Fultium-D_3 3,200 IU Capsules

PL 17871/0208

UKPAR

TABLE OF CONTENTS

LAY SUMMARY
Fultium-D_3 3,200 IU Capsules
(colecalciferol)

This is a summary of the Public Assessment Report (PAR) for Fultium-D_3 3,200 IU Capsules (PL 17871/0208). It explains how Fultium-D_3 3,200 IU Capsules 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 Fultium-D_3 3,200 IU Capsules.

For practical information about using Fultium-D_3 3,200 IU Capsules, patients should read the package leaflet or contact their doctor or pharmacist.

What are Fultium-D_3 3,200 IU Capsules and what are they used for?
Fultium-D_3 3,200 IU Capsules contain the active substance colecalciferol (equivalent to vitamin D3). Fultium-D_3 3,200 IU Capsules are used to treat vitamin D deficiency.

How are Fultium-D_3 3,200 IU Capsules used?
Fultium-D_3 3,200 IU Capsules are taken by mouth. A single capsule should be swallowed whole (not chewed) with water. The recommended dose for adults and the elderly is 1 capsule (3,200 IU) daily for up to 12 weeks dependent upon the severity of the disease and the patient's response to treatment.

Fultium-D_3 3,200 IU Capsules should not be used in children under 12 years.

Fultium-D_3 3,200 IU Capsules can only be obtained on prescription from a doctor.

For further information on how Fultium-D_3 3,200 IU Capsules are used, please refer to the Summary of Product Characteristics and the Patient Information Leaflet available on the MHRA website.

How do Fultium-D_3 3,200 IU Capsules work?
Fultium-D3 3,200 IU Capsules are vitamin products containing colecalciferol (equivalent to vitamin D3). Vitamin D3 acts to maintain normal concentrations of calcium and phosphate in plasma by facilitating their absorption from the small intestine, enhancing their mobilisation from bone and decreasing their excretion by the kidney.

How have Fultium-D_3 3,200 IU Capsules been studied?
As colecalciferol is a well-known substance and has a well-established use, the applicant (Jenson Pharmaceutical Services Ltd) presented data from the scientific literature. The literature provided confirmed the efficacy and safety of colecalciferol for the treatment of vitamin D deficiency.

What are the Benefits and risks of Fultium-D_3 3,200 IU Capsules?
Colecalciferol is a well-known active ingredient. Colecalciferol-containing products have been available in the European Union for many years and have an established favourable benefit-risk profile.

For information about side effects that may occur with taking Fultium-D_3 3,200 IU Capsules, please refer to the package leaflet or the Summary of Product Characteristics available on the MHRA website.

Why are Fultium-D_3 3,200 IU Capsules approved?
The use of Fultium-D_3 3,200 IU Capsules for the approved indications is well-established. Literature data have been submitted to support this application. No new or unexpected safety concerns arose from this application. It was, therefore, considered that the benefits of Fultium-D_3 3,200 IU Capsules outweigh the risks and the grant of a Marketing Authorisation was recommended.

What measures are being taken to ensure the safe and effective use of Fultium-D3 3,200 IU Capsules?

A Risk Management Plan has been developed to ensure that Fultium-D_3 3,200 IU Capsules are used as safely as possible. Based on this plan, safety information has been included in the Summary of Product Characteristics and the package leaflet for Fultium-D_3 3,200 IU Capsules, including the appropriate precautions to be followed by healthcare professionals and patients.

Other information about Fultium-D_3 3,200 IU Capsules

A Marketing Authorisation was granted in the UK on 17th April 2014.

The full PAR for Fultium-D_3 3,200 IU Capsules follows this summary.

For more information about treatment with Fultium-D_3 3,200 IU Capsules, read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in June 2014.

Fultium-D_3 3,200 IU Capsules

PL 17871/0208

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) granted Jenson Pharmaceutical Services Ltd a Marketing Authorisation for the medicinal product Fultium-D_3 3,200 IU Capsules (PL 17871/0208) on 17th April 2014. The product is a prescription-only medicine (POM) indicated for the treatment of vitamin D deficiency.

