyl, heterocyklyl, aryl, substituert aryl, aryloksy, arylalkoxsy, amino, alkylamino, dialkylamino hvor alkylgruppene i dialkylamino kan være like eller forskjellige, heteroaryl, karboksyl, okso, karbamoyl, alkylkarbamoyl, dialkylkarbamoyl hvor alkylgruppene i dialkylkarbamoyl kan være like eller forskjellige, og heterocyklylkarbonyl.
- 5
12. Forbindelse ifølge krav 1, hvor E er aryl, substituert aryl eller cykloalkyl.
13. Forbindelse ifølge krav 1, hvor E er substituert aryl.
- 10 14. Forbindelse ifølge krav 1, hvor A og B uavhengig av hverandre er alkyl; D er O, S eller NH; R₁ og R₂ uavhengig av hverandre er halogen, alkoxsy, alkyl eller H; X er N eller CH; G er alkyl, hvor alkylet kan være substituert med én, to eller tre grupper valgt fra gruppen bestående av alkanoyl, cykloalkyl, alkenyl, alkynyl, halogen, hydroksyl, alkoxsy, alkoxsykarbonyl, heterocyklyl, aryl, substituert aryl, aryloksy, arylalkoxsy, amino, alkylamino, dialkylamino hvor alkylgruppene i dialkylamino kan være like eller forskjellige, heteroaryl, karboksyl, okso, karbamoyl, alkylkarbamoyl, dialkylkarbamoyl hvor alkylgruppene i dialkylkarbamoyl kan være like eller forskjellige, og heterocyklylkarbonyl; og E er aryl, substituert aryl eller cykloalkyl.
- 15
- 20 15. Forbindelse ifølge krav 1 som er:
- 1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;
- 3-(4-Fluorfenyl)-1-metyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;
- 25 3-(4-Fluorfenyl)-1-(2-metoksyethyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;
- 1-(2-Etoksyethyl)-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

1-Cyklopropylmetyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

5 3-(4-Fluorfenyl)-1-(3-metoksypropyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

3-(4-Fluorfenyl)-1-isobutyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

10 1-Allyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

1-(2-Benzylloksyethyl)-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

3-(4-Fluorfenyl)-2,4-diokso-1-propyl-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

15 3-(4-Fluorfenyl)-1-(2-isopropoxysyethyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

1-(3-Benzylloksypropyl)-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

20 1-(3,3-Difluorallyl)-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

3-(4-Fluorfenyl)-1-(3-metyl-but-2-enyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

3-(4-Fluorfenyl)-1-(2-morfolin-4-yletyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

25 3-(4-Fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

3-(4-Fluorfenyl)-1-metyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)fenyl]amid;

1-(2-Benzyloksyetyl)-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)fenyl]amid;

5 1-(2-Dimethylaminoetyl)-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

1-(3-Benzyloksypropyl)-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)fenyl]amid;

10 1-(3-Benzyloksypropyl)-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-2-fluorfenyl]amid;

3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)fenyl]amid;

3-(4-Fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)fenyl]amid;

15 3-Cykloheksyl-1-etyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

3-(4-Fluorfenyl)-2,4-diokso-1-(2-pyrrolidin-1-yletyl)-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

20 3-(4-Fluorfenyl)-2,4-diokso-1-(2-piperidin-1-yletyl)-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)fenyl]amid;

1-Cyklobutyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

25 3-(4-Fluorfenyl)-2,4-diokso-1-(tetrahydropyran-4-yl)-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[5-(6,7-dimetoksykinolin-4-yloksy)pyridin-2-yl]amid ble syntetisert utgående fra 5-(6,7-dimetoksykinolin-4-yloksy)pyridin-2-ylamin;

1-Etyl-3-(4-fluorfenyl)-6-metyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dietoksykinolin-4-yloksy)-3-fluorfenyl]amid;

3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[5-(6,7-dimetoksykinolin-4-yloksy)pyridin-2-yl]amid;

10 1-Cyklopropylmetyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[5-(6,7-dimetoksykinolin-4-yloksy)pyridin-2-yl]amid;

3-(4-Fluorfenyl)-2,4-diokso-1-pentyl-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

15 3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dietoksykinolin-4-yloksy)-3-fluorfenyl]amid;

