COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Trederol 5,000 IU, 10,000 IU, 20,000 IU film-coated tablets (cholecalciferol concentrate)

NL/H/5374/001-003/DC

Date: 5 January 2023

This module reflects the scientific discussion for the approval of Trederol 5,000 IU, 10,000 IU, 20,000 IU film-coated tablets. The procedure was finalised at 16 June 2022. For information on changes after this date please refer to the 'steps taken after finalisation' at the end of this PAR.

List of abbreviations

ASMF	Active Substance Master File
CEP	Certificate of Suitability to the monographs of the European Pharmacopoeia
CHMP	Committee for Medicinal Products for Human Use
CMD(h)	Coordination group for Mutual recognition and Decentralised procedure for human medicinal products
CMS	Concerned Member State
EDMF	European Drug Master File
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
ERA	Environmental Risk Assessment
FDA	Food and Drug Administration (of the United States of America)
ICH	International Conference of Harmonisation
MAH	Marketing Authorisation Holder
Ph.Eur.	European Pharmacopoeia
PL	Package Leaflet
RH	Relative Humidity
RMP	Risk Management Plan
SmPC	Summary of Product Characteristics
TSE	Transmissible Spongiform Encephalopathy
WHO	World Health Organisation

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have granted a marketing authorisation for Trederol 5,000 IU, 10,000 IU, 20,000 IU film-coated tablets, from Wörwag Pharma GmbH & Co. KG.

The product is indicated for initial treatment of clinically relevant vitamin D deficiency (serum level < 25 nmol/L (10 ng/mL)) in adults.

A comprehensive description of the indication and posology is given in the SmPC.

The marketing authorisation has been granted via a decentralised procedure under Article 10a of Directive 2001/83/EC (well-established use (WEU) application). Well-established medicinal use needs to be demonstrated for the active substance of the medicinal product for at least 10 years in the specific therapeutic area. In a WEU application, results of non-clinical and clinical trials are replaced by detailed references to published scientific literature. Therefore, no clinical studies have been performed by the marked authorisation holder (MAH) and instead, bibliographical data are submitted.

Cholecalciferol as active substance in medicinal products have been in well-established medicinal use within the Community for more than ten years, with recognised efficacy and an acceptable level of safety.

The concerned member states (CMS) involved in this procedure were Austria, Bulgaria, Czechia, Germany, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Slovakia and Spain.

Indication

Other indications which were initially applied for included “Prevention of vitamin D deficiency in adults with an identified risk” and “As an adjunctive therapy for osteoporosis in patients with vitamin D deficiency or at risk of vitamin D insufficiency”. Following comments of the involved member states, these two indications were dropped during the application procedure.

Scientific advice

Scientific advice was sought prior to this application with the Medical Evaluation Board in the Netherlands on 5 August 2019.

II. QUALITY ASPECTS

II.1 Introduction

- Trederol of 5,000 IU is a round film-coated tablet, white to slightly yellow, embossed with logo “5”. Each tablet contains 125 micrograms cholecalciferol (Vitamin D3, corresponding to 5,000 IU as cholecalciferol-concentrate powder form).

- Trederol of 10,000 IU is an elongated film-coated tablet, white to slightly yellow, embossed with logo "10". Each tablet contains 250 micrograms cholecalciferol (Vitamin D3, corresponding to 10,000 IU as cholecalciferol-concentrate powder form).
- Trederol of 20,000 IU is an oval film-coated tablet, white to slightly yellow, with a double score line which is to facilitate breaking for ease of swallowing and not to divide into equal doses. Each tablet contains 500 micrograms cholecalciferol (Vitamin D3, corresponding to 20,000 IU as cholecalciferol-concentrate powder form).

The excipients are:
Tablet core – sodium ascorbate (E301), all-rac-alpha-tocopherol, starch sodium octenyl succinate (E1450), sucrose, medium chain triglycerides, colloidal anhydrous silica (E551), croscarmellose sodium (E468), microcrystalline cellulose (PH102, E460) and magnesium stearate (E470b);
Tablet coating – white Opadry PVA (contains: polyvinyl alcohol (E1203), titanium dioxide (E171), macrogol 3350 and talc (E553B)).

The tablets are packed in PVC/PVDC-Al blisters. The excipients and packaging are usual for this type of dosage form.

The cores of the three tablet strengths are fully dose proportional.

II.2 Drug Substance

The active substance is cholecalciferol concentrate (powder form), i.e. Dry Vitamin D3 100 SD/S with cholecalciferol as active ingredient (with all-rac-α-tocopherol and sodium ascorbate), an established active substance described in the European Pharmacopoeia (Ph.Eur.). It is a crystalline powder and is practically insoluble in water. Polymorphism is not applicable for the spray dried drug substance mixture.

The CEP procedure is used for the active substance. Under the official Certification Procedures of the EDQM of the Council of Europe, manufacturers or suppliers of substances for pharmaceutical use can apply for a certificate of suitability concerning the control of the chemical purity and microbiological quality of their substance according to the corresponding specific monograph, or the evaluation of reduction of Transmissible Spongiform Encephalopathy (TSE) risk, according to the general monograph, or both. This procedure is meant to ensure that the quality of substances is guaranteed and that these substances comply with the Ph.Eur.

Manufacturing process
A CEP has been submitted; therefore no details on the manufacturing process have been included.

Quality control of drug substance
The active substance specification is considered adequate to control the quality and meets the requirements of the monograph in the Ph.Eur. for cholecalciferol concentrate (powder

form) and the CEP, with additional requirements for microbiological purity. Batch analytical data demonstrating compliance with the specifications have been provided for three batches.

Stability of drug substance

The active substance is stable for 24 months when stored under the stated conditions. Assessment thereof was part of granting the CEP and has been granted by the EDQM.

II.3 Medicinal Product

Pharmaceutical development

This is a well-established use application. No bioequivalence or clinical studies have been performed. In order to support the well-established use claim, comparative dissolution data have been provided for the test product and two reference products at three different pH's and the quality control (QC) medium. Also, full dissolution profiles in the QC medium have been provided for the test product for all three strengths. The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

Manufacturing process

The manufacturing consists of the following steps: weighing, homogenisation, tablet compression, film-coating and packaging. The process has been validated according to relevant European guidelines. The product is manufactured using conventional manufacturing techniques. However, as cholecalciferol comprises only 0.083% of the tablet core weight, the drug product is considered a specialised pharmaceutical dose form. Process validation data on the product has been presented for three full scaled batches of each strength. Process validation for the packaging and leak test will be performed for the first three commercial batches.

Control of excipients

All excipients comply with the Ph.Eur. requirements, except Opadry (the film coating), for which an in-house specification is provided. These specifications are acceptable.

Quality control of drug product

The finished product specifications are adequate to control the relevant parameters for the dosage form. The specification is based on the monograph in the Ph.Eur and includes tests for appearance, dimensions, water content, identification, assay of vitamin D3, assay of alpha-tocopherol, impurities, dissolution, uniformity of mass, uniformity of dosage units, and microbiological purity. The release and shelf life limits are mostly the same, except for water content, assay of vitamin D3, assay of alpha-tocopherol and total impurities. Limits in the specification have been justified and are considered appropriate for adequate quality control of the product. The analytical methods have been adequately described and validated. Batch analytical data from three batches per strength from the proposed production site have been provided, demonstrating compliance with the specification.

Stability of drug product

Stability data on the product have been provided for three production scale batches of each strength. The batches are stored at 25°C/60% RH (18 months), 30°C/75% RH (12 months) and 40°C/75% RH (6 months). The conditions used in the stability studies are according to the ICH stability guideline. The batches were stored in PVC/PVDC-Al blisters and for each strength two batches were packaged in bulk packaging, i.e. transparent polyethylene bags (LDPE), packed in a black bag, desiccant, packed in an HDPE container. Photostability studies were performed in accordance with ICH recommendations and showed that the product is stable when exposed to light.

The drug product is unstable at accelerated storage conditions. At the intermediate and long term condition, a significant decrease in dissolution and assay was observed. Hence, extrapolation is not considered appropriate and the shelf life should be based on the long term stability data. On basis of the data submitted, a shelf life was granted of 18 months. The labelled storage conditions are: store below 30°C. The bulk is considered stable for a period of 6 months at 25°C/60% RH.

Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies

Certificates of suitability issued by the EDQM have been provided for an animal product used in the manufacture of the drug substance and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via medicinal products has been satisfactorily demonstrated.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Based on the submitted dossier, the member states consider that Trederol has a proven chemical-pharmaceutical quality. Sufficient controls have been laid down for the active substance and finished product. No post-approval commitments were made.

III. NON-CLINICAL ASPECTS

III.1 Pharmacology

The MAH provided a literature overview on the pharmacodynamic effects of cholecalciferol. The primary pharmacodynamic effect of cholecalciferol is its absorption into the bloodstream and subsequent hydroxylation to form calcidiol. A substantial amount of clinical literature regarding this process is available. The lack of non-clinical data is accepted because of the extensive clinical experience with the product and its well-established use. Further primary pharmacodynamic effects of cholecalciferol are related to the development and maintenance of bones and muscles. Vitamin D promotes the development of bone by stimulating the osteogenic differentiation of mesenchymal stem cells. In addition, calcidiol and calcitriol regulate bone remodelling and mineralisation by maintaining plasma calcium levels and phosphorus concentrations. Studies have shown effects on diphosphate uptake by

osteoporotic bones by cholecalciferol, and calcitriol supplementation may prevent cellular processes of osteoporosis. In guinea pigs, a single high dose of cholecalciferol stimulated fracture healing. Bone quality was also found to be improved by alfacalcidol, a prodrug of calcitriol, which enhanced collagen deposition and the maturation and stability of collagen in osteoporotic bones. A highly potent analogue of calcitriol stimulated osteoblast-mediated bone calcium mobilization and promoted osteoblast-mediated osteoclast formation *in vitro*, supporting indirectly the importance of vitamin D for bone health.

Table 1. Synonyms of compounds

Term used in this document	*Synonym*
Calcidiol	25(OH)D3; Calcifediol
Calcitriol	1,25 $(OH)_2$D3; 1α,25-dihydroxyvitamin D
Cholecalciferol	Vitamin D3; Calciol

Several studies have investigated the effects of vitamin D on muscle tissue. A study on skeletal muscle derived satellite cells showed that calcitriol promotes myotube formation and induces the expression of pro-myogenic skeletal muscle markers, indicating that vitamin D promotes muscle regeneration. In rats, vitamin D deficiency was associated with a 40% reduction in muscle protein fractional synthesis rate, which was restored upon dietary vitamin D supplementation with cholecalciferol. Further, calcitriol has been shown to regulate the internalization of vitamin D binding protein (DBP) by skeletal muscle cells *in vitro,* supporting the role of skeletal muscle in the maintenance of vitamin D levels.

Secondary pharmacodynamic effects include the control of vitamin D homeostasis in the kidneys by regulation of the metabolism of calcitriol. In addition, cholecalciferol may have protective effects on the kidneys, which have been demonstrated in studies on cholecalciferol supplementation in animals with induced kidney damage. Vitamin D deficiency results in parathyroid hyperplasia and increased parathyroid hormone (PTH) synthesis and secretion. Calcitriol administration inhibits PTH synthesis and parathyroid cell growth, and may also act to increase the sensitivity of the parathyroid gland to calcium. Calcitriol can suppress the adaptive immune system, which appeared beneficial in suppressing autoimmunity and slowing down inflammatory diseases in experimental models. Studies have shown vitamin D to act upon hormonal regulation, production of insulin and protein homeostasis. Furthermore, vitamin D has effects on cell differentiation and proliferation, with potential impact on tumour suppression, as well as positive effects on the cardiovascular system and oxidative stress and effects against viral infections.

Formal safety pharmacology studies according to ICH S7A/B have not been performed. The accepted justification is based on the fact that cholecalciferol is a naturally occurring intermediary metabolite in humans. The MAH reported a small number of non-clinical data on pharmacodynamic drug-drug interactions, these were without clinical evidence and described to not have a negative impact.

The non-clinical literature overview presents data on cholecalciferol. The primary, secondary and safety pharmacology have been adequately discussed based on available literature for the purpose of a well-established use application.

III.2 Pharmacokinetics

The information provided by the MAH on the absorption of cholecalciferol is considered limited. Non-clinical data on cholecalciferol absorption is scarce since most data have been collected in clinical studies. One study investigated the intestinal absorption of cholecalciferol and its active metabolite, calcitriol through intact jejunal segments of rats. It was demonstrated that intracellular binding proteins may be involved in the transport of cholecalciferol and calcitriol through rat enterocytes. Vitamin D and its metabolites bind in the serum with high affinity to DBP and distributes to plasma, ileum, kidney and bones.

Vitamin D is metabolised in three distinct steps. The first step is cytochrome P450 enzymes converting cholecalciferol to calcidiol in the liver. The second step is the conversion of calcidiol to calcitriol in the kidney through CYP27B1 hydroxylase. Finally, this is followed by hydroxylation through the action of mitochondrial CYP24A1 located in several different tissue types of the body leading to inactivation, the formation of end products and excretion. The submitted literature describes that cholecalciferol is eliminated mainly through the bile or is excreted in urine after conversion into water-soluble metabolites. Metabolites that are transformed into less polar components can be reabsorbed in the intestine after excretion in the bile (enterohepatic recirculation).

The available non-clinical literature suggests that the metabolism of cholecalciferol can be influenced by interactions with anticonvulsants, cephalosporins, adefovir, thiazides, glucocorticoids, cholestyramine, buspirone, actinomycin and clotrimazole. Interactions of cholecalciferol with anticonvulsants, thiazides, glucocorticoids and actinomycin are reflected in the SmPC.

