INN Working Doc 24.590
May 2024
Distr.: PUBLIC
ENGLISH ONLY

55th MEETING OF THE WHO INTERNATIONAL WORKING GROUP FOR DRUG STATISTICS METHODOLOGY

Oslo, 14-15 March 2024 (hybrid face-to-face/virtual meeting)

Executive Summary

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World Health Organization, Geneva

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EXECUTIVE SUMMARY

Welcome and opening remarks

Dr Raffaella Balocco, Unit Head, International Nonproprietary Names (INN) Programme and Classification of Medical Products, welcomed all participants to the 55th meeting and proceeded directly to the election of the Chair and rapporteur.

Election of Chair and rapporteur

Professor Vera Vlahović-Palčevski was proposed for the Chair and elected unopposed. Professor Vlahović-Palčevski thanked the members and led the election of the rapporteur. Dr Kerry Atkins was elected as rapporteur.

Minutes of the 54th meeting

The minutes of the 54th meeting were adopted without objection.

Report from the WHO Collaborating Centre for Drug Statistics Methodology

Dr Mohammad Nouri Sharikabad, Director, WHO Collaborating Centre for Drug Statistics Methodology (the 'Centre'), provided an update on the work being undertaken by the Centre. Dr Sharikabad noted key initiatives towards the modernisation of product delivery from the Centre, including the development of an Application Programming Interface (API) and the updating of its websites.

Points for discussion from the WHO Headquarters

Dr Raffaella Balocco emphasized the need to strengthen collaborative efforts among the experts, the Centre, the INN, and the EML. A brief update was provided regarding the establishment of the *ad hoc* working group on DDDs for antineoplastic agents, detailing the initial progress and the development of a preliminary road map (see 3a). There was a good discussion about the importance of fortifying the ATC/DDD system to meet the evolving demands of the new era effectively. Many countries use the methodology to tailor a customised or modified version of the system by augmenting the official ATC/DDD Index with national "ATC" codes or "DDDs". It is, therefore, essential to properly identify and comprehend the reasons driving this necessity to effectively develop the methodology in line with its mission. It is vital to find ways to facilitate feedback and proactively seek opportunities for strategically crafted improvements that are meaningful to the users. In line with that, Dr Raffaella Balocco underscored the significance of two ongoing initiatives: the ATC/DDD online course for the School of INN and the ATC/DDD Questionnaire.

ATC classification items

The Working Group discussed two challenges, one objection to a decision from the previous meeting, and one proposed alteration for ATC codes and made the following decisions:

- Due to a limited number of codes left under L01XX *Other antineoplastic agents*, a new ATC 4th level for "other" antineoplastic agents in L01XU *Other antineoplastic agents (cont.)* was established as a continuation of the ATC 4th level L01XX *Other antineoplastic agents.* The Working Group recommended that clarifying comments should be added to the Guidelines to explain that there are two "other" groups in this third ATC level. The Working Group requested that it should be further investigated how the ATC system can be developed to manage similar situations in the future.
- To assign a new ATC 5th level for patritumab deruxtecan in L01FX *Other monoclonal antibodies and antibody drug conjugates.*
- To maintain the decision from M54 to classify zuranolone in N06AX *Other antidepressants.* It was decided to consider a reclassification of substances in N06AX at a future meeting.
- A request to assign topical formulations of fluorouracil in a separate ATC code in D *Dermatologicals* was considered. The Working Group noted that the local and systemic formulations of fluorouracil were classified together in the ATC group L01BC *Pyrimidine analogues* and a comment was included in the Guidelines to note that L01BC includes both formulations. A suggestion to establish D06BX *Other chemotherapeutics* under D06B *Chemotherapeutics for topical use* was discussed which identified that the use of the term "chemotherapeutic" had changed and that it may be beneficial to revise the use of the terms "antibiotic", "antimicrobial" and "chemotherapeutics" in the Guidelines. In order to keep the classification system stable, it was decided to not alter the classification of topical fluorouracil and maintain the current classification of the topical formulations together with systemic formulations in L01BC. The Working Group requested for the Centre to examine if revisions to the text in the Guidelines in D06 were required.

