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National Health Care Institute
Care
Medicinal products

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Our reference
2022020138

Date 13 July 2022
Subject Advisory report on the clustering of combination preparations and ghost clusters in the Medicine Reimbursement System (part 3)

Dear Mr Kuipers,

In your letter of 12 May 2020, your predecessor asked the National Health Care Institute for advice on the clustering of combination preparations and the ghost clusters in the Medicine Reimbursement System, GVS (your reference 1681288-204715-GMT). For this analysis, the National Health Care Institute uses the overviews from the G-standard that were provided at your request by CIBG/Farmatec. Because these involve a large number of medicinal products, we have to give our advice in stages and in parts.

The first part of our advisory report was issued to you on 4 May 2021 (our reference 2021012702).[1] On 13 April 2022, the second part was delivered to you (our reference 2021044712).[2] For the fixed combination of colecalciferol/calcium, the National Health Care Institute issued a separate package advice to you on 9 May 2022.[3]

In the parliamentary letter of 19 April 2022, you indicated your intention to implement the recalculation of the reimbursement limits as of 1 January 2023 (modernising the Medicine Reimbursement System).[4] In response, your ministry asked the National Health Care Institute to bring the handling of the remaining combination preparations forward. After issuing this advisory report (part 3), the National Health Care Institute completed its recommendations about clustering all combination preparations, as requested in your letter of 12 May 2020.[5]

Advisory reports for remaining combination preparations (part 3)
In this advisory report, the National Health Care Institute addresses combination preparations that were not discussed previously. This is about the assessment of

[1] https://www.zorginstituutnederland.nl/werkagenda/publicaties/adviezen/2021/05/04/advies-clustering-van-combinatiepreparaten-en-spookclusters-in-gvs-deel-1

[2] https://www.zorginstituutnederland.nl/werkagenda/publicaties/adviezen/2022/04/13/advies-clustering-van-combinatiepreparaten-en-spookclusters-in-gvs-deel-2

[3] https://www.zorginstituutnederland.nl/publicaties/adviezen/2022/05/09/pakketadvies-vitamine-d

[4] Parliamentary letter 29477-749 of 19 April 2022. Available at: https://www.tweedekamer.nl/downloads/document?id=af98cdb3-fd08-4021-b1b8-82af9cc365dd

[5] National Health Care Institute. 9 May 2022. Additional package advice for vitamin D. Available at: https://www.zorginstituutnederland.nl/publicaties/adviezen/2022/05/09/pakketadvies-vitamine-d

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their interchangeability within the Medicine Reimbursement System. The following drugs are being considered: Augmentin®, Cofact® and combination preparations where one of the substances in the combination preparation is not included in the Medicine Reimbursement System as a monopreparation (see *Appendix 15 to part 1*). In our advisory process, it is assumed that clustering of combination products is possible after the amendments to articles 2.40 and 2.47 of the Health Insurance Regulation.
The substantive discussion of these combination preparations can be found in Appendix 1. The responses of the various parties can be found in Appendix 2.

Based on our assessments, the National Health Care Institute has decided on the following advice:

- *Amoxicillin/clavulanic acid powder for suspension 125/31.5 mg/5 ml* and *250/62.5 mg/5 ml* that were included in paediatric cluster 0J01CRAO K can be moved to cluster 0J01CRAO V. Additionally, the *amoxicillin/clavulanic acid injection powder vial 1000/100 mg* that is included in paediatric cluster 0J01CRAP K can be moved to the 0J01CRAP V cluster. The positioning of other amoxicillin/clavulanic acid combination preparations in the Medicine Reimbursement System can be retained.
- The *prothrombin complex (Cofact®)* can be removed from the Medicine Reimbursement System. This medicinal product is already being funded via an add-on as part of medical care.
- *Insulin lispro/insulin lispro protamine* (Humalog Mix®) is interchangeable with *insulin aspart/insulin aspart protamine* (Novomix®). Both combination preparations are available as suspensions for injection in a *prefilled pen* and as suspensions for injection in a *cartridge*. Given the current structure of the Medicine Reimbursement System, these administration forms are not considered interchangeable. That is why the Humalog Mix® and Novomix® suspensions for injection can be placed in a cluster to be created in List 1A of the Health Insurance Regulation. The Humalog Mix® and Novomix® suspensions in prefilled pens can be placed in a different cluster (also to be created) in List 1A of the Health Insurance Regulation.
- *Sulfamethoxazole/trimethoprim (Bactrimel®) concentrate for infusion fluid* and *sulfametrole/trimethoprim (Rokiprim®) solution for infusion* can be grouped in a cluster to be created in List 1A of the Health Insurance Regulation.[6]
- *Artemether/lumefantrine (Riamet®) tablets of 20/120 mg* can be retained on List 1B. *Atovaquone/proguanil tablets of 250/100 mg* are offered by various manufacturers and can be grouped in a cluster (to be created). *Atovaquone/proguanil hydrochloride film-coated tablets of 62.5/25 mg* are specifically licensed for treating children and are offered by various manufacturers. This dosage of *atovaquone/proguanil* can be grouped in a paediatric cluster (to be created).
- *Flumethasone/clioquinol (Lococorten-Vioform®), dexamethasone/framycetin/gramicidin (Sofradex®), hydrocortisone/oxytetracycline/polymyxin B (Terra Cortil + Polymyxine B®), colistin/bacitracin/hydrocortisone (Bacicoline-B®)* and *fludrocortisone/neomycin/polymyxin B/lidocaine (Panotile®):* the positioning