The submitted literature data are adequate to assess the non-clinical absorption, distribution, metabolism and elimination of cholecalciferol for the purpose of a well-established use application.

III.3 Toxicology

The lowest possible toxic dose in humans was determined to be 39 mg/kg, whereas Trederol 5,000 IU, 10,000 IU, 20,000 IU film-coated tablets contain 125, 250 or 500 µg of Vitamin D3, respectively. Hence, a very large amount of tablets would have to be taken to reach (fatal) intoxication. Lethal cholecalciferol doses in animal species were not considered informative for the safety assessment because of how high they were. Toxicity was tested via repeated intravenous administration of calcitriol (not cholecalciferol) to rats, dogs and other canines, which resulted in hypercalcaemia, among other effects. The MAH indicates that the production of calcitriol is a well-regulated process *in vivo*, which is largely independent of the cholecalciferol doses given. As such, cholecalciferol cannot cause blood calcitriol concentrations to rise to such toxic values.

The overall evidence on genotoxicity indicates that cholecalciferol is not genotoxic. Limited literature studies on carcinogenicity have been reported. Evidence exists for carcinogenicity from rat studies where cases of phaechromocytoma (a usually benign tumour of cells in the

adrenal gland) were observed. However, the MAH indicates that this occurred with doses of cholecalciferol that are much higher than those that will be likely with the use of the current product. This is acknowledged.

Studies in rats and rabbits given calcitriol suggested adverse effects on reproductive or developmental events at clinically relevant doses. However, the MAH indicates that *in vivo* calcitriol production from cholecalciferol is a highly regulated process which is not linearly related to cholecalciferol or calcidiol concentrations. Hence, these effects observed after application of calcitriol to animals are not considered to be relevant to Trederol tablets. This is acknowledged.

No literature studies on local tolerance were submitted by the MAH. Considering that cholecalciferol will be administered by oral route, this is acceptable (see Guideline on non-clinical local tolerance testing of medicinal products, EMA/CHMP/SWP/2145/2000 Rev. 1, Corr. 1*).

The MAH evaluated all excipients present in the product, which are either naturally occurring substances or have been granted a "Generally Recognized as Safe" (GRAS) status by the FDA and are considered not to impact the safety of the product. As these substances are commonly used excipients. An evaluation on the presence of macrogol 3350 in the product indicated that the levels in the maximum daily doses of the tablets are far below the acceptable daily intake as proposed by the WHO.

The provided non-clinical overview on toxicology is adequate for the purpose of a well-established use application.

III.4 Ecotoxicity/environmental risk assessment (ERA)

The active substance is a natural substance, the use of which will not alter the concentration or distribution of the substance in the environment. Therefore, Trederol 5,000 IU, 10,000 IU, 20,000 IU film-coated tablets is not expected to pose a risk to the environment.

III.5 Discussion on the non-clinical aspects

This product has been granted a market authorisation for well-established use. A non-clinical overview on the pharmacology, pharmacokinetics and toxicology has been provided, which is based on up-to-date and adequate scientific literature. The overview justifies why there is no need to generate additional non-clinical pharmacology, pharmacokinetics and toxicology data. Therefore, the member states agreed that no further non-clinical studies are required.

IV. CLINICAL ASPECTS

IV.1 Introduction

Cholecalciferol is a well-known active substance with established efficacy and tolerability. A clinical overview has been provided, which is based on scientific literature regarding pharmacokinetics (absorption, metabolism and excretion of vitamin D and its metabolites, and its effects in special populations), pharmacodynamics (drug interactions and effects of vitamin D on molecular levels), efficacy (dosing and effects of vitamin D in the body) and safety (risks of toxicity and adverse events). The submitted information has been linked to clinical studies and is considered to be adequate. The overview justifies why there is no need to generate additional clinical data and the member states agreed that no further clinical studies were required.

IV.2 Pharmacokinetics

The pharmacokinetics of cholecalciferol have been widely studied and are well-known. Cholecalciferol (vitamin D3) from nutritional sources is actively absorbed from the gastro-intestinal tract in the presence of dietary lipids and bile acids. At high doses, cholecalciferol is absorbed by passive diffusion. Bile is important for a good absorption of cholecalciferol, specifically deoxycholic acid. Being a lipid-soluble compound, intake of a fat meal seems to facilitate a good absorption of cholecalciferol and therefore intake with food is recommended. Absorbed cholecalciferol circulates in the blood in association with vitamin D-binding protein (DBP), a specific alpha-globulin. Cholecalciferol is stored in fat depots. It is a lipophilic compound which explains its adipose tissue distribution and its slow turnover in the body (the half-life is approximately 2 months).

Cholecalciferol is metabolised by microsomal hydroxylase to form calcidiol (25-hydroxycolecalciferol), the primary storage form of vitamin D3. Calcidiol undergoes a secondary hydroxylation within the kidney to form the predominant active metabolite calcitriol (1,25-hydroxycolecalciferol). Calcidiol is the most abundant cholecalciferol metabolite in circulation, where approximately 90% is bound to DBP.

In the kidney, the calcidiol–DBP complex is filtered through the glomerulus into the proximal tubule and then is taken up by the proximal tubular cell via the cell surface receptors megalin and cubilin. Within the proximal tubular cell, enzyme CYP27B1 can hydrolyse calcidiol into calcitriol. Calcitriol is delivered to target tissues bound to DBP, then binds to the vitamin D receptor to regulate a wide variety of genes. Catabolism is an essential component of vitamin D metabolism. Calcidiol and calcitriol undergo catabolism via multiple side chain hydroxylations to become more polar metabolites, which subsequently are excreted in the urine and the feces. CYP24A1 is capable of catalysing all of the hydroxylation steps in the catabolism of both calcidiol and calcitriol. Another P450 enzyme, CYP3A4, also plays a role in vitamin D catabolism. CYP3A4 catabolizes calcidiol and calcitriol in a manner similar to CYP24A1, with production of 1,24,25-trihydroxyvitamin D and 24,25-dihydroxyvitamin D.

The primary route of cholecalciferol excretion is the bile; only a small percentage is found in urine. Metabolites destined for excretion are calcitroic acid and 24,25-OH2D3. Elimination half-life for cholecalciferol is about 4,5 days, for calcidiol it is approximately 15 days, for calcitriol it is 1 to 5 hours.

There appears to be no age-related effect and no gender effect on the pharmacokinetics. Patients with chronic kidney disease are at a higher risk of vitamin D deficiency due to either renal losses or decreased synthesis of calcitriol. In patients with chronic liver disease, absorption of vitamin D is reduced, related to the severity of the disease and limited bile secretion. Considering different SmPCs, there are no specific dose recommendations regarding dosing for supplementation of vitamin D in patients with hepatic impairment. An increased BMI is associated with greater doses required to achieve the same serum calcidiol concentrations. The discussed interactions are known from other SmPCs of vitamin D products.

It is expected that the bioavailability of cholecalciferol from the MAH's formulation will be in the range of the formulations mentioned in literature, based upon the comparison of the excipients' solubility and dissolution data. Bridging is sufficiently supported.

The literature supported pharmacokinetics, efficacy and safety. The clinical overview discussed the pharmacokinetics of cholecalciferol sufficiently.

IV.3 Pharmacodynamics

The MAH has provided a brief overview of general pharmacodynamic properties of vitamin D. Section 4.5 of the SmPC reflects the interactions of vitamin D with other medicinal products, including: antiepileptic medicinal products and barbiturates, glucocorticoids, ion exchange resins, laxatives and orlistat, actinomycin and imidazole, rifampicin, isoniazid, thiazide diuretics and phosphate. The effects of vitamin D on bone mineral density, calcium and phosphate and its pharmacodynamics are considered sufficiently described.

IV.4 Clinical efficacy

The MAH has presented literature data of efficacy studies using different vitamin D doses. The therapeutic indication is initial treatment of clinically relevant vitamin D deficiency (serum level <25 nmol/L (10 ng/mL)) in adults. The MAH amended their original definition of vitamin D deficiency to be in alignment with registered SmPCs. For the indication, appropriate doses to be considered are in the range of 800-4,000 IU/day as also indicated for instance in the Dutch SmPCs of the Benferol (NL/H/3500/001-004) and Will Pharma (NL/H/2963/001-006) products. The initially proposed loading dose for Trederol was 20,000 IU per week for a duration of 8-12 weeks (leading to a loading dose of 160,000 to 240,000 IU). Since 2012, a 100,000 IU loading dose for the initial treatment of vitamin D deficiency has been registered in the Netherlands (DE/H/2903/001/DC). Since approval of the 100,000 IU loading dose, no new safety concerns were raised for this. Therefore, the loading dose regimen was amended to 4-5 weeks instead of 8-12 weeks. A dose of 20,000 IU per week was considered acceptable. Other proposed indications (prevention of vitamin D deficiency

and treatment of osteoporosis) were dropped. The MAH restricted the indication to initial treatment and aligned it with the approved products.

IV.5 Clinical safety

The safety profile of cholecalciferol is well-known. In general, vitamin D is well tolerated. However, there is a risk for toxicity with higher dosages, for which hypercalcaemia and hypercalciuria are the main adverse events. Most adverse events are reported in health care practice for gastrointestinal disorders, skin and subcutaneous disorders and metabolism and nutrition disorders. The safety profile appears to be generally in line with findings of other vitamin D medicinal products. The precautions of use in other special populations are described sufficiently in the SmPC.

IV.6 Risk Management Plan

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Trederol.

Table 2. Summary table of safety concerns as approved in RMP

Important identified risks	None
Important potential risks	None
Missing information	None

The member states agreed that routine pharmacovigilance activities and routine risk minimisation measures are sufficient for the risks and areas of missing information.

IV.7 Discussion on the clinical aspects

The clinical benefit of treating vitamin D deficiency is well known. The bibliographic data submitted showed vitamin D deficiency was resolved or improved as indicated by increases in serum calcidiol levels. The MAH submitted and discussed several studies to support the initial treatment of vitamin D deficiency. No new clinical studies were conducted. The proposed indication is widely used and known and sufficiently discussed in the provided literature and therefore acceptable.

V. USER CONSULTATION

The package leaflet (PL) has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PL was English. The test consisted of a pilot test with five participants, followed by two rounds with ten participants each. The questions covered the following areas sufficiently: traceability, comprehensibility and applicability. The results

show that the PL meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

Trederol 5,000 IU, 10,000 IU, 20,000 IU film-coated tablets have a proven chemical-pharmaceutical quality. The products have an adequate efficacy and safety profile and are considered widely established.

The Board followed the advice of the assessors.

There was no discussion in the CMD(h). Agreement between member states was reached during a written procedure. The member states, on the basis of the data submitted, have granted a marketing authorisation. The decentralised procedure was finalised with a positive outcome on 16 June 2022.

STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number*	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
N/A	N/A	N/A	N/A	N/A	N/A

LITERATURE REFERENCES

acis Arzneimittel GmbH (2018): Fachinformation: Colecalciferol acis 20.000 I.E. Weichkapseln. Lil- Dagover-Ring 7 82031 Grünwald.

Adams, John S.; Hewison, Martin (2010): Update in vitamin D. In The Journal of clinical endocrinology and metabolism 95 (2), pp. 471–478. DOI: 10.1210/jc.2009-1773.

Aghajafari, Fariba; Nagulesapillai, Tharsiya; Ronksley, Paul E.; Tough, Suzanne C.; O'Beirne, Maeve; Rabi, Doreen M. (2013): Association between maternal serum 25-hydroxyvitamin D level and pregnancy and neonatal outcomes: systematic review and meta-analysis of observational studies. In BMJ 346, f1169. DOI: 10.1136/bmj.f1169.

Al-Daghri, Nasser M.; Al-Saleh, Yousef; Aljohani, Naji; Sulimani, Riad; Al-Othman, Abdulaziz M.; Alfawaz, Hanan et al. (2017): Vitamin D status correction in Saudi Arabia: an experts' consensus under the auspices of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis, and Musculoskeletal Diseases (ESCEO). In Archives of osteoporosis 12 (1), p. 1. DOI: 10.1007/s11657-016- 0295-y.

Aloia, John F.; Katumuluwa, Subhashini; Stolberg, Alexandra; Usera, Gianina; Mikhail, Mageda; Hoofnagle, Andrew N.; Islam, Shahidul (2018): Safety of calcium and vitamin D supplements, a randomized controlled trial. In Clin. Endocrinol. (Oxf) 89 (6), pp. 742–749. DOI: 10.1111/cen.13848.

Alshahawey, Mona; El Borolossy, Radwa; El Wakeel, Lamia; Elsaid, Tamer; Sabri, Nagwa Ali (2021): The impact of cholecalciferol on markers of vascular calcification in hemodialysis patients: A randomized placebo controlled study. In Nutrition, metabolism, and cardiovascular diseases : NMCD 31 (2), pp. 626– 633. DOI: 10.1016/j.numecd.2020.09.014.

Alshahrani, Fahad; Aljohani, Naji (2013): Vitamin D: deficiency, sufficiency and toxicity. In Nutrients 5 (9), pp. 3605–3616. DOI: 10.3390/nu5093605.

Alvarez, Jessica; Wasse, Haimanot; Tangpricha, Vin (2012): Vitamin D supplementation in pre-dialysis chronic kidney disease: A systematic review. In Dermato-endocrinology 4 (2), pp. 118–127. DOI: 10.4161/derm.20014.

Alzaman, Naweed S.; Dawson-Hughes, Bess; Nelson, Jason; D'Alessio, David; Pittas, Anastassios G. (2016): Vitamin D status of black and white Americans and changes in vitamin D metabolites after varied doses of vitamin D supplementation. In Am. J. Clin. Nutr. 104 (1), pp. 205–214. DOI: 10.3945/ajcn.115.129478.

