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To the Minister of Health,
Welfare and Sport
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2021047270

Date 9 May 2022
Regarding Additional package advice Vitamin D

Dear Mr Kuipers,

In the letter of 10 March 2021 (Annex 1), your predecessor requested additional advice from the National Health Care Institute about the reimbursement of vitamin D medicinal products included in the Medicine Reimbursement System (GVS). Research by the Netherlands Institute for Health Services Research (Nivel) has shown that for users of vitamin D medicinal products that were removed from the package since 2019 as they could come at own expense, substitution has taken place for vitamin D medicinal products that are still reimbursed via the basic health care package.¹ As a result, the costs for vitamin D medicinal products have not decreased in recent years, but have even increased. This has created an undesirable effect, undoing the package measure of 2019.

National Health Care Institute advice

The National Health Care Institute recommends that all colecalciferol-containing medicinal products and calcifediol be removed from the GVS. These vitamin D medicinal products, intended for (the prevention of) vitamin D deficiency, can be paid out of pocket by users, and do not meet the package criterion 'essential care to be insured'. With this measure, the costs to be borne by the GVS will decrease by €129 million. This money can be spent more effectively on other essential insured care.

Colecalciferol (vitamin D3) in low dose is available over the counter as a self-care product at the chemist's or supermarket. In addition, there are colecalciferol medicinal products that are prescribed by a physician and delivered through the pharmacy (high dose, mostly weekly or monthly dosage).

At a standard dose of 800 international units (IU; 20 micrograms) per day, vitamin D is available for sale as a self-care product from €7.30 per person per year.² A treatment with colecalciferol on prescription costs on average €79 per person per year. Approximately half of these costs consist of delivery costs for the pharmacy, for the provision of pharmaceutical care. The costs of vitamin D

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Your reference

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Your letter of

10 March 2021

¹ Brabers, A., Heins, M., Meijer, M., et al. Monitor vitamins, minerals and paracetamol from the package: final report. Utrecht: Nivel, 2020. Viewed in June 2021 via: <https://www.nivel.nl/nl/project/monitoring-de-gevolgen-van-verwijdering-van-vitamines-mineralen-en-paracetamol-uit-het>

² Tablets with 10 micrograms (=400 IU) vitamin D are available from €0.01 per day. For a daily dose of 800 IU, the annual costs are €7.30 (price level August 2020). Source: Mul S. Mag het ietsje meer zijn? Vitamin D. Consumer Guide November 2020.

through reimbursement from the GVS is therefore on average ten times higher than that of a comparable product purchased over the counter.

By far the majority of prescription medication users are expected to be able to switch to a daily dosage with a self-care product. People with severe vitamin D deficiency can also use a high-dose prescription product for a short period, a so-called loading dose. The GIP database shows that the costs for the short-term use of the high dose of 100,000 IU are less than €25 per year (without delivery costs).

The National Health Care Institute has considered whether colecalciferol for users with a severe vitamin D deficiency or for long-term users could still remain insured care, subject to further conditions. However, the elaboration of further conditions was not feasible (see 'Considerations in this advisory report').

The National Health Care Institute expects that, if a prescription medication product is chosen, most persons can afford these costs of an average of 79 euros per person per year. For people who cannot afford certain costs, there are municipal and tax schemes from which they can claim.

Background

In our package advice of 2016@, we asked whether vitamin D is essential care to be insured. We concluded that medicinal products for which an equivalent or almost equivalent medicinal product or food supplement is available over the counter should, not be included in the basic insured package anyway (Annex 2). As a result, a number of vitamin D-containing medicinal products in low dose were removed from the GVS as from 1 January 2019. Annex 3 contains background information on vitamin D-containing medicinal products included in the GVS (status 2021).

In our 2016 advice, we warned about possible substitution for vitamin D products that are still in the GVS (high dose). When implementing the advice, the Ministry of Health, Welfare and Sport paid attention to this, but real-life practice is unpredictable. One consequence of substitution is that the savings intended by the package measure have not been achieved. In fact, the costs have even increased. One year after the package measure, the compensation for colecalciferol (only the price of the product itself, i.e. not including the delivery costs) increased from € 19.0 million (2018) to € 27.8 million per year (2019). More information from the GIP database on substitution for reimbursed alternatives and the cost development of colecalciferol in 2016-2020 can be found in Annex 4.

If the most effective products are not chosen when prescribing and delivering medicines, but for products that are still reimbursed, then there is no appropriate care from a collective perspective.

Approach request for advice

In the preparation for this advice, the National Health Care Institute explored various options (see Annexes 5-7). The current proposal (total withdrawal of all colecalciferol-containing medicinal products and calcifediol) is substantiated by an impact analysis (Annex 8). This proposal was submitted to the parties for consultation in March 2022. This advice was then discussed with the ACP at the

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meeting of 8 April 2022 (Annex 9).

