Part VI: Summary of the risk management plan

Summary of risk management plan for Decurol hard capsules (25,000 IU, 12,500 IU and 5,600 IU) (Cholecalciferol)

This is a summary of the risk management plan (RMP) of Decurol hard capsules (25,000 IU, 12,500 IU and 5,600 IU). The RMP details important risks of Decurol hard capsules (25,000 IU, 12,500 IU and 5,600 IU) and how more information will be obtained about Decurol hard capsules (25,000 IU, 12,500 IU and 5,600 IU)'s risks and uncertainties (missing information).

Decurol hard capsules (25,000 IU, 12,500 IU and 5,600 IU)'s summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Decurol hard capsules (25,000 IU, 12,500 IU and 5,600 IU) should be used.

Important new concerns or changes to the current ones will be included in updates of Decurol's RMP.

I. The medicine and what it is used for

Decurol hard capsules (25,000 IU, 12,500 IU and 5,600 IU) is indicated for the initial treatment of symptomatic vitamin D deficiency in adults. It contains CHOLECALCIFEROL as active substance and is given by oral route.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Decurol hard capsules (25,000 IU, 12,500 IU and 5,600 IU), together with measures to minimise such risks and the proposed studies for learning more about Decurol hard capsules (25,000 IU, 12,500 IU and 5,600 IU)'s risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g., with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

II.A List of important risks and missing information

Important risks of Decurol hard capsules (25,000 IU, 12,500 IU and 5,600 IU) are risks that need

special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken.
Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Decurol hard capsules (25,000 IU, 12,500 IU and 5,600 IU). Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine);

List of important risks and missing information	
Important identified risks	• Hypercalcemia and associated disorders, especially in patients with recognized risk factors
Important potential risks	• Overdose in patients who concomitantly receive vitamin D from other sources
Missing information	• None

II.B Summary of important risks

Important identified risk 1: Hypercalcemia and associated disorders, especially in patients with recognized risk factors	
Evidence for linking the risk to the medicine	Patients with vitamin D intoxication usually present with hypercalcemia, normal or high serum phosphorus levels, normal or low alkaline phosphatase levels, high levels of 25(OH)D, low serum parathyroid hormone and high urine calcium/creatinine. Many scientific publications have described cases of hypercalcemia related to the use of cholecalciferol. Among others, Lodh M *et al*. and Koul PA *et al.* published about respectively 8 and 10 cases of hypercalcemia and hypervitaminosis D. In the latter case series, all patients received high doses of vitamin D and no other cause of hypercalcemia was identified. The signal "Hypercalcaemia (associated with CYP24A1 and triggered by Vitamin D supplementation)" was initially triggered by a publication on case reports on infantile hypercalcaemia caused by CYP24A1 mutations and intake of recommended doses of vitamin D. It should be noted that vitamin D intoxication remains extremely rare but can be caused by inadvertent or intentional ingestion of excessively high doses. Doses of more than 50,000 IU per day raise levels of 25-hydroxyvitamin D to more than 150 ng per millilitre (374 nmol per litre) and are associated with hypercalcemia and hyperphosphatemia.
Risk factors and risk groups	- Concomitant intake of calcium supplements - Concomitant intake of glycosides or diuretics - Overdose of vitamin D - Elderly - Children - Renal impaired patients

	- Sarcoidosis - Total body immobilization - Vitamin D hypersensitivity - Patients with idiopathic infantile hypercalcaemia (e.g. CYP24A1 or SLC34A1 mutation)
Risk minimization measures	Routine risk minimisation measures: - SmPC section 4.3 (& PIL Section 2) Contraindications - SmPC section 4.4 (& PIL Section 2, Section 3) Special warnings and precaution - SmPC section 4.5 (& PIL Section 2) Interaction with other medicinal products - SmPC section 4.6 (& PIL Section 2) Fertility, pregnancy and lactation - SmPC section 4.8 (& PIL Section 4) Undesirable effects - SmPC section 4.9 (& PIL Section 3) Overdose - SmPC section 5.2 Pharmacokinetic properties In SmPC section 4.4, advice is given on monitoring serum and urinary calcium. Legal status: Under medical prescription (in some countries).
Important potential risk 1: Overdose in patients who concomitantly receive vitamin D from other sources	
Evidence for linking the risk to the medicine	Vitamin D is a particularly important sterol hormone, with evidence emerging of its beneficial effects well beyond bone. In consequence of this and increased global recognition of vitamin D deficiency in the general population, there has been a resurgence in treatment with vitamin D preparations. These preparations include over-the-counter products (including multivitamin preparations) and fortified foods which can be taken without medical supervision and could potentially be concomitantly taken with Decurol hard capsules (25,000 IU, 12,500 IU and 5,600 IU).
Risk factors and risk groups	Patients taking vitamin D from other sources.
Risk minimization measures	Routine risk minimisation measures: - SmPC section 4.4 (& PIL Section 2/3) Special warnings and precaution - SmPC section 4.5 (& PIL Section 2) Interaction with other medicinal products - SmPC section 4.6 (& PIL Section 2) Fertility, pregnancy and lactation - SmPC section 4.8 (& PIL Section 4) Undesirable effects - SmPC section 4.9 (& PIL Section 3) Overdose - SmPC section 5.2 Pharmacokinetic properties Legal status: Under medical prescription (in some countries).

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Decurol hard capsules (25,000 IU, 12,500 IU and 5,600 IU).

II.C.2 Other studies in post-authorisation development plan

There are no studies required for Decurol hard capsules (25,000 IU, 12,500 IU and 5,600 IU).