American Geriatrics Society Workgroup (2014): American Geriatrics Society Workgroup on Vitamin D. Supplementation for Older Adults: Consensus Statement on vitamin D for Prevention of Falls and Their Consequences Recommendations abstracted from the American Geriatrics Society Consensus Statement on vitamin D for Prevention of Falls and Their Consequences. In J. Am. Geriatr. Soc. 62 (1), pp. 147–152. DOI: 10.1111/jgs.12631.

Amrein, K.; McNally, J. D.; Dobnig, H.; Pieber, T. R. (2016): High-dose cholecalciferol in critically ill patients with liver cirrhosis. In Journal of internal medicine 279 (3), pp. 309–310. DOI: 10.1111/joim.12457.

Appel, Lawrence J.; Michos, Erin D.; Mitchell, Christine M.; Blackford, Amanda L.; Sternberg, Alice L.; Miller, Edgar R. et al. (2021): The Effects of Four Doses of Vitamin D Supplements on Falls in Older Adults: A Response-Adaptive, Randomized Clinical Trial. In Annals of internal medicine 174 (2), pp. 145–156. DOI: 10.7326/M20-3812.

Armas, Laura A. G.; Hollis, Bruce W.; Heaney, Robert P. (2004): Vitamin D2 is much less effective than vitamin D3 in humans. In The Journal of clinical endocrinology and metabolism 89 (11), pp. 5387–5391. DOI: 10.1210/jc.2004-0360.

Arroyo-Maya, Izlia J.; McClements, David Julian (2016): Application of ITC in foods: A powerful tool for understanding the gastrointestinal fate of lipophilic compounds. In Biochim. Biophys. Acta 1860 (5), pp. 1026–1035. DOI: 10.1016/j.bbagen.2015.10.001.

Auguste, Bourne L.; Avila-Casado, Carmen; Bargman, Joanne M. (2019): Use of vitamin D drops leading to kidney failure in a 54-year-old man. In CMAJ 191 (14), E390-E394. DOI: 10.1503/cmaj.180465.

Avenell, Alison; Gillespie, William J.; Gillespie, Lesley D.; O'Connell, Dianne (2009): Vitamin D and vitamin D analogues for preventing fractures associated with involutional and post-menopausal osteoporosis. In Cochrane Database Syst. Rev. (2), CD000227. DOI: 10.1002/14651858.CD000227.pub3.

Avenell, Alison; Mak, Jenson C. S.; O'Connell, Dianne (2014): Vitamin D and vitamin D analogues for preventing fractures in post-menopausal women and older men. In Cochrane Database Syst. Rev. (4), CD000227. DOI: 10.1002/14651858.CD000227.pub4.

Baughman, R. P.; Janovcik, J.; Ray, M.; Sweiss, N.; Lower, E. E. (2013): Calcium and vitamin D metabolism in sarcoidosis. In Sarcoidosis, vasculitis, and diffuse lung diseases : official journal of WASOG 30 (2), pp. 113–120.

Baughman, Robert P.; Lower, Elyse E. (2014): Goldilocks, vitamin D and sarcoidosis. In Arthritis research & therapy 16 (3), p. 111. DOI: 10.1186/ar4568.

Beaudart, Charlotte; Buckinx, Fanny; Rabenda, Véronique; Gillain, Sophie; Cavalier, Etienne; Slomian, Justine et al. (2014): The effects of vitamin D on skeletal muscle strength, muscle mass, and muscle power: a systematic review and meta-analysis of randomized controlled trials. In The Journal of clinical endocrinology and metabolism 99 (11), pp. 4336–4345. DOI: 10.1210/jc.2014-1742.

Bergman, Gert J. D.; Fan, Tao; McFetridge, Jeffrey T.; Sen, Shuvayu S. (2010): Efficacy of vitamin D3 supplementation in preventing fractures in elderly women: a meta-analysis. In Current medical research and opinion 26 (5), pp. 1193–1201. DOI: 10.1185/03007991003659814.

BfArM-Mustertext: Colecalciferol Tabletten. Wortlaut der für die Fachinformation vorgesehenen Angaben (FI280009), checked on 4/9/2001.

Bhan, Ishir; Burnett-Bowie, Sherri-Ann M.; Ye, Jun; Tonelli, Marcello; Thadhani, Ravi (2010): Clinical measures identify vitamin D deficiency in dialysis. In Clinical journal of the American Society of Nephrology : CJASN 5 (3), pp. 460–467. DOI: 10.2215/CJN.06440909.

Bikle, Daniel (2000): Endotext Vitamin D: Production, Metabolism, and Mechanisms of Action. Edited by Kenneth R. Feingold, Bradley Anawalt, Alison Boyce, George Chrousos, Kathleen Dungan, Ashley Grossman et al. South Dartmouth (MA).

Billington, E. O.; Burt, L. A.; Plett, R.; Rose, M. S.; Boyd, S. K.; Hanley, D. A. (2020a): Effect of high-dose vitamin D supplementation on peripheral arterial calcification: secondary analysis of a randomized controlled trial. In Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA 31 (11), pp. 2141–2150. DOI: 10.1007/s00198-020-05500-2.

Billington, E. O.; La Burt; Rose, M. S.; Davison, E. M.; Gaudet, S.; Kan, M. et al. (2020b): Safety of High- Dose Vitamin D Supplementation: Secondary Analysis of a Randomized Controlled Trial. In J Clin Endocrinol Metab 105 (4), pp. 1261–1273. DOI: 10.1210/clinem/dgz212.

Bischoff-Ferrari, H. A.; Dawson-Hughes, B.; Orav, E. J.; Staehelin, H. B.; Meyer, O. W.; Theiler, R. et al. (2016): Monthly High-Dose Vitamin D Treatment for the Prevention of Functional Decline: A Randomized Clinical Trial. In JAMA internal medicine 176 (2), pp. 175–183. DOI: 10.1001/jamainternmed.2015.7148.

Bischoff-Ferrari, Heike A.; Fischer, Karina; Orav, Endel J.; Dawson-Hughes, Bess; Meyer, Ursina; Chocano-Bedoya, Patricia O. et al. (2017): Statin Use and 25-Hydroxyvitamin D Blood Level Response to Vitamin D Treatment of Older Adults. In J. Am. Geriatr. Soc. 65 (6), pp. 1267–1273. DOI: 10.1111/jgs.14784.

Bischoff-Ferrari, Heike A.; Giovannucci, Edward; Willett, Walter C.; Dietrich, Thomas; Dawson-Hughes, Bess (2006): Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. In Am. J. Clin. Nutr. 84 (1), pp. 18–28. DOI: 10.1093/ajcn/84.1.18.

Bjelakovic, Goran; Nikolova, Dimitrinka; Bjelakovic, Marko; Gluud, Christian (2017): Vitamin D supplementation for chronic liver diseases in adults. In Cochrane Database Syst. Rev. 11, CD011564. DOI: 10.1002/14651858.CD011564.pub2.

Boonen, Steven; Lips, Paul; Bouillon, Roger; Bischoff-Ferrari, Heike A.; Vanderschueren, Dirk; Haentjens, Patrick (2007): Need for additional calcium to reduce the risk of hip fracture with vitamin d supplementation: evidence from a comparative metaanalysis of randomized controlled trials. In The Journal of clinical endocrinology and metabolism 92 (4), pp. 1415–1423. DOI: 10.1210/jc.2006-1404.

Borel, P.; Caillaud, D.; Cano, N. J. (2015): Vitamin D bioavailability: state of the art. In Critical reviews in food science and nutrition 55 (9), pp. 1193–1205. DOI: 10.1080/10408398.2012.688897.

Bowyer, Lucy; Catling-Paull, Christine; Diamond, Terrence; Homer, Caroline; Davis, Gregory; Craig, Maria E. (2009): Vitamin D, PTH and calcium levels in pregnant women and their neonates. In Clin. Endocrinol. (Oxf) 70 (3), pp. 372–377. DOI: 10.1111/j.1365-2265.2008.03316.x.

Brannon, Patsy M.; Yetley, Elizabeth A.; Bailey, Regan L.; Picciano, Mary Frances (2008): Overview of the conference "Vitamin D and Health in the 21st Century: an Update". In Am. J. Clin. Nutr. 88 (2), 483S-490S. DOI: 10.1093/ajcn/88.2.483S.

Cai, Lei; Eckhardt, Erik R. M.; Shi, Wei; Zhao, Zhenze; Nasser, Munira; Villiers, Willem J. S. de; van der Westhuyzen, Deneys R. (2004): Scavenger receptor class B type I reduces cholesterol absorption in cultured enterocyte CaCo-2 cells. In Journal of lipid research 45 (2), pp. 253–262. DOI: 10.1194/jlr.M300303-JLR200.

Cavalier, Etienne; Jandrain, Bernard; Coffiner, Monte; Da Silva, Stéphanie; Niet, Sophie de; Vanderbist, Francis; Souberbielle, Jean-Claude (2016): A Randomised, Cross-Over Study to Estimate the Influence of Food on the 25-Hydroxyvitamin D_3 Serum Level after Vitamin D_3 Supplementation. In Nutrients 8 (5). DOI: 10.3390/nu8050309.

Cediel, Gustavo; Pacheco-Acosta, Johanna; CastiUo-Durdn, Carlos (2018): Deficiencia de vitamina D en la práctica clínica pediátrica. In Archivos argentinos de pediatria 116 (1), e75-e81. DOI: 10.5546/aap.2018.eng.e75.

Cesareo, Roberto; Attanasio, Roberto; Caputo, Marco; Castello, Roberto; Chiodini, Iacopo; Falchetti, Alberto et al. (2018): Italian Association of Clinical Endocrinologists (AME) and Italian Chapter of the American Association of Clinical Endocrinologists (AACE) Position Statement: Clinical Management of Vitamin D Deficiency in Adults. In Nutrients 10 (5). DOI: 10.3390/nu10050546.

Chandler, Paulette D.; Scott, Jamil B.; Drake, Bettina F.; Ng, Kimmie; Forman, John P.; Chan, Andrew T. et al. (2014): Risk of hypercalcemia in blacks taking hydrochlorothiazide and vitamin D. In Am. J. Med. 127 (8), pp. 772–778. DOI: 10.1016/j.amjmed.2014.02.044.

Chandra, Prakash; José, Binongo; Thomas, Ziegler; Lynn, Schlanger; Wenli, Wang; James, Someren; Vin, Tangpricha (2008): Cholecalciferol (vitamin D3) therapy and vitamin D insufficiency in patients with chronic kidney disease: a randomized controlled pilot study. In Endocrine Practice 14 (1), pp. 10–17. DOI: 10.22334/jbhost.v6i2.217.s47.

Chandy, David D.; Kare, Jahnavi; Singh, Shakal N.; Agarwal, Anjoo; Das, Vinita; Singh, Urmila et al. (2016): Effect of vitamin D supplementation, directly or via breast milk for term infants, on serum 25 hydroxyvitamin D and related biochemistry, and propensity to infection: a randomised placebo- controlled trial. In The British journal of nutrition 116 (1), pp. 52–58. DOI: 10.1017/S0007114516001756.

Chel, V.; Wijnhoven, H. A. H.; Smit, J. H.; Ooms, M.; Lips, P. (2008): Efficacy of different doses and time intervals of oral vitamin D supplementation with or without calcium in elderly nursing home residents. In Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA 19 (5), pp. 663–671. DOI: 10.1007/s00198-007-0465-2.

Chen, Pei-Zhan; Li, Mian; Duan, Xiao-Hua; Jia, Jing-Ying; Li, Jing-Quan; Chu, Rui-Ai et al. (2016): Pharmacokinetics and effects of demographic factors on blood 25(OH)D3 levels after a single orally administered high dose of vitamin D3. In Acta Pharmacol. Sin. 37 (11), pp. 1509–1515. DOI: 10.1038/aps.2016.82.

Coelho, Iara Maria Gomes; Andrade, Luena Dias de; Saldanha, Lunnara; Diniz, Erik Trovão; Griz, Luiz; Bandeira, Francisco (2010): Bioavailability of vitamin D3 in non-oily capsules: the role of formulated compounds and implications for intermittent replacement. In Arquivos brasileiros de endocrinologia e metabologia 54 (2), pp. 239–243. DOI: 10.1590/s0004-27302010000200022.

College ter Beoordeling van Geneesmiddelen (2019): Public Assessment Report Scientific discussion, Osferol-D3 800 IE, 1000 IE, 7000 IE, and 30000 IE film-coated tablets (cholecalciferol). College ter Beoordeling van Geneesmiddelen. /H/4073/001-004/DC. College ter Beoordeling van Geneesmiddelen. Graadt van Roggenweg 500, 3531 AH Utrecht.

Colonis Pharma Ltd: Colecalciferol 20 000 IU Capsules - Summary of Product Characteristics (SmPC) - print friendly - (eMC), checked on 3/6/2018.

Cowan, Abigail; Pugh, Rachael; McCaughey, Aileen (2017): Treatment of Vitamin D Deficiency in Adults, checked on 12/19/2019.

Crandall, Carolyn J.; Newberry, Sydne J.; Diamant, Allison; Lim, Yee-Wei; Gellad, Walid F.; Suttorp, Marika J. et al. (2012): Treatment To Prevent Fractures in Men and Women With Low Bone Density or Osteoporosis: Update of a 2007 Report. Rockville (MD).

Cranney, Ann; Horsley, Tanya; O'Donnell, Siobhan; Weiler, Hope; Puil, Lorri; Ooi, Daylily et al. (2007): Effectiveness and safety of vitamin D in relation to bone health. In Evidence report/technology assessment (158), pp. 1–235.

Crockett, Seth D.; Barry, Elizabeth L.; Mott, Leila A.; Ahnen, Dennis J.; Robertson, Douglas J.; Anderson, Joseph C. et al. (2018): Calcium and vitamin D supplementation and increased risk of serrated polyps: results from a randomised clinical trial. In Gut. DOI: 10.1136/gutjnl-2017-315242.

