Medicines & Healthcare products
Regulatory Agency

# Public Assessment Report

# National Procedure

# Colecalciferol 3,200 IU Soft Capsules
# Colecalciferol 20,000 IU Soft Capsules

## colecalciferol

## PL 40861/0014-0015

## Internis Pharmaceuticals Ltd. (trading as 'STADA')

# LAY SUMMARY

## Colecalciferol 3,200 & 20,000 IU Soft Capsules
## colecalciferol

This is a summary of the Public Assessment Report (PAR) for Colecalciferol 3,200 & 20,000 IU Soft Capsules. It explains how these products were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use these products.

These products will be referred to as Colecalciferol Capsules in this lay summary for ease of reading.

For practical information about using Colecalciferol Capsules, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

**What are Colecalciferol Capsules and what are they used for?**
These applications are the same as Fultium-D3 3200 IU and Fultium-D3 20000 IU Capsules (PL 40861/0003-0004) which are already authorised.

The Company responsible for Fultium-D3 3200 IU and Fultium-D3 20000 IU Capsules has agreed that its scientific data can be used as the basis for the grant of an identical licences for Colecalciferol Capsules.

Colecalciferol Capsules are used to treat or prevent vitamin D deficiency. Deficiency of vitamin D may occur when a patient's diet or lifestyle does not provide them enough vitamin D or when the body requires more vitamin D (for instance when a patient are pregnant).

Colecalciferol 20,000 IU Soft Capsules may also be prescribed for certain bone conditions, such as thinning of the bone (osteoporosis) when it will be given to a patient with other medicines.

**How do Colecalciferol Capsules work?**
Colecalciferol are soft capsules. They contain the active ingredient Vitamin D3 (3,200 IU colecalciferol is equivalent to 80 micrograms Vitamin D3 and 20,000 IU colecalciferol is equivalent to 500 micrograms Vitamin D3).

Vitamin D is found in the diet and is also produced in the skin after exposure to the sun. Often vitamin D is given in combination with calcium. Colecalciferol is recommended for use when a patient has a normal intake of dietary calcium.

**How are Colecalciferol Capsules used?**
The pharmaceutical form of these medicines is a soft capsule and the route of administration is oral (by mouth).

**<u>Colecalciferol 3,200 IU soft capsules</u>**
**Dose**
<u>In severe vitamin D deficiency (for adults and the elderly)</u>
The patient's doctor will usually prescribe them a dose of 1 capsule daily for up to 12 weeks. The amount will depend on how low the patient's vitamin D levels are and how they respond to treatment.

Use in pregnancy and breast feeding
To treat vitamin D deficiency the patient's doctor will usually prescribe 1 capsule daily for up to 12 weeks.

The capsules should be swallowed whole (not chewed) with water.

Colecalciferol 3,200 IU soft capsules should not be used in children under the age of 12.

**Colecalciferol 20,000IU soft capsules**
**Dose**
Use in children and adolescents
The recommended dose for:

- Prevention of vitamin D deficiency 12-18 years is 20,000 IU (1 capsule) every 6 weeks.
- Treatment of vitamin D deficiency 12-18 years is 20,000 IU (1 capsule) every 2 weeks for 6 weeks.

Colecalciferol 20,000IU soft capsules are not suitable for children under 12 years.

Use in pregnancy and breast-feeding
Colecalciferol 20,000 IU soft capsules are not recommended.

Use in adults
The recommended dose for:

- prevention of vitamin D deficiency is 20,000 IU/month (1 capsule), higher doses may be required in certain situations.
- Treatment of vitamin D deficiency is 40,000 IU/week (2 capsules) for 7 weeks, followed by maintenance therapy, (equivalent to 1,400-2,000 IU/day, such as 2-3 capsules per month), based on the advice of the patient's doctor.

The capsule should be swallowed whole with water, preferably with the main meal of the day.

For further information on how Colecalciferol Capsules are used, refer to the PILs and Summaries of Product Characteristics (SmPCs) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

These medicines can only be obtained with a prescription.

The patient should always take the medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

**What benefits of Colecalciferol Capsules have been shown in studies?**
Colecalciferol Capsules are considered identical to the previously authorised products with the same benefits and risks. No new studies have been provided for Colecalciferol Capsules, however, reference is made to the studies for Fultium-D3 3200 IU and Fultium-D3 20000 IU Capsules.

**What are the possible side effects of Colecalciferol Capsules?**
For the full list of all side effects reported with these medicines, see Section 4 of the PIL or the SmPCs available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Colecalciferol Capsules are considered to be identical to the previously authorised products with the same benefits and risks.

**Why were Colecalciferol Capsules approved?**
The MHRA decided that the benefits of Colecalciferol Capsules are greater than the risks and recommended that these medicines are approved for use.

**What measures are being taken to ensure the safe and effective use of Colecalciferol Capsules?**
As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Colecalciferol Capsules The RMP details the important risks of Colecalciferol Capsules, how these risks can be minimised, any uncertainties about Colecalciferol Capsules (missing information), and how more information will be obtained about the important risks and uncertainties.

There are no safety concerns associated with use of Colecalciferol Capsules.

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Colecalciferol Capsules are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

**Other information about Colecalciferol Capsules**
Marketing Authorisations were granted in the UK on 19 February 2024.

The full PAR for Colecalciferol Capsules follows this summary.

This summary was last updated in April 2024.

