**Proposed new classification of the L01XE Protein kinase inhibitors and**

**L01XX Other antineoplastic agents**

A revision of the classification of the above mentioned ATC groups is needed due to the increasing number of new agents that are developed in cancer therapy area. A new classification in these groups was discussed by the WHO International Working Group for Drug Statistics Methodology at the latest meeting in October 2019. The Working Group would like to have feedback from the users of the ATC system to ensure that the new classification is considered to be useful.

**The following alterations are suggested:**

*Protein kinase inhibitors*

A new ATC 3rd level *L01E Protein kinase inhibitors* with 13 new ATC 4th levels are proposed (see enclosure 1). The substances are divided in subgroups according to “their main targets”. All protein kinase inhibitors in L01XE will be included in the new ATC 3rd level, L01E. In addition, the phosphatidylinositol-3-kinase (Pi3K) inhibitors, currently classified in L01XX, are suggested included in the new L01E.

*Other antineoplastic agents (L01XX)*

This group contains many ATC 5th levels and is a heterogeneous group. It is proposed to establish five new ATC 4th levels (see enclosure 2) based on the agents main mode of actions. In addition, it is suggested to alter the classification of the topoisomerase 1 inhibitors (currently classified in L01XX) and to establish a new ATC 4th level *L01CE* *Topoisomerase 1 inhibitors*.

|  |
| --- |
| *Our aim is to improve the usefulness of the ATC system and we would appreciate your feedback related to the new proposed classification.* *If you have alternative suggestions for subdivisions, or you consider the new classification contains too many ATC 4th sublevels we would appreciate your comments. If you think that some the subgroups should be combined we would also like to have your inputs.* |

The proposed new classification will be discussed again based on the feedback from the users at the next meeting in the Working Group in March 2019.

We will appreciate your comments as soon as possible and not later than 1 February, 2020.