Dachverband Osteologie (2017): DVO-LEITLINIE zur Prophylaxe, Diagnostik und Therapie der Osteoporose bei postmenopausalen Frauen und bei Männern, checked on 12/19/2019.

Davis, Harry R.; Zhu, Li-Ji; Hoos, Lizbeth M.; Tetzloff, Glen; Maguire, Maureen; Liu, Jianjun et al. (2004): Niemann-Pick C1 Like 1 (NPC1L1) is the intestinal phytosterol and cholesterol transporter and a key modulator of whole-body cholesterol homeostasis. In J. Biol. Chem. 279 (32), pp. 33586–33592. DOI: 10.1074/jbc.M405817200.

Dawodu, Adekunle; Saadi, Hussein F.; Bekdache, Gharid; Javed, Yasin; Altaye, Mekibib; Hollis, Bruce W. (2013): Randomized controlled trial (RCT) of vitamin D supplementation in pregnancy in a population with endemic vitamin D deficiency. In The Journal of clinical endocrinology and metabolism 98 (6), pp. 2337–2346. DOI: 10.1210/jc.2013-1154.

Dawson-Hughes, B. (2011): Treatment of vitamin D deficiency in adults.

Dawson-Hughes, Bess; Harris, Susan S.; Lichtenstein, Alice H.; Dolnikowski, Gregory; Palermo, Nancy J.; Rasmussen, Helen (2015): Dietary fat increases vitamin D-3 absorption. In Journal of the Academy of Nutrition and Dietetics 115 (2), pp. 225–230. DOI: 10.1016/j.jand.2014.09.014.

Dawson-Hughes, Bess; Harris, Susan S.; Palermo, Nancy J.; Ceglia, Lisa; Rasmussen, Helen (2013): Meal conditions affect the absorption of supplemental vitamin D3 but not the plasma 25-hydroxyvitamin D response to supplementation. In J. Bone Miner. Res. 28 (8), pp. 1778–1783. DOI: 10.1002/jbmr.1896.

Deb, Subrata; Pandey, Mitali; Adomat, Hans; Guns, Emma S. Tomlinson (2012): Cytochrome P450 3A- mediated microsomal biotransformation of 1α,25-dihydroxyvitamin D3 in mouse and human liver: drug- related induction and inhibition of catabolism. In Drug metabolism and disposition: the biological fate of chemicals 40 (5), pp. 907–918. DOI: 10.1124/dmd.111.041681.

deBoer, Ian H. de; Levin, Gregory; Robinson-Cohen, Cassianne; Biggs, Mary L.; Hoofnagle, Andy N.; Siscovick, David S.; Kestenbaum, Bryan (2012): Serum 25-hydroxyvitamin D concentration and risk for major clinical disease events in a community-based population of older adults: a cohort study. In Ann. Intern. Med. 156 (9), pp. 627–634. DOI: 10.7326/0003-4819-156-9-201205010-00004.

DeLuca, Hector F. (2009): Vitamin D and the parenteral nutrition patient. In Gastroenterology 137 (5 Suppl), S79-91. DOI: 10.1053/j.gastro.2009.07.075.

deNiet, Sophie de; Coffiner, Monte; Da Silva, Stéphanie; Jandrain, Bernard; Souberbielle, Jean-Claude; Cavalier, Etienne (2018): A Randomized Study to Compare a Monthly to a Daily Administration of Vitamin D_3 Supplementation. In Nutrients 10 (6). DOI: 10.3390/nu10060659.

Denker, Andrew E.; Lazarus, Nicole; Porras, Arturo; Ramakrishnan, Rohini; Constanzer, Marvin; Scott, Boyd B. et al. (2011): Bioavailability of alendronate and vitamin D(3) in an alendronate/vitamin D(3) combination tablet. In J. Clin. Pharmacol. 51 (10), pp. 1439–1448. DOI: 10.1177/0091270010382010.

DeRegil, Luz Maria; Palacios, Cristina; Lombardo, Lia K.; Peña-Rosas, Juan Pablo (2016): Vitamin D supplementation for women during pregnancy. In Cochrane Database Syst. Rev. (1), CD008873. DOI: 10.1002/14651858.CD008873.pub3.

Didriksen, Allan; Grimnes, Guri; Hutchinson, Moira Strand; Kjærgaard, Marie; Svartberg, Johan; Joakimsen, Ragnar M.; Jorde, Rolf (2013): The serum 25-hydroxyvitamin D response to vitamin D supplementation is related to genetic factors, BMI, and baseline levels. In Eur. J. Endocrinol. 169 (5), pp. 559–567. DOI: 10.1530/EJE-13-0233.

Djokovic, J.; Tomic Lucic, A.; Milovanovic, O; Bazic, D.; Veselinovic, M.; Djukic, A. et al. (2019): Population pharmacokinetics of 25-hydroxy vitamin D in non-elderly postmenopausal women. In Acta Poloniae Pharmaceutica - Drug Research 76 (1), pp. 129–

136. DOI: 10.32383/appdr/93982.

Drincic, Andjela; Fuller, Eileen; Heaney, Robert P.; Armas, Laura A. G. (2013): 25-Hydroxyvitamin D response to graded vitamin D_3 supplementation among obese adults. In The Journal of clinical endocrinology and metabolism 98 (12), pp. 4845–4851. DOI: 10.1210/jc.2012-4103.

Drugs and Lactation Database (Ed.) (2019): Vitamin D. (Drugs and Lactation Database (LactMed). Bethesda (MD):: National Library of Medicine (US).

Duan, Leizhen; Xue, Zonggui; Ji, Huanwen; Zhang, Dongdong; Wang, Yan (2018): Effects of CYP2R1 gene variants on vitamin D levels and status: A systematic review and meta-analysis. In Gene 678, pp. 361–

369. DOI: 10.1016/j.gene.2018.08.056.

Ebeling, Peter R. (2014): Vitamin D and bone health: Epidemiologic studies. In BoneKEy reports 3, p. 511. DOI: 10.1038/bonekey.2014.6.

EFSA NDA Panel (2016): Dietary reference values for vitamin D. In EFS2 14 (10), e04547. DOI: 10.2903/j.efsa.2016.4547.

Ekwaru, John Paul; Zwicker, Jennifer D.; Holick, Michael F.; Giovannucci, Edward; Veugelers, Paul J. (2014): The importance of body weight for the dose response relationship of oral vitamin D supplementation and serum 25-hydroxyvitamin D in healthy volunteers. In PLoS ONE 9 (11), e111265. DOI: 10.1371/journal.pone.0111265.

Elangovan, Harendran; Chahal, Sarinder; Gunton, Jenny E. (2017): Vitamin D in liver disease: Current evidence and potential directions. In Biochimica et biophysica acta. Molecular basis of disease 1863 (4), pp. 907–916. DOI: 10.1016/j.bbadis.2017.01.001.

El-Desouki, Mahmoud I.; Othman, Saleh M.; Fouda, Mona A. (2004): Bone mineral density and bone scintigraphy in adult Saudi female patients with osteomalacia. In Saudi Med. J. 25 (3), pp. 355–358.

Fassio, Angelo; Adami, Giovanni; Rossini, Maurizio; Giollo, Alessandro; Caimmi, Cristian; Bixio, Riccardo et al. (2020): Pharmacokinetics of Oral Cholecalciferol in Healthy Subjects with Vitamin D Deficiency: A Randomized Open-Label Study. In Nutrients 12 (6). DOI: 10.3390/nu12061553.

Feng, Haixia; Xun, Pengcheng; Pike, Katharine; Wills, Andrew K.; Chawes, Bo L.; Bisgaard, Hans et al. (2017): In utero exposure to 25-hydroxyvitamin D and risk of childhood asthma, wheeze, and respiratory tract infections: A meta-analysis of birth cohort studies. In The Journal of allergy and clinical immunology 139 (5), pp. 1508–1517. DOI: 10.1016/j.jaci.2016.06.065.

Flood-Nichols, Shannon K.; Tinnemore, Deborah; Huang, Raywin R.; Napolitano, Peter G.; Ippolito, Danielle L. (2015): Vitamin D deficiency in early pregnancy. In PLoS ONE 10 (4), e0123763. DOI: 10.1371/journal.pone.0123763.

Francis, R.; Aspray, T.; Fraser, W.; Gittoes, N.; Javaid, K.; Macdonald, H. et al. (2013): Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management. In Society, checked on 1/13/2020.

Francis, R.; Aspray, T.; Fraser, W.; Macdonald, H.; Patel, S.; Mavroeidi, A. et al. (2018): Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management (version 2),. In National Osteoporosis Society 2018, checked on 1/13/2020.

Ganji, Mohammad Reza; Shafii, Zahra; Hakemi, Monir Sadat (2019): Vitamin D Supplementation and Risk of Hypercalciuria in Stone Formers. In iranian journal of kidney diseases 13 (1), pp. 27–31.

Glass, A. R.; Eil, C. (1986): Ketoconazole-induced reduction in serum 1,25-dihydroxyvitamin D. In The Journal of clinical endocrinology and metabolism 63 (3), pp. 766–769. DOI: 10.1210/jcem-63-3-766.

Glowka, Eliza; Stasiak, Joanna; Lulek, Janina (2019): Drug Delivery Systems for Vitamin D Supplementation and Therapy. In Pharmaceutics 11 (7). DOI: 10.3390/pharmaceutics11070347.

Golzarand, M.; Shab-Bidar, S.; Koochakpoor, G.; Speakman J, R.; Djafarian, K. (2016): Effect of vitamin D3 supplementation on blood pressure in adults: An updated meta-analysis. In Nutr. Metab. Cardiovasc. Dis. 26 (8), pp. 663–673. DOI: 10.1016/j.numecd.2016.04.011.

Goncalves, Aurélie; Roi, Stéphanie; Nowicki, Marion; Dhaussy, Amélie; Huertas, Alain; Amiot, Marie- Josèphe; Reboul, Emmanuelle (2015): Fat-soluble vitamin intestinal absorption: absorption sites in the intestine and interactions for absorption. In Food chemistry 172, pp. 155–160. DOI: 10.1016/j.foodchem.2014.09.021.

González-Castro, Thelma Beatriz; Blachman-Braun, Ruben; Hernández-Díaz, Yazmín; Tovilla-Zárate, Carlos Alfonso; Pérez-Hernández, Nonanzit; Moscardi, Paulo Renato Marcelo et al. (2019): Association of vitamin D receptor polymorphisms and nephrolithiasis: A meta-analysis. In Gene 711, p. 143936. DOI: 10.1016/j.gene.2019.06.026.

Gopal-Kothandapani, Jaya Sujatha; Evans, Lucy Faith; Walsh, Jennifer S.; Gossiel, Fatma; Rigby, Alan S.; Eastell, Richard; Bishop, Nick J. (2019): Effect of vitamin D supplementation on free and total vitamin D: A comparison of Asians and Caucasians. In Clin. Endocrinol. (Oxf) 90 (1), pp. 222–231. DOI: 10.1111/cen.13825.

Grant, Cameron C.; Stewart, Alistair W.; Scragg, Robert; Milne, Tania; Rowden, Judy; Ekeroma, Alec et al. (2014): Vitamin D during pregnancy and infancy and infant serum 25-hydroxyvitamin D concentration. In Pediatrics 133 (1), e143-53. DOI: 10.1542/peds.2013-2602.

Greene-Finestone, L. S.; Berger, C.; Groh, M. de; Hanley, D. A.; Hidiroglou, N.; Sarafin, K. et al. (2011): 25-Hydroxyvitamin D in Canadian adults: biological, environmental, and behavioral correlates. In Osteoporos. Int. 22 (5), pp. 1389–1399. DOI: 10.1007/s00198-010-1362-7.

Gröber, Uwe; Reichrath, Jörg; Holick, Michael F. (2015): Live longer with vitamin D? In Nutrients 7 (3), pp. 1871–1880. DOI: 10.3390/nu7031871.

Grossmann, Ruth E.; Tangpricha, Vin (2010): Evaluation of vehicle substances on vitamin D bioavailability: a systematic review. In Mol. Nutr. Food Res. 54 (8), pp. 1055–1061. DOI: 10.1002/mnfr.200900578.

Gupta, A.; Gupta, N.; Singh, N.; Goswami, R. (2010): Presence of impaired intestinal calcium absorption in chronic hypovitaminosis D and its change after cholecalciferol supplementation: assessment by the calcium load test. In Journal of human nutrition and dietetics : the official journal of the British Dietetic Association 23 (1), pp. 54–60. DOI: 10.1111/j.1365-277X.2009.01003.x.

Hammami, Muhammad M.; Yusuf, Ahmed (2017): Differential effects of vitamin D2 and D3 supplements on 25-hydroxyvitamin D level are dose, sex, and time dependent: a randomized controlled trial. In BMC Endocr. Disord. 17 (1), p. 12. DOI: 10.1186/s12902-017-0163-9.

Hannan, Marian T.; Litman, Heather J.; Araujo, Andre B.; McLennan, Christine E.; McLean, Robert R.; McKinlay, John B. et al. (2008): Serum 25-hydroxyvitamin D and bone mineral density in a racially and ethnically diverse group of men. In The Journal of clinical endocrinology and metabolism 93 (1), pp. 40–

46. DOI: 10.1210/jc.2007-1217.

Hansen, C. S.; Fleischer, J.; Vistisen, D.; Ridderstråle, M.; Jensen, J. S.; Jørgensen, M. E. (2017): High and low vitamin D level is associated with cardiovascular autonomic neuropathy in people with Type 1 and Type 2 diabetes. In Diabet. Med. 34 (3), pp. 364–371. DOI: 10.1111/dme.13269.