This is a line extension application submitted under Article 10a, well-established use, of Directive 2001/83/EC, as amended, and concerns a new strength of the currently licensed product, Fultium-D_3 800 IU Capsules (PL 17871/0151).

In its biologically active form vitamin D_3 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 D_3. PTH secretion is inhibited additionally by the increased calcium uptake in the small intestine under the influence of biologically active vitamin D_3.

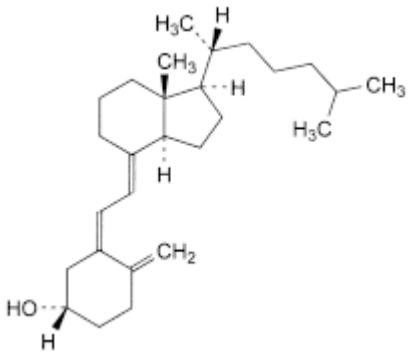
No new non-clinical or clinical studies were necessary for this application, which is acceptable given that this is a bibliographic application for a product containing an active of well-established use. Bioequivalence studies are not necessary to support this application.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product type at all sites responsible for the manufacturing and assembly of this product. Evidence of compliance with GMP has been provided for the named manufacturing and assembly sites.

PHARMACEUTICAL ASSESSMENT

ACTIVE SUBSTANCE

INN: Colecalciferol
Chemical name: (5*Z*,7*E*)-9,10-Secocholesta-5,7,10(19)-trien-3β-ol
Structure:



Molecular formula: $C_{27}H_{44}O$
Molecular weight: 384.6 g/mol
Appearance: White or almost white crystalline powder
Solubility Practically insoluble in water, freely soluble in ethanol (96 per cent) and soluble in trimethylpentane and in fatty oils.

Colecalciferol is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance colecalciferol are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

DRUG PRODUCT

Other Ingredients

Other ingredients consist of the pharmaceutical excipients arachis Oil (peanut oil), butylated hydroxytoluene (BHT) (E321) making up the capsule content. The capsule shell is composed of glycerol (E422), chlorophyllin copper complex sodium (E141), gelatin (E441) and purified water. Appropriate justification for the inclusion of each excipient has been provided.

All excipients comply with their respective European Pharmacopoeia monographs with the exception of chlorophyllin copper complex sodium (E14) which complies with the United States Pharmacopeia.

The only excipient used that contains material of animal or human origin is gelatin. Satisfactory documentation has been provided by the gelatin suppliers stating that the gelatin they provide complies with the criteria described in the current version of the monograph 'Products with risk of transmitting agents of animal spongiform encephalopathies'. Confirmation has also been given that the glycerol used in the capsules is of vegetable origin.

Satisfactory Certificates of Analysis have been provided for all excipients showing compliance with the proposed specifications.

Pharmaceutical Development

The objective of the development programme was to formulate a safe, efficacious, stable line extension presentation containing 3,200 IU of colecalciferol.

Suitable pharmaceutical development data have been provided for this application.

Manufacturing Process
A satisfactory batch formula has been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results. Process validation data on commercial batches have been provided. The results are satisfactory.

Control of Finished Product
The finished product specification is satisfactory. The test methods have been described and have been adequately validated, as appropriate. Batch data have been provided that comply with the release specification. Certificates of Analysis have been provided for any working standards used.

Container Closure System
The product is packed in an opaque, white polyvinylchloride (PVC), polyvinylidenechloride (PVDC) blister tray with aluminium foil. The pack sizes are 7, 10, 14, 20, 28, 30, 56, 60, 84 and 90 capsules. Not all pack sizes may be marketed.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current European regulations concerning materials in contact with food.

Stability
Finished product stability studies were performed in accordance with current guidelines on batches of finished product packed in the packaging proposed for marketing.

Based on the results, a shelf-life of 12 months with storage conditions “Do not store above 30°C” and “Store blister foil in original container in order to protect from light” have been set. These are satisfactory.

Suitable post approval stability commitments have been provided to continue stability studies on batches of the finished product.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labelling
The SmPC, PIL and labelling are satisfactory from a pharmaceutical perspective.