**Please reply by mail to** **whocc@fhi.no****.**

Your sincerely

WHO Collaborating Centre for Drug Statistics Methodology

**Enclosure 1 Proposed new ATC level L01E Protein kinase inhibitors decided at the Working Group meeting October 2019**

|  |  |  |  |
| --- | --- | --- | --- |
| **L01E** | **Protein kinase inhibitors** |  | **Current ATC code L01XE--** |
| **L01EA** | **BCR-ABL tyrosine-kinase inhibitors** |  |
|  | 01 | imatinib |  |  | 01 |
|  | 02 | dasatinib |  |  | 06 |
|  | 03 | nilotinib |  |  | 08 |
|  | 04 | bosutinib |  |  | 14 |
|  | 05 | ponatinib |  |  | 24 |
| **L01EB** | **Epidermal growth factor receptor (EGFR)-tyrosin kinase inhibitors** |
|  | 01 | gefitinib |  |  | 02 |
|  | 02 | erlotinib |  |  | 03 |
|  | 03 | afatinib |  |  | 13 |
|  | 04 | osimertinib |  |  | 35 |
|  | 05 | rociletinib |  |  | 37 |
|  | 06 | olmutinib |  |  | 40 |
|  | 07 | dacomitinib |  |  | 47 |
|  | 08 | icotinib |  |  | 48 |
| **L01EC** | **B-Raf serine-threonine kinase (BRAF) inhibitors** |
|  | 01 | vemurafenib |  | 15 |
|  | 02 | dabrafenib |  |  | 23 |
|  | 03 | encorafenib |  |  | 46 |
| **L01ED** | **Anaplastic lymphoma kinase (ALK) inhibitors** |
|  | 01 | crizotinib  |  |  | 16 |
|  | 02 | ceritinib |  |  | 28 |
|  | 03 | alectinib |  |  | 36 |
|  | 04 | brigatinib |  |  | 43 |
|  | 05 | lorlatinib |  |  | 44 |
| **L01EE** | **Mitogen-activated protein kinase (MEK) inhibitors** |
|  | 01 | trametinib |  |  | 25 |
|  | 02 | cobimetinib |  |  | 38 |
|  | 03 | binimetinib |  |  | 41 |
|  | 04 | selumetinib |  |  | -- |
| **L01EF** | **Cyclin-dependent kinase (CDK) inhibitors** |  |
|  | 01 | palbociclib |  |  | 33 |
|  | 02 | ribociclib |  |  | 42 |
|  | 03 | abemaciclib |  |  | 50 |
| **L01EG** | **Mammalian target of rapamycin (mTOR) kinase inhibitors** |
|  | 01 | temsirolimus |  | 09 |
|  | 02 | everolimus |  |  | 10 |
|  | 03 | ridaforolimus |  | 19 |
| **L01EH** | **Human epidermal growth factor receptor 2 (HER2) tyrosine kinase inhibitors** |
|  | 01 | lapatinib |  |  | 07 |
|  | 02 | neratinib |  |  | 45 |
|  | 03 | tucatinib |  |  | -- |
| **L01EJ** | **Janus Associated Kinase (JAK) inhibitors** |  |
|  | 01 | ruxolitinib |  |  | 18 |
|  | 02 | fedratinib |  |  | 57 |
| **L01EK** | **Vascular endothelial growth factor receptor (VEGFR)-tyrosine kinase inhibitors** |
|  | 01 | axitinib |  |  | 17 |
|  | 02 | cediranib |  |  | 32 |
|  | 03 | tivozanib |  |  | 34 |
| **L01EL** | **Bruton`s tyrosine kinase (BTK) inhibitors** |  |
|  | 01 | ibrutinib |  |  | 27 |
|  | 02 | acalabrutinib |  | 51 |
| **L01EM** | **Phosphatidylinositol-3-kinase (Pi3K) inhibitors** |  |  |
|  | 01 | idelalisib |  | L01XX47 |
|  | 02 | copanlisib |  | L01XX61 |
|  | 03 | alpelisib |  | L01XX65 |
|  | 04 | duvelisib |  | -- |
| **L01EX** | **Other protein kinase inhibitors** |  |  |
|  | 01 | sunitinib |  |  | 04 |
|  | 02 | sorafenib |  |  | 05 |
|  | 03 | pazopanib |  |  | 11 |
|  | 04 | vandetanib |  |  | 12 |
|  | 05 | regorafenib |  |  | 21 |
|  | 06 | masitinib |  |  | 22 |
|  | 07 | cabozantinib |  | 26 |
|  | 08 | lenvatinib |  |  | 29 |
|  | 09 | nintedanib |  |  | 31 |
|  | 10 | midostaurin |  |  | 39 |
|  | 11 | quizartinib |  |  | 52 |
|  | 12 | larotrectinib |  | 53 |
|  | 13 | gilteritinib |  |  | 54 |
|  | 14 | entrectinib |  |  | 56 |
|  | 15 | pexidartinib |  | -- |
|  | 16 | erdafitinib |  |  | -- |
|  | 17 | capmatinib |  |  | -- |
|  | 18 | avapritinib |  |  | -- |

**Enclosure 2**

**Proposed new ATC 4th levels in L01X Other antineoplastic agents decided at Working Group meeting October 2019**

|  |  |  |
| --- | --- | --- |
| **L01XF** | **Retinoids for cancer treatment** | **Current ATC code L01XX--** |
|  | 01 | tretinoin | 14 |
|  | 02 | alitretinoin | 22 |
|  | 03 | bexarotene | 25 |
| **L01XG** | **Proteasome inhibitors** |  |
|  | 01 | bortezomib | 32 |
|  | 02 | carfilzomib | 45 |
|  | 03 | ixazomib  | 50 |
| **L01XH** | **Histone deacetylase (HDAC) inhibitors** |
|  | 01 | vorinostat | 38 |
|  | 02 | romidepsin | 39 |
|  | 03 | panobinostat | 42 |
|  | 04 | belinostat | 49 |
|  | 05 | entinostat | 64 |
| **L01XJ** | **Hedgehog pathway inhibitors** |  |
|  | 01 | vismodegib | 43 |
|  | 02 | sonidegib | 48 |
|  | 03 | glasdegib | 63 |
| **L01XK** | **Poly (ADP-ribose) polymerase (PARP) inhibitors** |
|  | 01 | olaparib | 46 |
|  | 02 | niraparib  | 54 |
|  | 03 | rucaparib  | 55 |
|  | 04 | talazoparib | 60 |

**Proposed new ATC 4th level in L01C Plant alkaloids and other natural products**

|  |  |  |
| --- | --- | --- |
| **L01CE** | **Topoisomerase 1 inhibitors** | **Current ATC code L01XX—** |
|  |
|  | 01 | topotecan | 17 |
|  | 02 | irinotecan | 19 |
|  | 03 | etirinotecan pegol  | 56 |
|  | 04 | belotecan | 68 |