Hansen, Karen E.; Johnson, R. Erin; Chambers, Kaitlin R.; Johnson, Michael G.; Lemon, Christina C.; Vo, Tien Nguyen Thuy; Marvdashti, Sheeva (2015): Treatment of Vitamin D Insufficiency in Postmenopausal Women: A Randomized Clinical Trial. In JAMA internal medicine 175 (10), pp. 1612–1621. DOI: 10.1001/jamainternmed.2015.3874.

Harris, Ryan A.; Pedersen-White, Jennifer; Guo, De-Huang; Stallmann-Jorgensen, Inger S.; Keeton, Daniel; Huang, Ying et al. (2011): Vitamin D3 supplementation for 16 weeks improves flow-mediated dilation in overweight African-American adults. In American journal of hypertension 24 (5), pp. 557–562. DOI: 10.1038/ajh.2011.12.

Hassan, Adla Bakri; Hozayen, Reham Fathi; Alotaibi, Raed Aqshan; Tayem, Yasin Ibrahim (2018): Therapeutic and maintenance regimens of vitamin D3 supplementation in healthy adults: A systematic review. In Cell. Mol. Biol. (Noisy-le-grand) 64 (14), pp. 8–14.

Hathcock, John N.; Shao, Andrew; Vieth, Reinhold; Heaney, Robert (2007): Risk assessment for vitamin D. In Am. J. Clin. Nutr. 85 (1), pp. 6–18. DOI: 10.1093/ajcn/85.1.6.

Hawkes, Colin Patrick; Li, Dong; Hakonarson, Hakon; Meyers, Kevin E.; Thummel, Kenneth E.; Levine, Michael A. (2017): CYP3A4 Induction by Rifampin: An Alternative Pathway for Vitamin D Inactivation in Patients With CYP24A1 Mutations. In The Journal of clinical endocrinology and metabolism 102 (5), pp. 1440–1446. DOI: 10.1210/jc.2016-4048.

He, Silu; Hao, Xiyuan (2019): The effect of vitamin D3 on blood pressure in people with vitamin D deficiency: A system review and meta-analysis. In Medicine (Baltimore) 98 (19), e15284. DOI: 10.1097/MD.0000000000015284.

Heaney, Robert P.; Armas, Laura A. G. (2015): Quantifying the vitamin D economy. In Nutr. Rev. 73 (1), pp. 51–67. DOI: 10.1093/nutrit/nuu004.

Heaney, Robert P.; Armas, Laura A. G.; Shary, Judith R.; Bell, Norman H.; Binkley, Neil; Hollis, Bruce W. (2008): 25-Hydroxylation of vitamin D3: relation to circulating vitamin D3 under various input conditions. In Am. J. Clin. Nutr. 87 (6), pp. 1738–1742. DOI: 10.1093/ajcn/87.6.1738.

Helde Frankling, Maria; Norlin, Anna-Carin; Hansen, Susanne; Wahren Borgström, Emilie; Bergman, Peter; Björkhem-Bergman, Linda (2020): Are Vitamin D3 Tablets and Oil Drops Equally Effective in Raising S-25-Hydroxyvitamin D Concentrations? A Post-Hoc Analysis of an Observational Study on Immunodeficient Patients. In Nutrients 12 (5). DOI: 10.3390/nu12051230.

Hernlund, E.; Svedbom, A.; Ivergård, M.; Compston, J.; Cooper, C.; Stenmark, J. et al. (2013): Osteoporosis in the European Union: medical management, epidemiology and economic burden. A report prepared in collaboration with the International Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA). In Archives of osteoporosis 8, p. 136. DOI: 10.1007/s11657-013-0136-1.

Heubi, J. E.; Hollis, B. W.; Specker, B.; Tsang, R. C. (1989): Bone disease in chronic childhood cholestasis. I. Vitamin D absorption and metabolism. In Hepatology 9 (2), pp. 258–264.

Heubi, J. E.; Hollis, B. W.; Tsang, R. C. (1990): Bone disease in chronic childhood cholestasis II. Better absorption of 25-OH vitamin D than vitamin D in extrahepatic biliary atresia. In Pediatric Research 27 (1), pp. 26–31.

Hii, Charles S.; Ferrante, Antonio (2016): The Non-Genomic Actions of Vitamin D. In Nutrients 8 (3), p. 135. DOI: 10.3390/nu8030135.

Hilger, Jennifer; Friedel, Angelika; Herr, Raphael; Rausch, Tamara; Roos, Franz; Wahl, Denys A. et al. (2014): A systematic review of vitamin D status in populations worldwide. In The British journal of nutrition 111 (1), pp. 23–45. DOI: 10.1017/S0007114513001840.

Hiller, Amie L.; Murchison, Charles F.; Lobb, Brenna M.; O'Connor, Susan; O'Connor, Morgan; Quinn, Joseph F. (2018): A randomized, controlled pilot study of the effects of vitamin D supplementation on balance in Parkinson's disease: Does age matter? In PloS one 13 (9), e0203637. DOI: 10.1371/journal.pone.0203637.

Holick, Michael F. (2007): Vitamin Deficiency. In The New England Journal of Medicine 357, pp. 266–281. DOI: 10.1007/SpringerReference_137754.

Holick, Michael F. (2012): Evidence-based D-bate on health benefits of vitamin D revisited. In Dermato-endocrinology 4 (2), pp. 183–190. DOI: 10.4161/derm.20015.

Holick, Michael F.; Binkley, Neil C.; Bischoff-Ferrari, Heike A.; Gordon, Catherine M.; Hanley, David A.; Heaney, Robert P. et al. (2011): Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. In The Journal of clinical endocrinology and metabolism 96 (7), pp. 1911–1930. DOI: 10.1210/jc.2011-0385.

Hollander, D.; Muralidhara, K. S.; Zimmerman, A. (1978): Vitamin D-3 intestinal absorption in vivo: influence of fatty acids, bile salts, and perfusate pH on absorption. In Gut 19 (4), pp. 267–272. DOI: 10.1136/gut.19.4.267.

Holmberg, I.; Aksnes, L.; Berlin, T.; Lindbäck, B.; Zemgals, J.; Lindeke, B. (1990): Absorption of a pharmacological dose of vitamin D3 from two different lipid vehicles in man: comparison of peanut oil and a medium chain triglyceride. In Biopharm. Drug Dispos. 11 (9), pp. 807–815. DOI: 10.1002/bdd.2510110908.

Holvik, Kristin; Ahmed, Luai A.; Forsmo, Siri; Gjesdal, Clara G.; Grimnes, Guri; Samuelsen, Sven Ove et al. (2013): Low serum levels of 25-hydroxyvitamin D predict hip fracture in the elderly: a NOREPOS study. In The Journal of clinical endocrinology and metabolism 98 (8), pp. 3341–3350. DOI: 10.1210/jc.2013-1468.

Holvik, Kristin; Madar, Ahmed A.; Meyer, Haakon E.; Lofthus, Cathrine M.; Stene, Lars C. (2007): A randomised comparison of increase in serum 25-hydroxyvitamin D concentration after 4 weeks of daily oral intake of 10 microg cholecalciferol from multivitamin tablets or fish oil capsules in healthy young adults. In Br. J. Nutr. 98 (3), pp. 620–625. DOI: 10.1017/S000711450773074X.

Hossein-nezhad, Arash; Holick, Michael F. (2013): Vitamin D for health: a global perspective. In Mayo Clinic proceedings 88 (7), pp. 720–755. DOI: 10.1016/j.mayocp.2013.05.011.

Hu, Henglong; Zhang, Jiaqiao; Lu, Yuchao; Zhang, Zongbiao; Qin, Baolong; Gao, Hongbin et al. (2017): Association between Circulating Vitamin D Level and Urolithiasis: A Systematic Review and Meta- Analysis. In Nutrients 9 (3). DOI: 10.3390/nu9030301.

Hwang, Jawl-Shan; Tsai, Keh-Sung; Cheng, Yuh-Min; Chen, Wen-Jer; Tu, Shih-Te; Lu, Ko-Hsiu et al. (2014): Vitamin D status in non-supplemented postmenopausal Taiwanese women with osteoporosis and fragility fracture. In BMC musculoskeletal disorders 15, p. 257. DOI: 10.1186/1471-2474-15-257.

Ilahi, Marium; Armas, Laura A. G.; Heaney, Robert P. (2008): Pharmacokinetics of a single, large dose of cholecalciferol. In Am. J. Clin. Nutr. 87 (3), pp. 688–691. DOI: 10.1093/ajcn/87.3.688.

Institute of Medicine (Ed.) (2011): Dietary reference intakes for Calcium and Vitamin D. With assistance of A. Catharine Ross, Christine L. Taylor, Ann L. Yaktine, Heather B. Del Valle. Institue of Medicine. Washington, D.C.: National Academies Press.

International Osteoporosis Foundation (2011): Three steps to unbreakable bones: Vitamin D, calcium and exercise. 2011. In International Osteoporosis Foundation. Available online at

https://www.iofbonehealth.org/sites/default/files/PDFs/WOD%20Reports/WOD11_Report.pdf, checked on 1/13/2020.

Internis Pharmaceuticals Ltd (2019): Fultium-D3 20,000IU capsules - Summary of Product Characteristics (SmPC) - print friendly - (eMC), checked on Text revision date: 1/9/2019.

Ish-Shalom, Sophia; Segal, Elena; Salganik, Tina; Raz, Batia; Bromberg, Irvin L.; Vieth, Reinhold (2008): Comparison of daily, weekly, and monthly vitamin D3 in ethanol dosing protocols for two months in elderly hip fracture patients. In The Journal of clinical endocrinology and metabolism 93 (9), pp. 3430– 3435. DOI: 10.1210/jc.2008-0241.

Jacobs, Thomas P.; Kaufman, Martin; Jones, Glenville; Kumar, Rajiv; Schlingmann, Karl-Peter; Shapses, Sue; Bilezikian, John P. (2014): A lifetime of hypercalcemia and hypercalciuria, finally explained. In The Journal of clinical endocrinology and metabolism 99 (3), pp. 708–712. DOI: 10.1210/jc.2013-3802.

Janjetovic, Zorica; Tuckey, Robert C.; Nguyen, Minh N.; Thorpe, Edwin M.; Slominski, Andrzej T. (2010): 20,23-dihydroxyvitamin D3, novel P450scc product, stimulates differentiation and inhibits proliferation and NF-kappaB activity in human keratinocytes. In Journal of cellular physiology 223 (1), pp. 36–48. DOI: 10.1002/jcp.21992.

Jansen, Rasmus Bo; Svendsen, Ole Lander (2014): The effect of oral loading doses of cholecalciferol on the serum concentration of 25-OH-vitamin-D. In Int. J. Vitam. Nutr. Res. 84 (1-2), pp. 45–54. DOI: 10.1024/0300-9831/a000192.

Jean, Guillaume; Souberbielle, Jean Claude; Chazot, Charles (2017): Vitamin D in Chronic Kidney Disease and Dialysis Patients. In Nutrients 9 (4). DOI: 10.3390/nu9040328.

Jeon, Ji-Young; Lee, Sun Young; Im, Yong-Jin; Kim, Eun-Young; Kim, Yunjeong; Park, Tae Sun et al. (2014): Comparison of the pharmacokinetics, safety, and tolerability of vitamin D3 in DP-R206 (150-mg ibandronate/24,000-IU vitamin D3 tablet) and as monotherapy (24,000 iu) in healthy male Korean adults. In Clin. Ther. 36 (1), pp. 48–57. DOI: 10.1016/j.clinthera.2013.12.001.

Jetter, Alexander; Egli, Andreas; Dawson-Hughes, Bess; Staehelin, Hannes B.; Stoecklin, Elisabeth; Goessl, Richard et al. (2014): Pharmacokinetics of oral vitamin D3 and calcifediol. In Bone 59, pp. 14–19. DOI: 10.1016/j.bone.2013.10.014.

Joh, Hee-Kyung; Hwang, Seung-Sik; Cho, BeLong; Lim, Chun Soo; Jung, Sung-Eun (2019): Effect of sun exposure versus oral vitamin D supplementation on serum 25-hydroxyvitamin D concentrations in young adults: A randomized clinical trial. In Clin. Nutr. DOI: 10.1016/j.clnu.2019.03.021.

Johnson, J. L.; Mistry, V. V.; Vukovich, M. D.; Hogie-Lorenzen, T.; Hollis, B. W.; Specker, B. L. (2005): Bioavailability of Vitamin D from Fortified Process Cheese and Effects on Vitamin D Status in the Elderly. In Journal of Dairy Science 88 (7), pp. 2295–2301. DOI: 10.3168/jds.S0022-0302(05)72907-6.

Jones, Glenville (2008): Pharmacokinetics of vitamin D toxicity. In The American journal of clinical nutrition 88 (2), 582S-586S. DOI: 10.1093/ajcn/88.2.582S.

Jones, Glenville; Prosser, David E.; Kaufmann, Martin (2014): Cytochrome P450-mediated metabolism of vitamin D. In Journal of lipid research 55 (1), pp. 13–31. DOI: 10.1194/jlr.R031534.

Kanis, J. A.; McCloskey, E. V.; Johansson, H.; Cooper, C.; Rizzoli, R.; Reginster, J-Y (2013): European guidance for the diagnosis and management of osteoporosis in postmenopausal women. In Osteoporos. Int. 24 (1), pp. 23–57. DOI: 10.1007/s00198-012-2074-y.

Karras, Spyridon N.; Anagnostis, Panagiotis; Beauchet, Olivier; Goulis, Dimitrios G.; Annweiler, Cedric (2014): Vitamin D supplements and bone mineral density. In Lancet 383 (9925), pp. 1292–1293. DOI: 10.1016/S0140-6736(14)60640-1.