3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(5,7-dimetoksykinolin-4-yloksy)fenyl]amid;

1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(5,7-dimetoksykinolin-4-yloksy)fenyl]amid;

20 1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(7-benzyloksy-6-metoksykinolin-4-yloksy)-3-fluorfenyl]amid;

3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(7-benzyloksy-6-metoksykinolin-4-yloksy)-3-fluorfenyl]amid;

25 1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[3-fluor-4-(7-hydroksy-6-metoksykinolin-4-yloksy)fenyl]amid;

- 1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-{ 3-fluor-4-[6-metoksy-7-(3-morfolin-4-ylpropoksy)kinolin-4-yloksy]fenyl} amid;
- 1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-{ 3-fluor-4-[6-metoksy-7-(2-metoksyetoksy)kinolin-4-yloksy]fenyl} amid;
- 5 1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-{ 3-fluor-4-[6-metoksy-7-(2-morfolin-4-yl-etoksy)kinolin-4-yloksy]fenyl} amid;
- 3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[3-fluor-4-(7-hydroksy-6-metoksykinolin-4-yloksy)fenyl]amid;
- 10 3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-{ 3-fluor-4-[6-metoksy-7-(3-morfolin-4-ylpropoksy)kinolin-4-yloksy]fenyl} amid;
- 3-(4-Fluorfenyl)-1-(2-hydroksyethyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;
- 15 3-(4-Fluorfenyl)-1-(3-hydroksypropyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;
- 3-(4-Fluorfenyl)-1-(3-hydroksypropyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-2-fluorfenyl]amid;
- 3-(4-Fluorfenyl)-1-(3-hydroksypropyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)fenyl]amid;
- 20 3-(4-Fluorfenyl)-1-(2-hydroksyethyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)fenyl]amid;
- 1-((S)-2,3-Dihydroksypropyl)-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;
- 25 3-(4-Fluorfenyl)-1-(4-hydroksybutyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6-cyano-7-metoksykinolin-4-yloksy)fenyl]amid;

3-(4-fluorfenyl)-1-metyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-[(6,7-dimetoksykinolin-4-yl)hydroksymetyl]-3-fluorfenyl] amid;

5 3-(4-fluorfenyl)-1-metyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-ylmetyl)-3-fluorfenyl]amid;

1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[3-cyklopropyl-4-(6,7-dimetoksykinolin-4-yloksy)fenyl]amid;

10 3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[3-cyklopropyl-4-(6,7-dimetoksykinolin-4-yloksy)fenyl]amid;

3-(4-Fluorfenyl)-2,4-diokso-1-prop-2-ynyl-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

3-(4-Fluorfenyl)-1-(2-imidazol-1-yletyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

15 3-(4-Fluorfenyl)-2,4-diokso-1-(2-pyrazol-1-yletyl)-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

3-(4-Fluorfenyl)-2,4-diokso-1-fenetyl-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

20 1-[2-(1,3-Dioksolan-2-yletyl)]-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

1-Dietylkarbamoylmethyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

25 3-(4-Fluorfenyl)-1-(2-morfolin-4-yl-2-okso-etyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

3-(4-Fluorfenyl)-2,4-diokso-1-[2-(2-oksopyrrolidin-1-yl)etyl]-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

1-(2-Fluor-etyl)-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

[5-[4-(6,7-Dimetoksykinolin-4-yloksy)-3-fluorfenylkarbamoyl]-3-(4-fluorfenyl)-2,4-diokso-3,4-dihydro-2H-pyrimidin-1-yl]eddiksyre-tert-butylester;

[5-[4-(6,7-Dimetoksykinolin-4-yloksy)-3-fluorfenylkarbamoyl]-3-(4-fluorfenyl)-2,4-diokso-3,4-dihydro-2Hpyrimidin-1-yl]eddiksyre;

10 3-(4-Fluorfenyl)-1-oksazol-2-ylmetyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

3-(4-Fluorfenyl)-2,4-diokso-1-(tetrahydrofuran-2-ylmetyl)-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

15 3-(4-Fluorfenyl)-2,4-diokso-1-(tetrahydropyran-4-ylmetyl)-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

