Supplementary notice to the Information Bulletin of 27 January 2021 "Vitamin D for children: use medicines and not food supplements to prevent the risk of overdose"

Context and reported cases

The health authorities have been alerted to several cases of severe hypercalcaemia, sometimes with lithiasis/nephrocalcinosis requiring hospitalisation, in previously healthy infants exposed to vitamin D supplementation in the form of food supplements:

- poison control centres have been called on numerous occasions about children who were given a vitamin D food supplement for several weeks, resulting in an overdose. Doses more than double the recommended dose lead to a risk of hypercalcaemia;
- in 2020, two serious cases of vitamin D poisoning were also reported to ANSES (nutrivigilance) after infants were given food supplements purchased on the internet and whose vitamin D content was particularly high (10,000 IU per drop).

In addition, we have become aware that healthcare professionals or parents sometimes prefer to substitute certain vitamin D medicines with food supplements fortified with this vitamin, because of the preservatives or essential oils these medicines may contain.

Recommended medicines

Review of the leaflet and the pharmaceutical quality

Although food supplements comply with regulations designed to ensure their safety, the leaflets of medicines containing vitamin D guarantee legible information on doses, precautions for use, the risk of adverse effects and overdose. Furthermore, medicines are subject to higher standards than food supplements with regard to the quality of raw materials, manufacturing and dosage control in each manufacturing batch.
We would like to reiterate that medicines are safe, verified, high-quality products that ensure reliable intake and safe use.

Commercial products available

To prevent vitamin D deficiency, the medicines administered in drop form are as follows:

Product	Dose of vitamin D per drop	Other components in the formulation (excipients)
Adrigyl	1 drop = 333 IU of vitamin D3	Butylated hydroxytoluene (BHT), saccharin, sorbic acid, lemon essential oil, unsaturated polyglycolysed glycerides
Deltius	1 drop = 200 IU of vitamin D3	Refined olive oil
ZymaD	1 drop = 300 IU of vitamin D3	Sweet orange essential oil, refined olive oil for injectable preparations, blend of natural tocopherols in alpha, beta, gamma and delta forms

1 international unit (IU) = 0.025 µg

There is also a product, Sterogyl, containing vitamin D2, which is not recommended for use as a first-line treatment for children.

Focus on the components

The vitamin D contained in medicines, as in food supplements, is of natural animal (lanolin derived from ruminant wool) or vegetable origin.

The other components in the medicines comply with the safety standards currently in force:

- butylated hydroxytoluene (BHT) is an antioxidant used as a preservative. It is found in food. In 2012, the acceptable daily intake (ADI) was set by the European Food Safety Authority (EFSA) at 0.25 mg/kg/day[1] on the basis of carcinogenesis and reprotoxicity studies. For example, for a newborn weighing 4 kg, the amount of BHT per dose contained in Adrigyl is about 60 times less than the ADI (this amount is 150 times less than the ADI for a child weighing 10 kg).
  In 2016, after analysing all the data on BHT, ANSES concluded that it was not possible to confirm whether BHT had endocrine-disrupting properties[2]. BHT is currently being assessed by the European Chemicals Agency (ECHA) as part of the REACh process (Registration, Evaluation and Authorisation of Chemicals).
- sweet orange and lemon essential oils are included in the Community list of flavourings and source materials approved for use in and on foods[3];
- vitamin E (tocopherol) is a commonly used antioxidant, especially in food.

1 EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS); Scientific Opinion on the reevaluation of Butylated hydroxytoluene BHT (E 321) as a food additive. EFSA Journal 2012;10(3):2588. [43 pp.] doi:10.2903/j.efsa.2012.2588. Available online: www.efsa.europa.eu/efsajournal.htm

2 https://www.anses.fr/fr/system/files/REACH2016RE0001.pdf

3 Annex I of Regulation (EC) No 1334/2008 and amendments