Kaur, Parjeet; Mishra, Sunil Kumar; Mithal, Ambrish (2015): Vitamin D toxicity resulting from overzealous correction of vitamin D deficiency. In Clin. Endocrinol. (Oxf) 83 (3), pp. 327–331. DOI: 10.1111/cen.12836.

Kazemi, Abolfazl; Shayesteh Azar, Masoud; Razavipour, Mehran; Ghaffari, Salman; Khademloo, Mohammad; Azade, Hosein (2019): Novel Fracture Improvements via Vitamin D Supplementation. In Trauma Mon 24 (4). DOI: 10.5812/traumamon.90745.

Kearns, Malcolm D.; Alvarez, Jessica A.; Tangpricha, Vin (2014): Large, single-dose, oral vitamin D supplementation in adult populations: a systematic review. In Endocr. Pract. 20 (4), pp. 341–351. DOI: 10.4158/EP13265.RA.

Kennedy, Deborah A.; Cooley, Kieran; Skidmore, Becky; Fritz, Heidi; Campbell, Tara; Seely, Dugald (2013): Vitamin d: pharmacokinetics and safety when used in conjunction with the pharmaceutical drugs used in cancer patients: a systematic review. In Cancers 5 (1), pp. 255–280. DOI: 10.3390/cancers5010255.

Khan, Qamar J.; Fabian, Carol J. (2010): How I treat vitamin d deficiency. In Journal of oncology practice 6 (2), pp. 97–101. DOI: 10.1200/JOP.091087.

Khaw, Kay-Tee; Stewart, Alistair W.; Waayer, Debbie; Lawes, Carlene M. M.; Toop, Les; Camargo, Carlos A.; Scragg, Robert (2017): Effect of monthly high-dose vitamin D supplementation on falls and non- vertebral fractures: secondary and post-hoc outcomes from the randomised, double-blind, placebo- controlled ViDA trial. In The Lancet Diabetes & Endocrinology 5 (6), pp. 438–447. DOI: 10.1016/S2213- 8587(17)30103-1.

Korkor, A. B. (2009): Effect of fish oil on vitamin D absorption. In American Journal of Kidney Diseases 53 (2), p. 356. DOI: 10.1053/j.ajkd.2008.11.010.

Kubesch, Alica; Quenstedt, Leonie; Saleh, Maged; Rüschenbaum, Sabrina; Schwarzkopf, Katharina; Martinez, Yolanda et al. (2018): Vitamin D deficiency is associated with hepatic decompensation and inflammation in patients with liver cirrhosis: A prospective cohort study. In PloS one 13 (11), e0207162. DOI: 10.1371/journal.pone.0207162.

LeBoff, Meryl S.; Murata, Elle M.; Cook, Nancy R.; Cawthon, Peggy; Chou, Sharon H.; Kotler, Gregory et al. (2020): VITamin D and OmegA-3 TriaL (VITAL): Effects of Vitamin D Supplements on Risk of Falls in the US Population. In The Journal of clinical endocrinology and metabolism 105 (9). DOI: 10.1210/clinem/dgaa311.

Lips, P. (2001): Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. In Endocrine reviews 22 (4), pp. 477–501. DOI: 10.1210/edrv.22.4.0437.

Looker, Anne C. (2013): Serum 25-hydroxyvitamin D and risk of major osteoporotic fractures in older U.S. adults. In J. Bone Miner. Res. 28 (5), pp. 997–1006. DOI: 10.1002/jbmr.1828.

Lv, Qing-Bo; Gao, Xiang; Liu, Xiang; Shao, Zhen-Xuan; Xu, Qian-Hui; Tang, Li et al. (2017): The serum 25-hydroxyvitamin D levels and hip fracture risk: a meta-analysis of prospective cohort studies. In Oncotarget 8 (24), pp. 39849–39858. DOI: 10.18632/oncotarget.16337.

Lynch Cronin, Irene; Byrne, Fiona; Doyle, Ross; Fraser, William D.; Chipchase, Allison; Eustace, Joseph A. (2019): The Effect of Short-Term Vitamin D Supplementation on Calcium Status in Vitamin D Insufficient Renal Transplant Recipients at Risk of Hypercalcemia. In Journal of renal nutrition : the official journal of the Council on Renal Nutrition of the National Kidney Foundation 29 (3), pp. 181–187. DOI: 10.1053/j.jrn.2018.11.012.

Maalouf, Joyce; Nabulsi, Mona; Vieth, Reinhold; Kimball, Samantha; El-Rassi, Rola; Mahfoud, Ziyad; El- Hajj Fuleihan, Ghada (2008): Short- and long-term safety of weekly high-dose vitamin D3 supplementation in school children. In The Journal of clinical endocrinology and metabolism 93 (7), pp. 2693–2701. DOI: 10.1210/jc.2007-2530.

Maeda, Sergio Setsuo; Borba, Victoria Z. C.; Camargo, Marília Brasilio Rodrigues; Silva, Dalisbor Marcelo Weber; Borges, João Lindolfo Cunha; Bandeira, Francisco; Lazaretti-Castro, Marise (2014): Recommendations of the Brazilian Society of Endocrinology and Metabology (SBEM) for the diagnosis and treatment of hypovitaminosis D. In Arquivos brasileiros de endocrinologia e metabologia 58 (5), pp. 411–433. DOI: 10.1590/0004-2730000003388.

Malihi, Z.; Wu, Zhenqiang; Lawes, Carlene M. M.; Scragg, Robert (2019a): Adverse events from large dose vitamin D supplementation taken for one year or longer. In The Journal of steroid biochemistry and molecular biology 188, pp. 29–37. DOI: 10.1016/j.jsbmb.2018.12.002.

Malihi, Zarintaj; Lawes, Carlene M. M.; Wu, Zhenqiang; Huang, Ying; Waayer, Debbie; Toop, Les et al. (2019b): Monthly high-dose vitamin D supplementation does not increase kidney stone risk or serum calcium: results from a randomized controlled trial. In Am. J. Clin. Nutr. 109 (6), pp. 1578–1587. DOI: 10.1093/ajcn/nqy378.

Malihi, Zarintaj; Wu, Zhenqiang; Mm Lawes, Carlene; Scragg, Robert (2017): Noncalcemic adverse effects and withdrawals in randomized controlled trials of long-term vitamin D2 or D3 supplementation: a systematic review and meta-analysis. In Nutr. Rev. 75 (12), pp. 1007–1034. DOI: 10.1093/nutrit/nux059.

Malihi, Zarintaj; Wu, Zhenqiang; Stewart, Alistair W.; Lawes, Carlene Mm; Scragg, Robert (2016): Hypercalcemia, hypercalciuria, and kidney stones in long-term studies of vitamin D supplementation: a systematic review and meta-analysis. In Am. J. Clin. Nutr. 104 (4), pp. 1039–1051. DOI: 10.3945/ajcn.116.134981.

Margulies, Samantha L.; Kurian, Divya; Elliott, Mark S.; Han, Zhiyong (2015): Vitamin D deficiency in patients with intestinal malabsorption syndromes--think in and outside the gut. In Journal of digestive diseases 16 (11), pp. 617–633. DOI: 10.1111/1751-2980.12283.

Martineau, Adrian R.; Thummel, Kenneth E.; Wang, Zhican; Jolliffe, David A.; Boucher, Barbara J.; Griffin, Simon J. et al. (2019): Differential Effects of Oral Boluses of Vitamin D2 vs Vitamin D3 on Vitamin D Metabolism: A Randomized Controlled Trial. In J. Clin. Endocrinol. Metab. 104 (12), pp. 5831–5839. DOI: 10.1210/jc.2019-00207.

Maugeri, Andrea; Barchitta, Martina; Blanco, Isabella; Agodi, Antonella (2019): Effects of Vitamin D Supplementation During Pregnancy on Birth Size: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. In Nutrients 11 (2). DOI: 10.3390/nu11020442.

Maurya, Vaibhav Kumar; Aggarwal, Manjeet (2017): Factors influencing the absorption of vitamin D in GIT: an overview. In Journal of food science and technology 54 (12), pp. 3753–3765. DOI: 10.1007/s13197-017-2840-0.

Mazahery, H.; Stonehouse, W.; Hurst, P. R. von (2015): The effect of monthly 50,000 IU or 100,000 IU vitamin D supplements on vitamin D status in premenopausal Middle Eastern women living in Auckland. In European journal of clinical nutrition 69 (3), pp. 367–372. DOI: 10.1038/ejcn.2014.264.

Mazidi, Mohsen; Rezaie, Peyman; Vatanparast, Hassan; Kengne, Andre Pascal (2017): Effect of statins on serum vitamin D concentrations: a systematic review and meta-analysis. In Eur. J. Clin. Invest. 47 (1), pp. 93–101. DOI: 10.1111/eci.12698.

McDuffie, Jennifer R.; Calis, Karim A.; Booth, Sarah L.; Uwaifo, Gabriel I.; Yanovski, Jack A. (2002): Effects of orlistat on fat-soluble vitamins in obese adolescents. In Pharmacotherapy 22 (7), pp. 814–822. DOI: 10.1592/phco.22.11.814.33627.

Medical Advisory Secretariat (2010): Clinical utility of vitamin d testing: an evidence-based analysis. In Ontario health technology assessment series 10 (2), pp. 1–93.

Meekins, M. E.; Oberhelman, S. S.; Lee, B. R.; Gardner, B. M.; Cha, S. S.; Singh, R. J. et al. (2014): Pharmacokinetics of daily versus monthly vitamin D3 supplementation in non-lactating women. In Eur. J. Clin. Nutr. 68 (5), pp. 632–634. DOI: 10.1038/ejcn.2013.278.

mibe GmBH Arzneimittel (2015): Dekristol 20.000 I.E. Weichkapseln. In Fachinformation, checked on Stand 09/2015.

mibe GmBH Arzneimittel (2019): Dekristol 20.000 I.E. N, Hartkapseln. In Fachinformation, checked on Stand 04/2019.

Mínguez, Miguel; López Higueras, Antonio; Júdez, Javier (2016): Use of polyethylene glycol in functional constipation and fecal impaction. In Revista espanola de enfermedades digestivas : organo oficial de la Sociedad Espanola de Patologia Digestiva 108 (12), pp. 790–806. DOI: 10.17235/reed.2016.4571/2016.

Misra, Madhusmita; Pacaud, Danièle; Petryk, Anna; Collett-Solberg, Paulo Ferrez; Kappy, Michael (2008): Vitamin D deficiency in children and its management: review of current knowledge and recommendations. In Pediatrics 122 (2), pp. 398–417. DOI: 10.1542/peds.2007-1894.

Mo, Minjia; Wang, Shijie; Chen, Zun; Muyiduli, Xiamusiye; Wang, Shuojia; Shen, Yu et al. (2019): A systematic review and meta-analysis of the response of serum 25-hydroxyvitamin D concentration to vitamin D supplementation from RCTs from around the globe. In European journal of clinical nutrition 73 (6), pp. 816–834. DOI: 10.1038/s41430-019-0417-x.

Motamed, Soudabe; Nikooyeh, Bahareh; Kashanian, Maryam; Hollis, Bruce W.; Neyestani, Tirang R. (2019): Efficacy of two different doses of oral vitamin D supplementation on inflammatory biomarkers and maternal and neonatal outcomes. In Maternal & child nutrition 15 (4), e12867. DOI: 10.1111/mcn.12867.

Nair, S. (2010): Vitamin Deficiency and Liver Disease. In Gastrology and Hepatology 6 (8), pp. 491–493.

National Institutes of Health OoDS. (2014): Vitamin D — Health Professional Fact Sheet. Edited by U.S. Department of Health & Human Services. Available online at https://ods.od.nih.gov/factsheets/VitaminD-HealthProfessional/, checked on 1/13/2020.

National Kidney Foundation: A Clinical Update on Vitamin D Deficiency and Secondary Hyperthyroidism: Vitamin D Testing and Supplementation in CKD Stages 3-4 Part 2, checked on 4/20/2021.

National Osteoporosis Foundation (2014): Clinician's Guide to Prevention and Treatment of Osteoporosis. Washington, D.C.

Nechita, M. I.; Guillaume, B. (2018): The active vitamin D treatment is totally harmless? Abstracts presented at the 23rd Annual Congress of the Belgian Society of Internal Medicine. Dolce La Hulpe, La Hulpe, Belgium, checked on 12/14/2018.

Newberry, Sydne J.; Chung, Mei; Shekelle, Paul G.; Booth, Marika Suttorp; Liu, Jodi L.; Maher, Alicia Ruelaz et al. (2014): Vitamin D and Calcium: A Systematic Review of Health Outcomes (Update). In Evidence report/technology assessment (217), pp. 1–929. DOI: 10.23970/AHRQEPCERTA217.

Ng, Kimmie; Scott, Jamil B.; Drake, Bettina F.; Chan, Andrew T.; Hollis, Bruce W.; Chandler, Paulette D. et al. (2014): Dose response to vitamin D supplementation in African Americans: results of a 4-arm, randomized, placebo-controlled trial. In The American journal of clinical nutrition 99 (3), pp. 587–598. DOI: 10.3945/ajcn.113.067777.

Norman, Anthony W. (2008): From vitamin D to hormone D: fundamentals of the vitamin D endocrine system essential for good health. In The American journal of clinical nutrition 88 (2), 491S-499S. DOI: 10.1093/ajcn/88.2.491S.

Nowson, Caryl A.; McGrath, John J.; Ebeling, Peter R.; Haikerwal, Anjali; Daly, Robin M.; Sanders, Kerrie M. et al. (2012): Vitamin D and health in adults in Australia and New Zealand: a position statement. In The Medical journal of Australia 196 (11), pp. 686–687. DOI: 10.5694/mja11.10301.