A total of 28 new ATC 5th level codes were considered.

- Working Group decisions in relation to establishing new codes included:
  - To establish a new ATC 5th level code for seladelpar in A05AX *Other drugs for bile therapy*.
  - To establish a new ATC 5th level code for the combination of bifikafusp alfa and onfekafusp in L01XY *Combinations of antineoplastic agents*.
- Working Group decisions for existing codes included:
  - To classify the catheter lock solution with taurolidine and heparin in the existing ATC 5th level code B01AB51 *heparin, combinations* in the B01AB *Heparin group*.
  - To classify the 21-valent pneumococcal polysaccharide conjugate vaccine in the existing ATC 5th level code J07AL02 *pneumococcus, purified polysaccharides antigen conjugated* in J07AL *Pneumococcal vaccines*.
  - To classify the combination of abiraterone and methylprednisolone in the existing ATC 5th level code L02BX53 with a name alteration to abiraterone and corticosteroids in L02BX *Other hormone antagonists and related agents*.
  - To classify the ophthalmic solution of atropine in the existing ATC 5th level code S01FA01 *atropine* in S01FA *Anticholinergics.*

Defined Daily Dose Items

The Working Group agreed with the proposed DDDs and approved the dose protocol presented by the Centre.

DDDs for 6 new single substances and 2 DDDs for combination products were assigned.

One DDD alteration request was considered for fulvestrant. The Working group decided to change the DDD for fulvestrant (L02BA03) from 8.3 mg to 16.7 mg to align with the new global standard maintenance dose of 500 mg per month.

The three-year revisions of DDDs included in the ATC/DDD index from January 2022 were considered by the Working Group. It was decided that all reviewed DDDs should be kept unchanged, except for remdesivir, lenvatinib, pexidartinib, and ravulizumab where it was decided to:

- Increase the DDD for remdesivir (J05AB16) from 0.1 g to 0.12 g based on a change in the treatment duration to a 5-day regimen.
- Increase the DDD for lenvatinib (L01EX08) from 18 mg to 20 mg as the most prevalent indication was for the treatment of endometrial carcinoma.
- Decrease the DDD for pexidartinib (L01EX15) from 0.8 g to 0.5 g to reflect the change in the recommendation for a reduced dose due to hepatotoxicity.
- Increase the DDD for ravulizumab (L04AJ02) from 58.9 mg, based on intravenous infusion, to 70 mg based on a newly approved subcutaneous injection that was expected to become the preferred administration form.

Other items

Ad hoc Working Group on DDDs for cancer drugs

Professor Vera Vlahović-Palčevski gave an update from the first two meetings of the *ad hoc* Working Group on DDDs for cancer drugs, which was established at M54. Professor Vlahović-Palčevski discussed the decision to start with the medicines included on the WHO Model List of Essential Medicines (EML) with a standard dosing or a weight-based dosing before looking at the substances with a body surface area (BSA)-based dosing. The Working Group noted that there had been discussion of the methodology and whether specific principles were needed to assign DDDs to antineoplastic agents, similar to what had been done for some other ATC groups such as the anti-infectives regarding the definition of "maintenance" dose. The particular challenges in deciding on the appropriate main indication for each substance were also noted. The Working Group considered that before the work was finalised, an assessment could be conducted to see whether the proposed DDDs from the *ad hoc* Working group describe the utilisation pattern for cancer drugs better than grams, the current recommended unit of measurement for measuring consumption of these drugs.

Development of an online platform for ATC/DDD submissions

Dr Antonio Romeo presented a proposal from WHO for the development of an online platform aimed at facilitating communication between the Centre, the WHO, and experts in managing ATC/DDD requests. Dr Romeo discussed that the INN Integrated Data Management Information System (IDMIS) platform would be suitable as a basis for the design of the proposed system. The proposal was well-received by the experts and the Centre.