Detremin 20,000 I.U./ml oral drops, solution

2016-08-01, version 7

VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Detremin contains cholecalciferol (vitamin D_3). It is used to treat vitamin D deficiency or insufficiency, for example in the following conditions:

- rickets in infants and children
- bone fragility, together with calcium and possibly also other treatment
- secondary hyperparathyroidism (when low blood calcium levels lead to excessive secretion of parathyroid hormone, combined with enlargement of the parathyroid gland).

Detremin is also used as prophylaxis and treatment of vitamin D deficiency in persons with difficulties to absorb vitamin D and in persons with increased risk of fractures, e.g. elderly patients and patients treated with glucocorticoids.

VI.2.2 Summary of treatment benefits

Vitamin D is an endogenous substance, synthesised in the skin when exposed to UV light, it can also be supplied via food or as a drug. Poor intake of vitamin D, together with lack of sunlight exposure, disorders that decrease the absorption of vitamin D or the conversion of vitamin D into its active forms, can cause vitamin D deficiency.

Vitamin D deficiency results in a decrease in the efficiency of intestinal calcium uptake, which may lead to osteopenia, osteoporosis and increased risk of fracture. Vitamin D deficiency and secondary hyperparathyroidism may also result in a mineralization defect of the skeleton, that can cause bone softening diseases like rickets in children and osteomalacia in adults.

Cholecalciferol (vitamin D_3) is a well-known substance that has been on the market for decades.

Use of cholecalciferol to prevent and treat vitamin D deficiency, in order to maintain or reach physiological serum levels of its active form and avoid the consequences of vitamin D deficiency is supported by the published data.

VI.2.3 Unknowns relating to treatment benefits

None.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Overdose	Vitamin D is fat soluble and may accumulate in the body. This may cause toxic effects in case of overdose and long	Follow the recommendations provided in the product information which states that

Risk	What is known	Preventability
	term treatment with excessive doses. Acute or chronic overdose of vitamin D can cause too high levels of calcium in the blood.	the recommended treatment should not be exceeded.
Too high levels of calcium in the blood and urine (hypercalcaemia, hypercalciuria)	Too high levels of calcium in the blood and urine have been seen after intake of products containing vitamin D_3. Acute or chronic overdose of vitamin D can cause too high levels of calcium in the blood.	Follow the recommendations provided in the product information which states you should not take Detremin if you have too high levels of calcium in the blood, and you should tell your doctor if you have had kidney problems. At high doses of vitamin D_3, the calcium levels in the blood may be monitored and particular caution is recommended in patients with a history of kidney stones.
Allergic (hypersensitivity) reactions	Allergic (hypersensitivity) reactions such as itching, rash or hives have been seen after intake of products containing vitamin D_3.	Follow the recommendations provided in the product information which states that you should not take Detremin if you are allergic (hypersensitive) to vitamin D_3 or any of the other ingredients of Detremin.

Missing information

Risk	What is known
Teratogenic risk at overdoses	Studies in animals have shown reproductive toxicity of high doses of vitamin D. At doses far higher than the human therapeutic range teratogenicity has been observed in animal studies. There are no indications that vitamin D at therapeutic doses is teratogenic in humans.
Use in patients with severe impaired renal function	Detremin should not be used in combination with calcium in patients with severe impaired renal function. Vitamin D_3 should be used with caution in patients with impaired renal function, and the effect on calcium and phosphate levels should be monitored. The risk of soft tissue calcification should be taken into account. In patients with severe renal insufficiency, vitamin D in the form of cholecalciferol is not metabolized normally and another form of vitamin D may therefore be needed.

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 Summary of Product Characteristics and the Package leaflet for Detremin can be found on the authorities web pages.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

None.

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

Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
1	01/07/2010		New RMP
2	18/10/2010	Interactions	Interaction "Drugs leading to fat malabsorption, e.g. orlistat and colestyramin, may impair the absorption of vitamin D." added.
3	25/01/2011	Interaction Overdose	Interaction "Isoniazid may reduce the effectiveness of vitamin D_3 due to inhibition of the metabolic activation of vitamin D." included Additional risk minimization activities for overdose added i.e. text regarding risk with overdose in SPC and description of package.
4	21/11/2013	NA	Change to new RMP template
5	13/05/2015	Teratogenic risk	Update of the important potential risks "Teratogenic risk" due to approved variation SE/H/966/01/II/06. General update due to upcoming renewal application.
6	18/02/2016	Overdose (upgraded from important potential risk) Hypercalcaemia and hypercalciuria Hypersensitivity reactions Teratogenic risk at overdoses Use in patients with severe renal impairment	Updates requested during renewal procedure SE/H/966/01/R/01. Upgrade of "overdose" from an important potential to an important identified risk since reports of overdoses have been reported in previous PSURs. "hypercalcaemia and hypercalciuria" and "hypersensitivity reactions" added as important identified risks,

			since these events are labelled in the SmPC for Detremin. Deletion of "teratogenic risk" as an important potential risk since Detremin can be used during pregnancy and instead inclusion of "teratogenic risk at overdoses" as missing information**.**
7	01/08/2016	NA	Updates to Section VI.2.2 'Summary of treatment benefits' in the 'Elements for a public summary' requested during renewal procedure SE/H/966/01/R/01.