

Part VI: Summary of the risk management plan

Summary of risk management plan for ALFACALCIDOLO DOC (alphacalcidol)

This is a summary of the Risk Management Plan (RMP) for ALFACALCIDOLO DOC. The RMP details important risks of alphacalcidol, how these risks can be minimised, and how more information will be obtained about alphacalcidol's risks and uncertainties (missing information).

ALFACALCIDOLO DOC 's Summary of Product Characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how alphacalcidol should be used.

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

I. The medicine and what it is used for

ALFACALCIDOLO DOC is authorised for adults and children over 20 kg bodyweight and children under 20 kg bodyweight, for treatment osteodystrophy due to renal failure on dialysis or not, hypoparathyroidism, D-resistant or D-dependent (pseudo-deficient) rickets and osteomalacia, rickets and osteomalacia due to renal alterations in vitamin D metabolism and post-menopausal osteoporosis. It contains alphacalcidol as the active substance.

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

Important risks of alphacalcidol, together with measures to minimise such risks and the proposed studies for learning more about ALFACALCIDOLO DOC '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. Alphacalcidol is subject to restricted medical prescription.

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

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment, 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 ALFACALCIDOLO DOC 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 alphacalcidol. 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).

Summary of safety concerns	
Important identified risks	Hypercalcaemia
	Hyperphosphataemia
	Skin reaction
	Kidney failure
Important potential risks	Arrhythmia due to interaction with cardiac glycosides or digitalis
	Nephrolitiasis, Nephrocalcinosis
Missing information	Use in Pregnancy
	Use during breast feeding
	Fertility

II.B Summary of important risks

Summary of safety concerns	
Important identified risks	Hypercalcaemia
	Hyperphosphataemia
	Skin reaction
	Kidney failure
Important potential risks	Arrhythmia due to interaction with cardiac glycosides or digitalis
	Nephrolitiasis, Nephrocalcinosis

Important identified risks: Hypercalcaemia	
Evidence for linking the risk to the medicine	Cases of Hypercalcaemia (with a common frequency between $\geq 1/100$ and $< 1/10$), following administration of alphacalcidol, have been reported. (Drugs Today (Barc). 2012)
Risk factors and risk groups	Particular attention must be paid to patients suffering from arteriosclerosis, heart valve sclerosis or nephrolithiasis because hypercalcemia can worsen their condition. Overdose can cause Hypercalcaemia.
Risk minimisation measure	As hypercalcaemia may occur in patients treated with Alfacalcidol, patients should be informed of the associated clinical symptoms. Routine risk minimization measures: SmPC section 4.4, 4.8.
Additional pharmacovigilance activities	None

Important identified risk: Hyperphosphataemia	
Evidence for linking the risk to the medicine	Curr Vasc Pharmacol.2014
Risk factors and risk groups	Patients with renal insufficiency or patient taking bisphosphonates.
Risk minimisation measure	Patients are advised to regularly check the level of phosphate in blood while taking alphacalcidol.

	Routine risk minimization measures: SmPC section 4.4, 4.8
Additional pharmacovigilance activities	None

Important identified risk: Skin reaction	
Evidence for linking the risk to the medicine	Reactions linked to hypersensitivity as reported in SmPC.
Risk factors and risk groups	Patients with hypersensitivity to the active substance or components.
Risk minimisation measure	Patients are advised to tell their doctor if they develop itching or redness while taking alfacalcidol. Routine risk minimization measures: SmPC section 4.4, 4.8
Additional pharmacovigilance activities	None

Important identified risk: Kidney failure	
Evidence for linking the risk to the medicine	Kidney Int Suppl. 1999
Risk factors and risk groups	Patients with severe renal impairment or with decreased renal function.
Risk minimisation measure	Labelling: Risk has been highlighted in the SmPC in section 4.4,4.8.
Additional pharmacovigilance activities	None

Important identified risk: Arrhythmia due to interaction with cardiac glycosides or digitalis	
Evidence for linking the risk to the medicine	Drug Saf. 1995
Risk factors and risk groups	Patients taking alfacalcidol with a cardiac glycoside.
Risk minimisation measure	Monitor in advance symptoms and informing your doctor immediately, make sure you do not exceed the dose prescribed or indicated in the SmPC. Labelling: Risk has been highlighted in the SmPC in section 4.4,4.8.
Additional pharmacovigilance activities	None

Important identified risk: Nephrolithiasis, Nephrocalcinosis	
Evidence for linking the risk to the medicine	Nephrol Ther. 2018

Risk factors and risk groups	Patients with renal insufficiency including kidney stones and chronic kidney disease.
Risk minimisation measure	Patients are advised to inform their physician if they have kidney problems, including kidney stones. Labelling: Risk has been highlighted in the SmPC in section 4.4,4.8.
Additional pharmacovigilance activities	None

II.C Post-authorisation development plan

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

Not applicable. There are no studies which are conditions of the marketing authorisation or specific obligation of alphacalcidol.

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

Not applicable. There are no studies required for alphacalcidol.