The process of the current advisory report, the written responses of the stakeholders and how the National Health Care Institute has dealt with this input can be found in Annexes 10 and 11.

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Considerations in this advisory report

- Colecalciferol (vitamin D3) is available over the counter as a self-care product (food supplement), for example at the chemist's or supermarket. These are lower doses of colecalciferol, up to a daily intake of 75 micrograms (3,000 IU). These lower doses are used daily to prevent vitamin D deficiency or, if there is already a vitamin D shortage, to compensate for it. As a self-care product, vitamin D is for sale from €7.30 per person per year.³
- In addition, there are colecalciferol medicinal products that are prescribed by a physician and delivered through the pharmacy. These prescriptions relate to the higher doses. These high doses can be used to quickly compensate for a severe vitamin D deficiency. These are often weekly or monthly dosages. A treatment with prescription colecalciferol costs an average of €79 per person per year: €37 in costs for the product itself, a further €42 in delivery costs. These delivery costs are necessary for the pharmacy for the provision of pharmaceutical care.
- For the prevention and treatment of a vitamin D deficiency, the usual dosage is 800 IU per day or an equivalent per week (5,600 IU) or month (25,000 IU).⁴ In these cases, it is therefore a choice whether to take a self-care product or a prescription medicine.
- According to the 2021 concept guideline on osteoporosis and fracture prevention, periodic high doses of vitamin D (so-called bolus regimes with more than 60,000 IU per month) are not recommended because they are associated with an increased fall risk.⁵
- In case of proven severe vitamin D deficiency, a loading dose can be used. Depending on the shortage, a loading dose of e.g. 25,000 IU once a week may be used until the calculated deficit is compensated. If blood level monitoring is not possible or desirable, the following loading schedule may be followed: 1,600–2,400 IU per day or 11,200–16,800 IU per week for 8 weeks.⁴ It is therefore also possible to follow a loading schedule using self-care products.
- In the case of proven severe vitamin D deficiency, the higher doses are now mostly used. The GIP database shows that the group using the high dose of 100,000 IE usually does this for a short period of time (which corresponds to a loading dose). The average cost for this group that uses 100,000 IE is less than €25 per person per year (without delivery costs).
- The National Health Care Institute has considered keeping vitamin D in the health care package for the group of people with severe vitamin D deficiency. To limit the reimbursement to this group, further conditions should be determined for this purpose. For example, the reimbursement only applies to people with a calcidiol plasmalevel lower than 50 nanomoles per litre or to the elderly with a calcidiol level lower than 75 nanomole per litre. To demonstrate a vitamin D deficiency, laboratory diagnosis is needed. This will result in

³ Tablets with 10 micrograms (=400 IU) vitamin D are available from €0.01 per day. For a daily dose of 800 IU, the annual costs are €7.30 (checked in August 2020). Source: Mul S. Mag het ietsje meer zijn? Vitamin D. Consumer Guide November 2020.

⁴ Farmacotherapeutisch Kompas. Preparation text for cholecalciferol. Consulted in May 2022 via <https://www.farmacotherapeutischkompas.nl/bladeren/preparaatteksten/c/colecalciferol>

⁵ <https://www.nvr.nl/wp-content/uploads/2021/06/Conceptrichtlijn-Osteoporose-en-fractuurpreventie.pdf>

additional costs for laboratory testing and additional administrative burdens (see Annex 7). Therefore, this option has been found to be not feasible.

- Finally, there is a group of people who use higher doses of vitamin D long-term. For this group, too, the National Health Care Institute has considered maintaining the reimbursement by establishing further conditions for specific indications. This has not been possible, however, because there are too many different indications here, and it is often unclear whether this indication meets the established medical science and medical practice. If a product is applied outside the registered indication and that application is not justified in the guideline of the occupational group, there is no appropriate care.
- Within the registered indication and where there is also a well-founded guideline from the specialist medical occupational group, reimbursement from medical care (intramural) is possible. In specialized centres for patients with cystic fibrosis specialists can, for example, provide these products to their patients on the basis of a diagnosis treatment combination (DBC). The application is then part of (intramural) medical care.
- As explained above, it is possible for the vast majority of users of prescription drugs to return to self-care products. This means significantly reduced costs: instead of an average of €79, vitamin D then costs only €7.30. In case of loading doses, the use is short-term and the costs are also limited (at 100,000 IE to less than €25 per person per year).
- Due to reimbursement from the health care package, the cost of vitamin D is in any case much higher than through self-care, partly due to the additional delivery costs and partly due to the lack of incentives for suppliers to compete with self-care products.
- There will still be people who cannot pay the relatively low costs themselves. There are municipal and tax schemes that can help these people. The National Health Care Institute does not think it is a good solution to make these products available to all insured persons. The fact that such relatively low costs cannot be borne by someone is a social problem and not a problem that needs to be resolved within the health insurance system.
- People should not switch to reimbursed alternatives if the package measure is introduced. To prevent new substitution effects to other vitamin D analogues that are still included in the CVS, the National Health Care Institute also recommends that package measures be taken there. This relates to the following medical products:
 - Calcifediol is a new vitamin D medicinal product that has been included in the GVS since September 2021. Calcifediol has similar applications to colecalciferol. Both products are considered to be interchangeable and are therefore included in the same GVS cluster (0A11CCBO V). If colecalciferol is no longer reimbursed, the package eligibility for calcifediol also expires.
 - Other vitamin D analogues in oral form other than colecalciferol and calcifediol are included in the GVS. These are alfacalcidol, calcitriol and dihydrotachysterol. These products cannot be considered to be interchangeable with colecalciferol or calcifediol and have registered indications other than the prevention or treatment of vitamin D deficiency. It is recommended to keep these products in the GVS, but limit their reimbursement to the registered indications by placing them on List 2 of the Health Insurance Regulation.