User testing of the package leaflet has been accepted, based on a bridging report provided by the applicant making reference to the user-testing of the PIL for Fultium-D_3 800 IU Capsules (PL 17871/0151). The products are from the same therapeutic class and have similar indications. A critical analysis demonstrated that the key messages for safe and effective use for both leaflets were similar. The justification on the rationale for bridging is accepted.

Marketing Authorisation Application (MAA) Form
The MAA form is satisfactory from a pharmaceutical perspective.

Expert Report (Quality Overall Summary)
The quality overall summary is written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

Conclusion
The grant of a Marketing Authorisation is recommended.

NON-CLINICAL ASSESSMENT

As the pharmacodynamic, pharmacokinetic and toxicological properties of colecalciferol are well-known, no further non-clinical studies are required and none have been provided.

The applicant's non-clinical overview has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the relevant non-clinical pharmacology, pharmacokinetics and toxicology.

The Marketing Authorisation holder has provided adequate justification for not submitting an Environmental Risk Assessment (ERA). This is acceptable as vitamins are unlikely to result in significant risk to the environment.

There are no objections to the approval of this product from a non-clinical point of view.

CLINICAL ASSESSMENT

CLINICAL PHARMACOLOGY

No new clinical pharmacology data have been submitted and none are required for applications of this type. The clinical pharmacology of colecalciferol is well-known.

EFFICACY

No new efficacy data have been submitted and none are required for applications of this type. The clinical efficacy of colecalciferol is well-established. Efficacy is adequately reviewed in the clinical overview.

SAFETY

No new safety data were supplied or required for this bibliographic application. Safety is adequately reviewed in the clinical overview. The safety profile of colecalciferol is well-known.

CLINICAL EXPERT REPORT (CLINICAL OVERVIEW)

The clinical overview is written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

PHARMACOVIGILANCE SYSTEM AND RISK MANAGEMENT PLAN

The Pharmacovigilance System, as described by the applicant, fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance, and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

A satisfactory Risk Management Plan has been provided.

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC), PATIENT INFORMATION LEAFLET (PIL) AND LABELLING

The SmPC, PIL and labelling are acceptable from a clinical perspective. The PIL is consistent with the details in the SmPC and in line with the current guidance. The labelling is in line with the current guidance.

MAA FORM

This is satisfactory.

CONCLUSION

The grant of a Marketing Authorisation is recommended.

OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY

The important quality characteristics of Fultium-D_3 3,200 IU Capsules are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

NON-CLINICAL

No new non-clinical data were submitted. As the pharmacokinetics, pharmacodynamics and toxicology of colecalciferol are well-known, no additional data were required.

CLINICAL

No new clinical data were submitted and none were required for applications of this type.

The published literature supports the efficacy of this product in the proposed indications. The efficacy of colecalciferol is well-known. The presented evidence for well-established use of the active substance is sufficient.

The safety profile of colecalciferol is well-known. The literature review identified no new or unexpected safety issues or concerns.

PRODUCT LITERATURE

The SmPC, PIL and labelling are satisfactory and in line with current guidance.

BENEFIT/RISK ASSESSMENT

The quality of the product is acceptable, and no new non-clinical or clinical concerns have been identified. Extensive clinical experience with colecalciferol is considered to have demonstrated the therapeutic value of the compound. The benefit:risk is, therefore, considered to be positive.

Fultium-D_3 3,200 IU Capsules

PL 17871/0208

STEPS TAKEN FOR ASSESSMENT

1 The MHRA received the Marketing Authorisation application on 19th July 2013.

2 Following standard checks and communication with the applicant the MHRA considered the application valid on 21st October 2013.

3 Following assessment of the application the MHRA requested further information on 10th December 2013, 23rd December 2013, 18th February 2014, 3rd March 2014 and 5th March 2014.

4 The applicant responded to the MHRA's requests, providing further information on 3rd January 2014, 26th February 2014, 11th March 2014 and 19th March 2014.