3-(4-Fluorfenyl)-1-(2-metyltaiazol-4-ylmetyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

1-Cyklopentyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

1-Benzyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

25 3-(4-Fluorfenyl)-1-[2-(2-fluorfenyl)etyl]-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

- 3-(4-Fluorfenyl)-1-[2-(4-fluorfenyl)etyl]-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;
- 1-(2-Cykloheksyletil)-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;
- 5 3-(4-Fluorfenyl)-2,4-diokso-1-(3-fenylpropyl)-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;
- 3-(4-Fluorfenyl)-2,4-diokso-1-(2-okso-2-pyrrolidin-1-yletyl)-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;
- 10 1-Dimetylkarbamoylmethyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;
- 1-(1-Dimetylkarbamoyl-2-okso-propyl)-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;
- 15 3-(4-Fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-2-fluorfenyl]amid;
- 3-(4-Fluorfenyl)-1-metyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-2-fluorfenyl]amid;
- 20 1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-2-fluorfenyl]amid;
- 1-Allyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-2-fluorfenyl]amid;
- 3-(4-Fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3,5-difluorfenyl]amid;
- 25 1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3,5-difluorfenyl]amid;

3-Etyl-1-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

1,3-Dimetyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

5 1,3-Dietyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

1,3-Diisopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

10 1,3-Bis-cyklopropylmethyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

1,3-Diallyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

1,3-Bis-(3-metyl-but-2-enyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

15 2,4-Diokso-1,3-di-prop-2-ynyl-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

2,4-Diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

20 1-Etyl-2,4-diokso-3-fenyl-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

1-Isopropyl-2,4-diokso-3-fenyl-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

3-(4-Fluorfenyl)-2,4-diokso-1-propyl-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-karbonyl)-3-fluorfenyl]amid;

25 4-(4-Fluorfenyl)-2-isopropyl-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

4-(4-Fluorfenyl)-2-metyl-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

2-Etyl-4-(4-fluorfenyl)-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

5 4-(4-Fluorfenyl)-2-isopropyl-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(2,3-dihydro[1,4]dioksino[2,3-g]kinolin-9-yloksy)-3-fluorfenyl]amid;

4-(4-Fluorfenyl)-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

10 4-(4-Fluorfenyl)-2-(2-hydroksyetyl)-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

2-Etyl-4-(4-fluorfenyl)-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dietoksykinolin-4-yloksy)-3-fluorfenyl]amid;

15 4-(4-Fluorfenyl)-2-isopropyl-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[5-(6,7-dimetoksykinolin-4-yloksy)pyridin-2-yl]amid;

4-(4-Fluorfenyl)-2-isopropyl-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[3-fluor-4-(7-metoksykinolin-4-yloksy)fenyl]amid;

4-(4-Fluorfenyl)-3,5-diokso-2-(2-okso-propyl)-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

20 4-(4-Fluorfenyl)-3,5-diokso-2-prop-2-ynyl-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

2-Metyl-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

2-Metyl-3,5-diokso-4-prop-2-ynyl-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-

25 [4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

2-Metyl-4-(5-metylisosazol-3-ylmetyl)-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

5 2-Metyl-3,5-diokso-4-pent-2-ynyl-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

4-(4-Hydroksy-but-2-ynyl)-2-metyl-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

10 4-(1,5-Dimetyl-1H-pyrazol-3-ylmetyl)-2-metyl-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

2-Metyl-3,5-diokso-4-(2-pyrazol-1-yletyl)-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

15 2-Metyl-4-(1-metyl-1H-[1,2,4]triazol-3-ylmetyl)-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

4-Cyanometyl-2-metyl-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

4-Etyl-2-metyl-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

20 4-Allyl-2-metyl-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

4-Cyklopropylmetyl-2-metyl-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

25 2-Metyl-3,5-diokso-4-(tetrahydropyran-4-ylmetyl)-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

4-Isobutyl-2-metyl-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;

