VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Vitamin D (cholecalciferol) is necessary for the maintenance of healthy bones.

Vitamin D is made in the skin when the skin is exposed to sunlight and then converted to an active hormone in the kidney. However, some people may be unable to make enough cholecalciferol to cover the body's needs:

- People who do not live on the equator or in the tropics. There is not always enough sunlight outside these regions to create sufficient vitamin D.
- Elderly people. The skin gets thinner with age, which reduces the ability to make vitamin D.
- People who have darker skin. Darker skin pigments reduce the amount of sunlight reaching the right layer of the skin.
- Clothing and sunscreen also reduce the amount of sunlight reaching the right layer of the skin.
- Periods of growth, during childhood and adolescence, pregnancy and breastfeeding also affect vitamin D levels in the body.
- Poor diet also reduces the amount of vitamin D available to the body.

VI.2.2 Summary of treatment benefits

Vitamin D (cholecalciferol) is necessary for the maintenance of healthy bones.

Rickets and osteomalacia are the classical Vitamin D deficiency diseases. In children, Vitamin D deficiency can cause rickets, a disease which is characterized by a failure of bone tissue to properly mineralize, resulting in skeletal deformities and soft bones. In adults, osteomalcia causes bone pain and muscle weakness, but such symptoms can be subtle and can go undetected in the initial stages.

Although rickets and osteomalacia are extreme examples of the effects of Vitamin D deficiency, osteoporosis is an example of a long-term effect of Calcium and Vitamin D insufficiency. Osteoporosis is a disease characterized by fragile bones, which significantly increases the risk of bone fractures. Osteoporosis is most often associated with inadequate Calcium intakes (generally <1,000-1,200 mg/day), but insufficient Vitamin D contributes to osteoporosis by reducing Calcium absorption.

The Oral solution product is a medicinal preparation aimed at initial treatment of symptomatic vitamin D deficiency in adults.

Many of the cholecalciferol products prescribed in Europe are supplied using unlicensed, food supplement products which are not supported by the degree of control (licensing, good practices, pharmacovigilance, quality control etc) applicable to a product supported by a Marketing Authorisation. The product themselves, and their proposed use, offers good control of doses for patients requiring treatment of vitamin D deficiency as well as supplementation. The review of potential undesirable effects shows no risk of hypercalcaemia or renal stones. The review also shows applicability of the product for use in infants, children, adolescent, adult and pregnant / lactating patient groups. As such, there is an appropriate positive benefit: risk associated with the grant of these applications.

VI.2.3 Unknowns relating to treatment benefits

Vitamin D has been extensively studied in the scientific literature. Therefore, no unknowns relating to the treatment benefits for vitamin D deficiency are anticipated.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
If you have kidney disease, taking cholecalciferol may damage your kidneys	Vitamin D is converted to an active hormone in the kidney. If your kidneys do not work properly, the conversion is affected and your kidneys might be damaged.	If your kidney disease is severe, you should not take this medicine. Your doctor will prescribe a different type of vitamin D which doesn't require conversion in the kidney. If your kidney disease is mild, you can take this medicine. Your doctor will monitor you to make sure your kidneys remain healthy.
Certain heart medicines won't work properly if you take them with cholecalciferol	Digitalis and other heart medicines known as cardiac glycosides can interact with cholecalciferol. This can cause your heart to beat too fast or too slowly	If you are taking cardiac glycosides at the same time as this medicine, your doctor must monitor you very carefully to ensure your heart beats properly.
Certain medicines used to treat epilepsy (Phenytoin), or medicines which make you sleep (barbiturates) can make cholecalciferol less effective	The metabolic effects of Phenytoin and barbiturates decrease the effect of cholecalciferol	Your doctor will need to monitor you to make sure you are getting enough cholecalciferol.
Actinomycin (a medicine used to treat some forms of cancer) can make cholecalciferol less effective	This medicine interferes with the metabolism of cholecalciferol in the kidneys	Your doctor will need to monitor you to make sure you are getting enough cholecalciferol.
You may acquire a hypersensitive reaction when you take this medicine.	Some ingredients used may cause hypersensitive in some people.	If you are allergic to any of the ingredient listed, you should not take this medicine. Your doctor will prescribe a different vitamin D product,
If you are taking thiazide diuretics and cholecalciferol, you may damage your kidneys.	Vitamin D helps your body absorb calcium. Some thiazide diuretics increase the amount of calcium in the body. Taking large amounts of vitamin D along with thiazide diuretic might cause to be too much calcium in the body. This may cause serious side effects including kidney problems	You should not this medicine.
If you have hypervitaminosis D,	Hypervitaminosis D (Vitamin D	You should not take this

Risk	What is known	Preventability
taking cholecalciferol may cause further vitamin D intoxication.	intoxication) is condition that occurs in those who either self-prescribe mega doses of vitamin D or consume excess dairy products.	medicine if you have hypervitaminosis D.
If you have hypercalcaemia, taking cholecalciferol may damage your kidneys.	Excessively high levels of calcium in the blood known as hypercalcemia can cause renal insufficiency, vascular and soft tissue calcification, hypercalciuria (high levels of calcium in the urine) and kidney stones	You should not this medicine. Your doctor must make sure your kidney is functioning properly before prescribing this medicine and your doctor should continue to monitor you.
If you have hypercalciuria, taking cholecalciferol may damage your kidneys.	Chronic hypercalciuria may lead to impairment of renal function, nephrocalcinosis, and renal insufficiency.	You should not take this medicine. Your doctor must monitor your kidney function before you take this medication and during your treatment.
If you have conditions that modify vitamin D metabolism, taking medicine may affect the level of vitamin D in your body.	Conditions that modify vitamin D metabolism including sarcoidosis may affect the level of vitamin D produced and/or processed by your body	Your doctor should monitor you and prescribe accordingly.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Use in pregnancy and lactation	There are no or limited amount of data from the use of cholecalciferol in pregnant women. Cholecalciferol has been shown to be teratogenic in high doses in animals (4-15 times the human dose). Offspring from pregnant rabbits treated with high doses of vitamin D had lesions anatomically similar to those of supravalvular aortic stenosis and offspring not showing such changes show vasculotoxicity similar to that of adults following acute vitamin D toxicity.
Potential for medication errors	There is clear differentiation between the capsules, dropper and oral solution formulations The oral solution and is a completely different pharmaceutical form and as such misidentification is much lower.
Overdose	Cholecalciferol affects the metabolism of calcium. Too much cholecalciferol can lead to calcium deposits in the soft tissues of the body and result in serious side effects

Missing Information

Not applicable

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

The Summaries of Product Characteristics and the Package leaflets for the Atrium-D_3 product range can be found in Appendix 2.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

There are no planned post-authorisation clinical studies, or studies which are a condition of the marketing authorisation.

VI.2.7 Summary of changes to the Risk Management Plan over time

This is the first Risk Management Plan for Atrium D_3 25,000 IU Oral Solution and therefore, there are no changes to describe at present.