5 The application was determined on 17th April 2014.

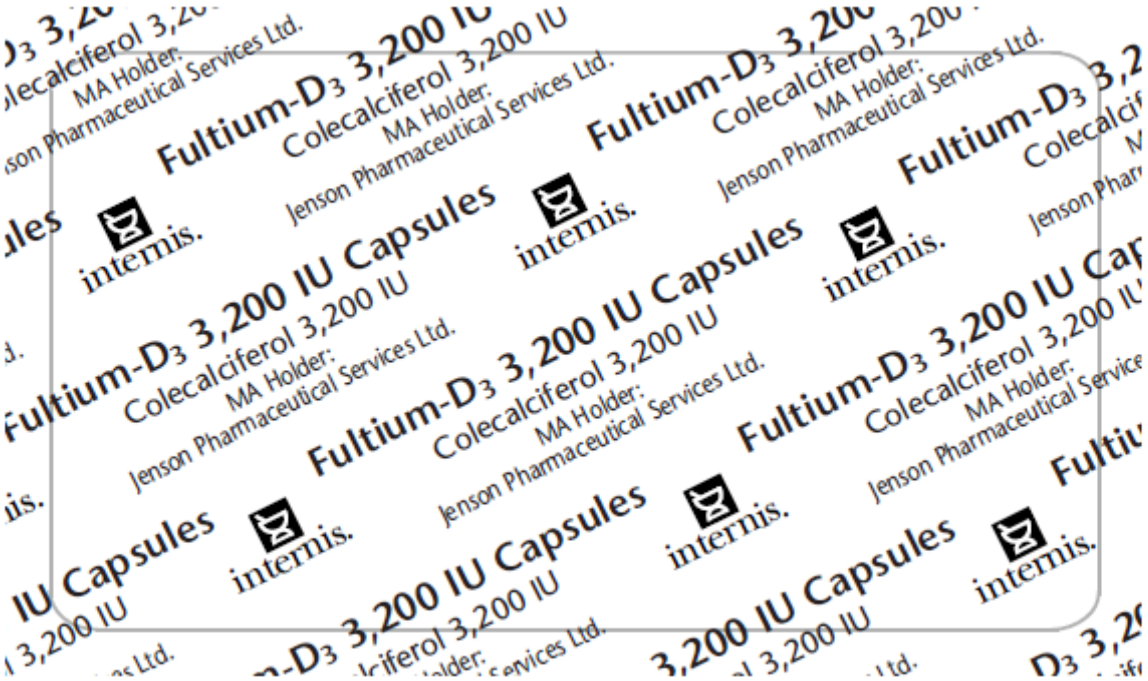
SUMMARY OF PRODUCT CHARACTERISTICS

In accordance with Directive 2010/84/EU, the Summaries of Product Characteristics (SmPCs) for products granted Marketing Authorisations at a national level are available on the MHRA website.

PATIENT INFORMATION LEAFLET

In accordance with Directive 2010/84/EU, the Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.

LABELLING


Fultium-D3 3,200 IU Capsules
Colecalciferol 3,200 IU
MA Holder:
Jenson Pharmaceutical Services Ltd.
intermis.


Unvarnished area
Space for dispersing label
B/N:
EXP:
Unvarnished area
Fultium®-D3 3,200 IU Capsules
Colecalciferol 3,200IU (equivalent to 80 micrograms Vitamin D3)
MA Holder: Jenson Pharmaceutical Services Ltd, Caradoc House, 237 Regents Park Road, London N3 3LF, UK. Distributed by: Interpharma Ltd, 237 Regents Park Road, London, N3 3LF, UK.
PL 17871/0208 POM
5 060222 940268
Fultium®-D3 3,200 IU Capsules
Colecalciferol 3,200IU (equivalent to 80 micrograms Vitamin D3)
Fultium®-D3 3,200 IU Capsules
Colecalciferol 3,200IU (equivalent to 80 micrograms Vitamin D3)
internis.
30 capsules
Active Substance: Colecalciferol 3,200IU (equivalent to 80 micrograms Vitamin D3). Excipients: Arachis Oil (peanut oil), Gelatin, Glycerol, E141, E321. Dosage: For Oral Use. Swallow whole, do not chew. Read the package information leaflet before use. Use as directed by your doctor. Do not store above 30°C. Store blister foil in original container in order to protect from light. Not recommended for children. DO NOT EXCEED THE STATED DAILY DOSE. Keep out of the reach and sight of children. Warning: Contains Arachis Oil (peanut oil). If you are allergic to peanut or soya, do not use this medicinal product.