O'Callaghan, Karen M.; Hennessy, Áine; Hull, George L. J.; Healy, Karina; Ritz, Christian; Kenny, Louise C. et al. (2018): Estimation of the maternal vitamin D intake that maintains circulating 25-hydroxyvitamin D in late gestation at a concentration sufficient to keep umbilical cord sera ≥25-30 nmol/L: a dose- response, double-blind, randomized placebo-controlled trial in pregnant women at northern latitude. In Am. J. Clin. Nutr. 108 (1), pp. 77–91. DOI: 10.1093/ajcn/nqy064.

Ozkan, Behzat; Hatun, Sükrü; Bereket, Abdullah (2012): Vitamin D intoxication. In The Turkish journal of pediatrics 54 (2), pp. 93–98.

Ozturk, Bengu; Argin, Sanem; Ozilgen, Mustafa; McClements, David Julian (2015): Nanoemulsion delivery systems for oil-soluble vitamins: Influence of carrier oil type on lipid digestion and vitamin D3 bioaccessibility. In Food chemistry 187, pp. 499–506. DOI: 10.1016/j.foodchem.2015.04.065.

Pérez-López, Faustino R.; Brincat, Marc; Erel, C. Tamer; Tremollieres, Florence; Gambacciani, Marco; Lambrinoudaki, Irene et al. (2012): EMAS position statement: Vitamin D and postmenopausal health. In Maturitas 71 (1), pp. 83–88. DOI: 10.1016/j.maturitas.2011.11.002.

Pfeifer, M.; Begerow, B.; Minne, H. W.; Suppan, K.; Fahrleitner-Pammer, A.; Dobnig, H. (2009): Effects of a long-term vitamin D and calcium supplementation on falls and parameters of muscle function in community-dwelling older individuals. In Osteoporos. Int. 20 (2), pp. 315–322. DOI: 10.1007/s00198-008- 0662-7.

Pigarova, Ekaterina A.; Rozhinskaya, Ludmila Ya.; Belaya, Janna E.; Dzeranova, Larisa K.; Karonova, Tatiana L.; Ilyin, Alexanrd V. et al. (2016): Russian Association of Endocrinologists recommendations for diagnosis, treatment and prevention of vitamin D deficiency in adults. In Probl Endokrinol (Mosk) 62 (4), pp. 60–84. DOI: 10.14341/probl201662460-84.

Płudowski, Paweł; Karczmarewicz, Elżbieta; Bayer, Milan; Carter, Graham; Chlebna-Sokół, Danuta; Czech-Kowalska, Justyna et al. (2013): Practical guidelines for the supplementation of vitamin D and the treatment of deficits in Central Europe - recommended vitamin D intakes in the general population and groups at risk of vitamin D deficiency. In Endokrynologia Polska 64 (4), pp. 319–327. DOI: 10.5603/ep.2013.0012.

Priambda, L.; Bhatia, V.; Singh, N.; Bhatia, E. (2014): Serum 25 hydroxyvitamin D profile after single large oral doses of cholecalciferol (vitamin D3) in medical staff in North India: A pilot study. In Journal of Postgraduate Medicine 60 (1), pp. 52–56.

Prytuła, Agnieszka; Cransberg, Karlien; Raes, Ann (2019): Drug-metabolizing enzymes CYP3A as a link between tacrolimus and vitamin D in renal transplant recipients: is it relevant in clinical practice? In Pediatr. Nephrol. 34 (7), pp. 1201–1210. DOI: 10.1007/s00467-018-4030-3.

PubChem (2021): Cholecalciferol. Available online at https://pubchem.ncbi.nlm.nih.gov/compound/5280795, checked on 2/24/2021.

Qi, Dan; Nie, Xiaolu; Cai, Jun (2017): The effect of vitamin D supplementation on hypertension in non- CKD populations: A systemic review and meta-analysis. In Int. J. Cardiol. 227, pp. 177–186. DOI: 10.1016/j.ijcard.2016.11.040.

Raed, Anas; Bhagatwala, Jigar; Zhu, Haidong; Pollock, Norman K.; Parikh, Samip J.; Huang, Ying et al. (2017): Dose responses of vitamin D3 supplementation on arterial stiffness in overweight African Americans with

vitamin D deficiency: A placebo controlled randomized trial. In PloS one 12 (12), e0188424. DOI: 10.1371/journal.pone.0188424.

Raef, Hussein; Al-Bugami, Munira; Balharith, Sakra; Moawad, Mahmoud; El-Shaker, Mohammad; Hassan, Anita et al. (2011): Updated recommendations for the diagnosis and management of osteoporosis: a local perspective. In Annals of Saudi medicine 31 (2), pp. 111–128. DOI: 10.4103/0256-4947.77502.

Ramasamy, Indra (2020): Vitamin D Metabolism and Guidelines for Vitamin D Supplementation. In The Clinical biochemist. Reviews 41 (3), pp. 103–126. DOI: 10.33176/AACB-20-00006.

Reboul, Emmanuelle; Goncalves, Aurélie; Comera, Christine; Bott, Romain; Nowicki, Marion; Landrier, Jean-François et al. (2011): Vitamin D intestinal absorption is not a simple passive diffusion: evidences for involvement of cholesterol transporters. In Mol. Nutr. Food Res. 55 (5), pp. 691–702. DOI: 10.1002/mnfr.201000553.

Reid, Ian R.; Bolland, Mark J.; Grey, Andrew (2014): Effects of vitamin D supplements on bone mineral density: a systematic review and meta-analysis. In Lancet 383 (9912), pp. 146–155. DOI: 10.1016/S0140-6736(13)61647-5.

Rhodes, Freya; Greenham, Olivia; Hunt, Emma; Shah, Sheetal; Ryan, Jennifer; Patch, David; Westbrook, Rachel (2019): SAT-102-Cirrhotic patients with vitamin d deficiency fail to respond to oral replacement therapy. In Journal of Hepatology 70 (1), e674. DOI: 10.1016/S0618-8278(19)31341-6.

Richy, F.; Schacht, E.; Bruyere, O.; Ethgen, O.; Gourlay, M.; Reginster, J-Y (2005): Vitamin D analogs versus native vitamin D in preventing bone loss and osteoporosis-related fractures: a comparative meta- analysis. In Calcified tissue international 76 (3), pp. 176–186. DOI: 10.1007/s00223-004-0005-4.

Rivera-Hernández, Gabriela; Antunes-Ricardo, Marilena; Martínez-Morales, Patricia; Sánchez, Mirna L. (2021): Polyvinyl alcohol based-drug delivery systems for cancer treatment. In International journal of pharmaceutics 600, p. 120478. DOI: 10.1016/j.ijpharm.2021.120478.

Rizzoli, R.; Boonen, S.; Brandi, M-L; Bruyère, O.; Cooper, C.; Kanis, J. A. et al. (2013): Vitamin D supplementation in elderly or postmenopausal women: a 2013 update of the 2008 recommendations from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). In Current medical research and opinion 29 (4), pp. 305–313. DOI: 10.1185/03007995.2013.766162.

Robien, Kim; Oppeneer, Sarah J.; Kelly, Julia A.; Hamilton-Reeves, Jill M. (2013): Drug-vitamin D interactions: a systematic review of the literature. In Nutr. Clin. Pract. 28 (2), pp. 194–208. DOI: 10.1177/0884533612467824.

Romagnoli, Elisabetta; Mascia, Maria Lucia; Cipriani, Cristiana; Fassino, Valeria; Mazzei, Franco; D'Erasmo, Emilio et al. (2008): Short and long-term variations in serum calciotropic hormones after a single very large dose of ergocalciferol (vitamin D2) or cholecalciferol (vitamin D3) in the elderly. In The Journal of clinical endocrinology and metabolism 93 (8), pp. 3015–3020. DOI: 10.1210/jc.2008-0350.

Rosen, Clifford J.; Abrams, Steven A.; Aloia, John F.; Brannon, Patsy M.; Clinton, Steven K.; Durazo-Arvizu, Ramon A. et al. (2012): IOM committee members respond to Endocrine Society vitamin D guideline. In The Journal of clinical endocrinology and metabolism 97 (4), pp. 1146–1152. DOI: 10.1210/jc.2011-2218.

Ross, S. G. (1952): Vitamin D intoxication in infancy; a report of four cases. In J. Pediatr. 41 (6), pp. 815– 822. DOI: 10.1016/s0022-3476(52)80301-4.

Roth, Daniel E.; Al Mahmud, Abdullah; Raqib, Rubhana; Akhtar, Evana; Black, Robert E.; Baqui, Abdullah H. (2013): Pharmacokinetics of high-dose weekly oral vitamin D3 supplementation during the third trimester of pregnancy in Dhaka, Bangladesh. In Nutrients 5 (3), pp. 788–810. DOI: 10.3390/nu5030788.

Roth, Daniel E.; Leung, Michael; Mesfin, Elnathan; Qamar, Huma; Watterworth, Jessica; Papp, Eszter (2017): Vitamin D supplementation during pregnancy: state of the evidence from a systematic review of randomised trials. In BMJ 359, j5237. DOI: 10.1136/bmj.j5237.

Rothen, Jean-Pierre; Rutishauser, Jonas; Walter, Philipp N.; Hersberger, Kurt E.; Arnet, Isabelle (2020): Oral intermittent vitamin D substitution: influence of pharmaceutical form and dosage frequency on medication adherence: a randomized clinical trial. In BMC pharmacology & toxicology 21 (1), p. 51. DOI: 10.1186/s40360-020-00430-5.

Rowe, Raymond C. (Ed.) (2009): Handbook of pharmaceutical excipients. 6. ed. London: APhA (PhP) Pharmaceutical Press.

Ruggiero, Carmelinda; Baroni, Marta; Bini, Vittorio; Brozzetti, Annalisa; Parretti, Luca; Zengarini, Elisa et al. (2019): Effects of Weekly Supplementation of Cholecalciferol and Calcifediol Among the Oldest-Old People: Findings From a Randomized Pragmatic Clinical Trial. In Nutrients 11 (11). DOI: 10.3390/nu11112778.

Rusińska, Agnieszka; Płudowski, Paweł; Walczak, Mieczysław; Borszewska-Kornacka, Maria K.; Bossowski, Artur; Chlebna-Sokół, Danuta et al. (2018): Vitamin D Supplementation Guidelines for General Population and Groups at Risk of Vitamin D Deficiency in Poland-Recommendations of the Polish Society of Pediatric Endocrinology and Diabetes and the Expert Panel With Participation of National Specialist Consultants and Representatives of Scientific Societies-2018 Update. In Frontiers in endocrinology 9, p. 246. DOI: 10.3389/fendo.2018.00246.

Sadat-Ali, Mir; Al-Turki, Haifa A. (2014): Vitamin D supplements and bone mineral density. In Lancet 383 (9925), p. 1293. DOI: 10.1016/S0140-6736(14)60641-3.

Sahebkar, Amirhossein; Reiner, Zeljko; Simental-Mendia, Luis E.; Ferretti, Gianna; Della Corte, Claudia; Nobili, Valerio (2017): Impact of Statin Therapy on Plasma Vitamin D Levels: A Systematic Review and Meta-Analysis. In Curr. Pharm. Des. 23 (6), pp. 861–869. DOI: 10.2174/1381612822666161006150542.

Sakaki, Toshiyuki; Kagawa, Norio; Yamamoto, Keiko; Inouye, Kuniyo (2005): Metabolism of vitamin D3 by cytochromes P450. In Frontiers in bioscience : a journal and virtual library 10, pp. 119–134. DOI: 10.2741/1514.

Samaan, Farid; Carvalho, Aluízio B.; Pillar, Roberta; Rocha, Lillian A.; Cassiolato, José L.; Cuppari, Lilian; Canziani, Maria Eugênia F. (2019): The Effect of Long-Term Cholecalciferol Supplementation on Vascular Calcification in Chronic Kidney Disease Patients With Hypovitaminosis D. In Journal of renal nutrition : the official journal of the Council on Renal Nutrition of the National Kidney Foundation 29 (5), pp. 407–415. DOI: 10.1053/j.jrn.2018.12.002.

Sanders, Kerrie M.; Stuart, A. L.; Williamson, E. J.; Simpson, J. A.; Kotowicz, M. A.; Young, D.; Nicholson GC. (2010): Anual High-Dose Oral Vitamin D and Falls and Fractures in Older Women. A Randomized Controlled Trial. In JAMA: The Journal of the American Medical Association 303 (18), pp. 1815–1822. DOI: 10.1001/jama.2010.594.

Saraf, Rajneeta; Morton, Susan M. B.; Camargo, Carlos A.; Grant, Cameron C. (2016): Global summary of maternal and newborn vitamin D status - a systematic review. In Matern. Child Nutr. 12 (4), pp. 647–668. DOI: 10.1111/mcn.12210.

Schleck, Marie-Louise; Souberbielle, Jean-Claude; Jandrain, Bernard; Da Silva, Stéphanie; Niet, Sophie de; Vanderbist, Francis et al. (2015): A Randomized, Double-Blind, Parallel Study to Evaluate the Dose- Response of Three Different Vitamin D Treatment Schemes on the 25-Hydroxyvitamin D Serum Concentration in Patients with Vitamin D Deficiency. In Nutrients 7 (7), pp. 5413–5422. DOI: 10.3390/nu7075227.

Schöttker, Ben; Haug, Ulrike; Schomburg, Lutz; Köhrle, Joseph; Perna, Laura; Müller, Heiko et al. (2013): Strong associations of 25-hydroxyvitamin D concentrations with all-cause, cardiovascular, cancer, and respiratory disease mortality in a large cohort study. In Am. J. Clin. Nutr. 97 (4), pp. 782–793. DOI: 10.3945/ajcn.112.047712.

Schwalfenberg, Gerry (2007): Not enough vitamin D: health consequences for Canadians. In Can. Fam. Physician 53 (5), pp. 841–854.