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Impact of the package advice on citizens and society

- A total ending of the compensation means that almost 1.5 million Dutch

people will no longer be reimbursed for their vitamin D medicinal product. They can buy vitamin D over the counter, or choose prescription medication but they will have to pay for it themselves.

- The National Health Care Institute realizes that losing reimbursement for a medicinal product can cause concern among current users. Prescribers can reduce or eliminate these concerns by discussing with users what the alternatives are and guiding their patients in making a responsible and affordable choice.
- The National Health Care Institute expects that virtually all people who now use and receive reimbursement for the high doses of vitamin D (administered weekly or monthly) can switch to less expensive products (lower dose self-care products for daily intake, or short-term use of product in a higher dose). To understand any unforeseen effects on, for example, adherence to therapy, particularly in vulnerable groups, the National Health Care Institute will monitor the practical effects of this product withdrawal of reimbursement, in the context of cyclical package management.
- If all medicinal products with colecalciferol and calcifediol are removed from the GVS, the policy is unambiguous. The measure is quite feasible. There are no administrative burdens.

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Financial impact

The overview below shows the financial impact of a withdrawal of colecalciferol-containing medicinal products (source: GIP figures 2020).

Calcifediol (A11CC06) has been included in the GVS since 2021, declaration figures are not yet available.

	Number of users	Costs medicinal product (including VAT)		Costs medicinal product + delivery fee (including VAT)	
		Total costs	Cost pppy#	Total costs	Cost pppy#
Colecalciferol (A11CC05)	914,602	€ 33,636,771	€ 37	€ 71,981,657	€ 79
Calcium/Colecalciferol (A12AX)	553,638	€ 31,194,042	€ 56	€ 55,900,773	€ 101
Alendronic acid/ colecalciferol (M05BB03)*	10,543	€ 800,699	€ 76	€ 1,500,878	€ 142
Alendronic acid/calcium carbonate/ colecalciferol (M05BB05)*	1,829	€ 207,602	€ 114	€ 240,676	€ 132
Total	1,480,612	€ 129 million**			
<p>#pppy= per person per year. *In case of the withdrawal of M05BB03 and M05BB05, the cost of the mono preparation with alendronic acid (M05BA04) will increase. It is estimated that this withdrawal will result in a cost reduction of €0.8 million. For details see the impact analysis (Annex 8). **this amount includes the cost of the alendronic acid mono preparation (see the impact analysis in Annex 8).</p>					

A total withdrawal of all cholecalciferol-containing medicinal products (and calcifediol) from GVS leads to an annual saving of € 129 million on the pharmaceutical budget. If all these people buy vitamin D through self-care over the counter, these costs will be approximately €11 million euros (1.5 million times € 7.30). For society as a whole, this would mean considerable savings. Because almost all current users of prescription medical products can switch to self-care products, we believe that reimbursing these products through the GVS is

not effective. This money can be spent more effectively. Because the practical effects of no longer reimbursing vitamin D cannot be predicted, the total savings on long-term healthcare costs are still uncertain.

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Package advice from the National Health Care Institute

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These are the following (groups of) medicinal products:

- The single products with colecalciferol (ATC code: A11CC05);
- The fixed combination preparations of colecalciferol/calcium (A12AX);
- The fixed combination preparations of alendronic acid/colecalciferol (M05BB03) and alendronic acid/calcium carbonate/colecalciferol (M05BB05);
- The product calcifediol (A11CC06).

In addition, the National Health Care Institute recommends that List 2 of the Health Insurance Regulation be extended with a new component. This point can be worded as follows:

Alfacalcidol, calcitriol and dihydrotachysterol

Condition:

only for an insured person who:

have a medical indication for the medicinal product for which the product is registered under the Medicines Act.

Yours sincerely,

Sjaak Wijma
Chairperson of the Executive Board

Annexes: see separate document with serial number 2021047290