[6] Furthermore, the National Health Care Institute notes that the medicinal product Lidatrim® (J01EE03) can be removed from the Medicine Reimbursement System. This medicinal product containing sulfametrole/trimethoprim is no longer on the market as of 2008. Lidaprim® is also no longer licensed as a medicinal product in the Netherlands.

of these medicinal products for ear conditions in the Medicine Reimbursement System does not need to be changed; the List 1B status can be retained.

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Looking ahead: planning for ghost clusters

After issuing part 3 (this advisory report), the National Health Care Institute will have answered all your questions about clustering combination preparations. A group of ghost products remains. As indicated previously, we will carry out the assessment of the ghost products in stages. It has not been possible to issue all the advisory reports about this at the same time. We have already made recommendations about a number of these ghost products in part 1 and part 2. The rest will be issued in 2023 and later, as per the planning.

In the advisory report of 13 April 2022, we explained our tiered approach: products that can be classified in the Medicine Reimbursement System for technical reasons were covered in parts 1 and 2 of the advisory report; medicinal products that need a pharmacotherapeutic assessment will be covered later. We prefer groupwise assessments for this. We will explain this approach further at your request.

Each ghost cluster has its own context: the reasons for their existence are diverse. This means that an assessment is needed in each situation of how the ghost product can be positioned in the Medicine Reimbursement System if the ghost cluster will be cancelled. This may need a technical or substantive assessment.

In a technical assessment, the reasons why it is possible to issue an advisory report will be obvious. Such reasons can be that the product is no longer available, that an auxiliary item was added to a medicinal product (combination packages with accessories), that it belongs to the group of medicinal products that were previously transferred to medical care, or that unambiguous cluster criteria have been applied (such as ages for paediatric clusters or administration by injection). We have already issued an advisory report about these ghost clusters as far as possible (see parts 1 and 2 of this advisory report).[1] [2]

When determining the status of the ghost clusters, a substantive assessment may be needed to test whether there is a clinically relevant difference in properties. The weighting of the criterion of 'clinically relevant differences in properties' is primarily based on an assessment of the favourable and unfavourable effects of the medicinal product compared to a different medicinal product in the Medication Reimbursement System. This type of pharmacotherapeutic assessment needs more time. An overview of ghost products that are still waiting for review and may require pharmacotherapeutic assessment can be found in Appendix 3.

The National Health Care Institute also notes that the medicinal product Skilarence® (dimethyl fumarate) is no longer a ghost product. Following a Supreme Court ruling on 21 March 2021, the medicinal product Tecfidera® (also containing dimethyl fumarate) was placed in cluster 0N06XXDO V in December 2021, the same cluster as Skilarence®. The medicinal product Vumerity® was later also placed in this cluster, in January 2022. Now that multiple products have been included in the cluster, it is no longer a ghost cluster, so an advisory report about it is no longer needed.

After issuing this advisory report about the combination preparations, the remaining ghost clusters are next to be tackled. First, we will begin with the assessment of the remaining injections, in the second half of 2022. This covers two insulin preparations (*Insuman® Infusat and Insulatard®*) and three parenteral administration forms (*ceftazidime injection powder, Erythrocine IV infusion powder and Haldol® injection fluid*).

Yours sincerely,

Sjaak Wijma
Chair of the Executive Board

Appendices: 3

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