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## I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the applications for Colecalciferol 3,200 & 20,000 IU Soft Capsules (PL 40861/0014-0015) could be approved.

The products are approved for the following indications:

Colecalciferol 3,200 IU Soft Capsules

- The treatment of vitamin D deficiency.

Colecalciferol 20,000 IU Soft Capsules

- The treatment and prevention of vitamin D deficiency.
- As an adjunct to specific therapy for osteoporosis in patients with vitamin D deficiency.

Colecalciferol is indicated for use in adolescents, adults and the elderly.

In its biologically active form vitamin D3 stimulates intestinal calcium absorption, incorporation of calcium into the osteoid, and release of calcium from bone tissue. In the small intestine it promotes rapid and delayed calcium uptake. The passive and active transport of phosphate is also stimulated. In the kidney, it inhibits the excretion of calcium and phosphate by promoting tubular resorption. The production of parathyroid hormone (PTH) in the parathyroids is inhibited directly by the biologically active form of vitamin D3. PTH secretion is inhibited additionally by the increased calcium uptake in the small intestine under the influence of biologically active vitamin D3.

These are national abridged applications approved under Regulation 56 of The Human Medicines Regulation 2012, as amended (previously Article 10c of Directive 2001/83/EC, as amended) as informed consent applications. The applications cross-refer to the reference products Fultium-D3 3200 IU and Fultium-D3 20000 IU Capsules (PL 40861/0003-0004).

No new non-clinical or clinical data have been supplied and none are required for these informed consent applications.

Suitable justification has been provided for non-submission of an Environmental Risk Assessment (ERA). As the applications are for identical versions of already authorised products, no increase in environmental exposure is anticipated and no ERA is required.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for these products at all sites responsible for the manufacture, assembly and batch release of these products.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

National marketing authorisations were granted in the UK on 19 February 2024.

## II. EXPERT REPORT

The applicant cross-refers to the data for Fultium-D3 3200 IU and Fultium-D3 20000 IU Capsules, Internis Pharmaceuticals Limited), to which these applications are claimed to be identical. This is acceptable.

## III. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION

**Summaries of Product Characteristics (SmPCs)**

The SmPCs are in line with those for Fultium-D3 3200 IU, dated 01/2018 and Fultium-D3 20000 IU Capsules, dated 05/2019.

**PATIENT INFORMATION LEAFLET**

A leaflet text and mock-up has been provided which has been aligned with that for Fultium-D3 3200 IU and Fultium-D3 20000 IU Capsules), dated for 01/2023.

**LABEL**

Label text and mock-ups have been provided.

## IV. QUALITY ASPECTS

### IV.1 Drug Substance

**Drug substance specification**

The source of the active substance is in line with the cross-reference products. The proposed drug substance specification is consistent with the details registered for the cross-reference products.

### IV.2. Drug Product

**Name**

The product has been named in line with current requirements.

**Strength, pharmaceutical form, route of administration, container and pack sizes**

Colecalciferol 3,200 IU Soft Capsules are available in PVC/PVdC blisters with aluminium foil in pack sizes of 7, 10, 14, 20, 28, 30, 56, 60, 84, 90 capsules.

Colecalciferol 3,200 IU Soft Capsules are available in PVC/PVdC blisters with aluminium foil in pack sizes of 7, 10, 14, 15, 20, 28, 30 capsules.

The appearance of the products is identical to that of the cross-reference products.

The proposed shelf life of the product is 24 months with the recommended storage condition store below 25°C, protect from light and store in the original package.

The proposed packaging, shelf life and storage conditions are consistent with the details registered for the reference product.

**Legal status**

Prescription only medicine (POM).

**Manufacturers**

The proposed manufacturing sites are consistent with the details registered for the cross-reference products and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

**Qualitative and quantitative compositions**
The composition of the proposed products are consistent with the details registered for the cross-reference products.

**Manufacturing process & control of critical steps**
The proposed manufacturing processes and process controls are consistent with the details registered for the reference products and the maximum batch size is stated.

**Finished product release/shelf life specifications**
The finished product specifications at release and shelf-life are in line with the details registered for the cross-reference products.

**TSE Compliance**
With the exception of gelatin, no excipients of animal or human origin are used in the final products.

Copies of the current TSE certificates for suppliers of gelatin capsules have been provided and are current in accordance with EDQM database.

These products do not contain or consist of genetically modified organisms (GMO).

## V. NON-CLINICAL ASPECTS

As these applications are submitted under Regulation 56 of The Human Medicines Regulation 2012, as amended, (as informed consent applications) no new non-clinical data have been supplied and none are required.

## VI. CLINICAL ASPECTS

As these applications are submitted under Regulation 56 of The Human Medicines Regulation 2012, as amended, (as informed consent applications) no new clinical data have been supplied and none are required.

## VII. RISK MANAGEMENT PLAN (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

## VIII. USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) was provided with the application in accordance with legal requirements, including user consultation.

## IX. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant's products are identical to the cross-reference products. The benefit/risk balance is, therefore, considered to be the same as for the cross-reference products and positive.

The Summaries of Product Characteristics (SmPCs), Patient Information Leaflets (PILs) and labelling are satisfactory, in line with current guidelines and consistent with the cross-reference products.

In accordance with legal requirements, the current approved UK versions of the SmPCs and PILs for these products are available on the MHRA website.

# TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

| **Application type** | **Scope** | **Product information affected** | **Date of grant** | **Outcome** | **Assessment report attached Y/N** |
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