Schwartz, Janice B.; Kane, Lynn; Bikle, Daniel (2016): Response of Vitamin D Concentration to Vitamin D3 Administration in Older Adults without Sun Exposure: A Randomized Double-Blind Trial. In J. Am. Geriatr. Soc. 64 (1), pp. 65–72. DOI: 10.1111/jgs.13774.

Shieh, Albert; Ma, Christina; Chun, Rene F.; Witzel, Sten; Rafison, Brandon; Contreras, Hannah T. M. et al. (2017): Effects of Cholecalciferol vs Calcifediol on Total and Free 25-Hydroxyvitamin D and Parathyroid Hormone. In The Journal of clinical endocrinology and metabolism 102 (4), pp. 1133–1140. DOI: 10.1210/jc.2016-3919.

Shroff, Rukshana; Wan, Mandy; Nagler, Evi V.; Bakkaloglu, Sevcan; Fischer, Dagmar-C; Bishop, Nicholas et al. (2017): Clinical practice recommendations for native vitamin D therapy in children with chronic kidney disease Stages 2-5 and on dialysis. In Nephrology Dialysis Transplantation 32 (7), pp. 1098–1113. DOI: 10.1093/ndt/gfx065.

Silva, Mariana Costa; Furlanetto, Tania Weber (2018): Intestinal absorption of vitamin D: a systematic review. In Nutr. Rev. 76 (1), pp. 60–76. DOI: 10.1093/nutrit/nux034.

Smith, H.; Anderson, F.; Raphael, H.; Maslin, P.; Crozier, S.; Cooper, C. (2007): Effect of annual intramuscular vitamin D on fracture risk in elderly men and women--a population-based, randomized, double-blind,

placebo-controlled trial. In Rheumatology (Oxford, England) 46 (12), pp. 1852–1857. DOI: 10.1093/rheumatology/kem240.

Smith, Lynette M.; Gallagher, J. Christopher; Suiter, Corinna (2017): Medium doses of daily vitamin D decrease falls and higher doses of daily vitamin D3 increase falls: A randomized clinical trial. In The Journal of steroid biochemistry and molecular biology 173, pp. 317–322. DOI: 10.1016/j.jsbmb.2017.03.015.

Song, Huihui; Yang, Lei; Jia, Chongqi (2017): Maternal vitamin D status during pregnancy and risk of childhood asthma: A meta-analysis of prospective studies. In Mol. Nutr. Food Res. 61 (5). DOI: 10.1002/mnfr.201600657.

Specker, Bonny (2004): Nutrition influences bone development from infancy through toddler years. In J. Nutr. 134 (3), 691S-695S. DOI: 10.1093/jn/134.3.691S.

Spiro, A.; Buttriss, J. L. (2014): Vitamin D: An overview of vitamin D status and intake in Europe. In Nutrition bulletin 39 (4), pp. 322–350. DOI: 10.1111/nbu.12108.

Stamp, T. C. (1974): Intestinal absorption of 25-hydroxycholecalciferol. In The Lancet 2 (7873), pp. 121– 123.

Szeto, Cheuk-Chun; Li, Philip Kam-Tao (2009): The use of vitamin D analogues in chronic kidney diseases: possible mechanisms beyond bone and mineral metabolism. In NDT plus 2 (3), pp. 205–212. DOI: 10.1093/ndtplus/sfp034.

Tabrizi, Reza; Moosazadeh, Mahmood; Lankarani, Kamran B.; Akbari, Maryam; Heydari, Seyed Taghi; Kolahdooz, Fariba et al. (2017): The effects of vitamin D supplementation on metabolic profiles and liver function in patients with non-alcoholic fatty liver disease: A systematic review and meta-analysis of randomized controlled trials. In Diabetes Metab. Syndr. 11 Suppl 2, S975-S982. DOI: 10.1016/j.dsx.2017.07.025.

Tafaro, Laura; Napoli, Nicola (2021): Orthogeriatrics: The Management of Older Patients with Fragility Fractures. Current and Emerging Treatment of Osteoporosis. Edited by Paolo Falaschi, David Marsh. Cham (CH).

Takács, István; Tóth, Béla E.; Szekeres, László; Szabó, Boglárka; Bakos, Bence; Lakatos, Péter (2017): Randomized clinical trial to comparing efficacy of daily, weekly and monthly administration of vitamin D3. In Endocrine 55 (1), pp. 60–65. DOI: 10.1007/s12020-016-1137-9.

Talib, Hina J.; Ponnapakkam, Tulasi; Gensure, Robert; Cohen, Hillel W.; Coupey, Susan M. (2016): Treatment of Vitamin D Deficiency in Predominantly Hispanic and Black Adolescents: A Randomized Clinical Trial. In J. Pediatr. 170, 266-72.e1. DOI: 10.1016/j.jpeds.2015.11.025.

Tangpricha, V.; Koutkia, P.; Rieke, S. M.; Chen, T. C.; Perez, A. A.; Holick, M. F. (2003): Fortification of orange juice with vitamin D: a nowvel approach for enhancing vitamin D nutritional health. In Am. J. Clin. Nutr. 77, pp. 1478–1483.

Tangpricha, Vin; Wasse, Haimanot (2014): Vitamin D therapy in kidney disease: more vitamin D is necessary. In Am. J. Kidney Dis. 64 (5), pp. 667–669. DOI: 10.1053/j.ajkd.2014.08.004.

Tavasoli, Sanaz; Taheri, Maryam (2019): Vitamin D and calcium kidney stones: a review and a proposal. In

Int. Urol. Nephrol. 51 (1), pp. 101–111. DOI: 10.1007/s11255-018-1965-z.

Tayem, Yasin; Alotaibi, Raed; Hozayen, Reham; Hassan, Adla (2019): Therapeutic regimens for vitamin D deficiency in postmenopausal women: a systematic review. In Przeglad menopauzalny = Menopause review 18 (1), pp. 57–62. DOI: 10.5114/pm.2019.84159.

Tebben, Peter J.; Singh, Ravinder J.; Kumar, Rajiv (2016): Vitamin D-Mediated Hypercalcemia: Mechanisms, Diagnosis, and Treatment. In Endocrine reviews 37 (5), pp. 521–547. DOI: 10.1210/er.2016- 1070.

Thacher, Tom D.; Clarke, Bart L. (2011): Vitamin D insufficiency. In Mayo Clinic proceedings 86 (1), pp. 50–60. DOI: 10.4065/mcp.2010.0567.

The Complete Drug Reference - Martindale (Ed.) (2012): The Complete Drug Reference. 37th ed (100).

Thorne-Lyman, Andrew; Fawzi, Wafaie W. (2012): Vitamin D during pregnancy and maternal, neonatal and infant health outcomes: a systematic review and meta-analysis. In Paediatr. Perinat. Epidemiol. 26 Suppl 1, pp. 75–90. DOI: 10.1111/j.1365-3016.2012.01283.x.

Tieroshyn, Vadim; Moroz, Larisa; Prishliak, Oleksandra; Shostakovich-Koretska, Lyudmila; Kruglova, Oksana; Gordienko, Lyudmila (2020): Colloidal Silicon Dioxide in Tablet form (Carbowhite) Efficacy in Patients with Acute Diarrhea: Results of Randomized, Double-Blind, Placebo-Controlled, Multi-Center Study. In Scientific Reports 10 (1), p. 6344. DOI: 10.1038/s41598-020-62386-0.

Toth, Bela E.; Takacs, Istvan; Szekeres, Laszlo; Szabo, Boglarka; Bakos, Bence; Lakatos, Peter (2017): Safety and Efficacy of Weekly 30,000 IU Vitamin D Supplementation as a Slower Loading Dose Administration Compared to a Daily Maintenance Schedule in Deficient Patients: A Randomized, Controlled Clinical Trial. In J Pharmacovigil 05 (04). DOI: 10.4172/2329-6887.1000233.

Traub, Michael L.; Finnell, John S.; Bhandiwad, Anup; Oberg, Erica; Suhaila, Lena; Bradley, Ryan (2014): Impact of vitamin D3 dietary supplement matrix on clinical response. In The Journal of clinical endocrinology and metabolism 99 (8), pp. 2720–2728. DOI: 10.1210/jc.2013-3162.

Trivedi, D. P.; Doll, R.; Khaw, K. T. (2003): Effect of four monthly oral vitamin D3 (cholecalciferol) supplementation on fractures and mortality in men and women living in the community: randomised double blind controlled trial. In BMJ 326 (7387).

van Groningen, Lenneke; Opdenoordt, Susanne; van Sorge, Adriaan; Telting, Darryl; Giesen, Astrid; Boer, Hans de (2010): Cholecalciferol loading dose guideline for vitamin D-deficient adults. In Eur. J. Endocrinol. 162 (4), pp. 805–811. DOI: 10.1530/EJE-09-0932.

van Orten-Luiten, Anne Claire B.; Janse, André; Dhonukshe-Rutten, Rosalie A. M.; Witkamp, Renger F. (2014): The association between drugs frequently used by the elderly and vitamin D blood levels: a review of observational and experimental studies. In Drugs Aging 31 (2), pp. 111–123. DOI: 10.1007/s40266-013-0137-1.

Vieth, Reinhold (2007): Vitamin D toxicity, policy, and science. In J. Bone Miner. Res. 22 Suppl 2, V64-8. DOI: 10.1359/jbmr.07s221.

VigiAccess (2021): Cholecalciferol safety data. Uppsala Monitoring Centre, WHO Collaborating Centre for International Drug Monitoring. Available online at http://www.vigiaccess.org/, updated on April 2021, checked on 4/22/2021.

Wacker, Matthias; Holick, Michael F. (2013): Vitamin D - effects on skeletal and extraskeletal health and the need for supplementation. In Nutrients 5 (1), pp. 111–148. DOI: 10.3390/nu5010111.

Wagner, Carol L.; Taylor, Sarah N.; Dawodu, Adekunle; Johnson, Donna D.; Hollis, Bruce W. (2012a): Vitamin D and its role during pregnancy in attaining optimal health of mother and fetus. In Nutrients 4 (3), pp. 208–230. DOI: 10.3390/nu4030208.

Wagner, Carol L.; Taylor, Sarah N.; Johnson, Donna D.; Hollis, Bruce W. (2012b): The role of vitamin D in pregnancy and lactation: emerging concepts. In Women's health (London, England) 8 (3), pp. 323–340. DOI: 10.2217/whe.12.17.

Wagner, Dennis; Sidhom, Gloria; Whiting, Susan J.; Rousseau, Dérick; Vieth, Reinhold (2008): The bioavailability of vitamin D from fortified cheeses and supplements is equivalent in adults. In The Journal of nutrition 138 (7), pp. 1365–1371. DOI: 10.1093/jn/138.7.1365.

Watts, Nelson B.; Bilezikian, John P.; Camacho, Pauline M.; Greenspan, Susan L.; Harris, Steven T.; Hodgson, Stephen F. et al. (2010): American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the diagnosis and treatment of postmenopausal osteoporosis. In Endocr. Pract. 16 Suppl 3, pp. 1–37. DOI: 10.4158/ep.16.s3.1.

Wei, Zhenzhen; Zhang, Jun; Yu, Xiaodan (2016): Maternal vitamin D status and childhood asthma, wheeze, and eczema: A systematic review and meta-analysis. In Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology 27 (6), pp. 612–619. DOI: 10.1111/pai.12593.

Willis, M. R.; Savory, J. (1984): Vitamin D metabolism and chronic liver disease. In Annals of clinical and laboratory science 14 (3), pp. 189–197.

Wortsman, J.; Matsuoka, L. Y.; Chen, T. C.; Lu, Z.; Holick, M. F. (2000): Decreased bioavailability of vitamin D in obesity. In Am. J. Clin. Nutr. 72 (3), pp. 690–693. DOI: 10.1093/ajcn/72.3.690.

Wu, L.; Sun, D. (2017): Effects of calcium plus vitamin D supplementation on blood pressure: a systematic review and meta-analysis of randomized controlled trials. In Journal of human hypertension 31 (9), pp. 547–554. DOI: 10.1038/jhh.2017.12.

Yildiz, Huseyin; Behiye, Deniz, Kosovali; Mustafa, Volkan, Demir (2018): Hypercalcemia and Hypertensive Pulmonary Edema associated with Vitamin D Toxicity: A case report. In Kuwait Medical Journal 2018 (50 (4)), pp. 467–469.

Zhang, Chenggui; Song, Chunli (2020): Combination Therapy of PTH and Antiresorptive Drugs on Osteoporosis: A Review of Treatment Alternatives. In Frontiers in pharmacology 11, p. 607017. DOI: 10.3389/fphar.2020.607017.

Zheng, Zhenfeng; Shi, Huilan; Jia, Junya; Li, Dong; Lin, Shan (2013): Vitamin D supplementation and mortality risk in chronic kidney disease: a meta-analysis of 20 observational studies. In BMC nephrology 14, p. 199. DOI: 10.1186/1471-2369-14-199.

Zhou, Changcheng; Assem, Mahfoud; Tay, Jessica C.; Watkins, Paul B.; Blumberg, Bruce; Schuetz, Erin G.; Thummel, Kenneth E. (2006): Steroid and xenobiotic receptor and vitamin D receptor crosstalk mediates CYP24 expression and drug-induced osteomalacia. In The Journal of clinical investigation 116 (6), pp. 1703–1712. DOI: 10.1172/JCI27793.

Žmitek, Katja; Hribar, Maša; Hristov, Hristo; Pravst, Igor (2020): Efficiency of Vitamin D Supplementation in Healthy Adults is Associated with Body Mass Index and Baseline Serum 25-Hydroxyvitamin D Level. In Nutrients 12 (5). DOI: 10.3390/nu12051268.