- 4-Cyklobutylmetyl-2-metyl-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;
- 4-(2,2-Dimetylpropyl)-2-metyl-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;
- 5 ±2-Metyl-4-(2-metyl-butyl)-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;
- 3-(4-Fluorfenyl)-1-metyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-([1,3]dioksolo[4,5-g]kinolin-8-yloksy)-3-fluorfenyl]amid;
- 1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(2,3-dihydro[1,4]dioksino[2,3-g]kinolin-9-yloksy)-3-fluorfenyl]amid;
- 10 2-Cyklopropylmetyl-4-(4-fluorfenyl)-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid;
- 1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-ylamino)fenyl]amid;
- 15 3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-ylamino)fenyl]amid;
- 4-(4-Fluorfenyl)-2-isopropyl-3,5-diokso-2,3,4,5-tetrahydro[1,2,4]triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-ylamino)fenyl]amid;
- 20 1-etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-ylsulfanyl)fenyl]amid;
- 3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-ylsulfanyl)fenyl]amid;
- 3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre{4-[(6,7-dimetoksykinolin-4-yl)methylamino]fenyl} amid;
- 25 1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-{4-[(6,7-dimetoksykinolin-4-yl)methylamino]fenyl} amid;

3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinazolin-4-yloksy)fenyl]amid;

1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksy-kinazolin-4-yloksy)fenyl]amid;

5 1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-2-metoksyfenyl]amid;

1-Metyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-2-metoksyfenyl]amid;

10 1-Isopropyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-2-metoksyfenyl]amid;

1-Metyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-2,3-difluorfenyl]amid;

1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-2,3-difluorfenyl]amid;

15 1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-metylfenyl]amid;

3-(4-Fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-metylfenyl]amid;

20 3-(4-Fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-metoksyfenyl]amid;

1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-metoksyfenyl]amid;

1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[3-klor-4-(6,7-dimetoksykinolin-4-yloksy)-3-metoksyfenyl]amid;

25 1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-2-dimethylaminofenyl]amid;

3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-2-dimethylaminofenyl]amid;

1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-isopropylfenyl]amid;

5 3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-isopropylfenyl]amid;

1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-2,3-dimethylfenyl]amid;

10 3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-2,3-dimethylfenyl]amid;

1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-trifluormetylfenyl]amid;

3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-trifluormetylfenyl]amid;

15 1-Etyl-3-(4-fluorfenyl)-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3,5-dimethylfenyl]amid;

3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3,5-dimethylfenyl]amid;

20 3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-metylfenyl]amid;

2-Etyl-4-(4-fluorfenyl)-3,5-diokso-2,3,4,5-tetrahydro-1,2,4-triazin-6-karboksylsyre-[5-(6,7-dimetoksykinolin-4-yloksy)pyridin-2-yl]amid;

2-Etyl-4-(4-fluorfenyl)-3,5-diokso-2,3,4,5-tetrahydro-1,2,4-triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-isopropylfenyl]amid; eller

25 4-(4-Fluorfenyl)-2-isopropyl-3,5-diokso-2,3,4,5-tetrahydro-1,2,4-triazin-6-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-2-metoksyfenyl]amid; eller

et farmasøytisk akseptabelt salt derav.

16. Forbindelse ifølge krav 1 som er 3-(4-Fluorfenyl)-1-isopropyl-2,4-diokso-1,2,3,4-tetrahydropyrimidin-5-karboksylsyre-[4-(6,7-dimetoksykinolin-4-yloksy)-3-fluorfenyl]amid.

5 17. Farmasøytisk sammensetning omfattende en forbindelse ifølge et av kravene 1-16 eller et salt derav og en farmasøytisk akseptabel eksipiens.

18. Forbindelse ifølge et hvilket som helst av kravene 1-17 for anvendelse ved behandling av en proliferativ forstyrrelse.

10 19. Forbindelse for anvendelse ifølge krav 18, hvor den proliferative forstyrrelse er kreft.

20. Forbindelse for anvendelse ifølge krav 18, hvor den proliferative forstyrrelse er valgt fra kronisk myelogen leukemi, kronisk myeloproliferativ forstyrrelse, lungekreft, prostatakreft, spiserørskreft, eggstokkrekf, bukspyttkjertelkreft, magekreft, leverkreft, skjoldbruskkjertelkreft, nyrecellekarsinom, glioblastom, 15 brystkreft, akutt myeloid leukemi, tykktarmskreft, livmorkrekf, ondartet glioma, uvealt melanom, osteosarkom og bløtvevssarkom.