SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ergocalciferol 300,000 IU solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ampoule of 1 ml solution for injection contains 300,000 IU of ergocalciferol.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for Injection

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Intramuscular therapy with Ergocalciferol Injection is used in patients with gastrointestinal, liver or biliary disease associated with malabsorption of Vitamin D, resulting in hypophosphataemia, rickets, and osteomalacia.

4.2 Posology and method of administration

Route of Administration: IM injection

Posology

Adults and Elderly

Ergocalciferol Injection is typically administered as a single dose of 300,000 IU every 3-6 months.

Paediatric population

In children 1-12 years, a bolus dose 300,000IU ergocalciferol is generally given in 2 divided doses.

However, for all age groups dosage should be individualised by the clinician for each patient dependent upon clinical response and requirements.

Serum and urinary calcium concentrations, phosphate and BUN should be monitored at regular intervals, initially weekly, in order to achieve optimum clinical response and to avoid hypercalcaemia.

Calcium and phosphorous supplements should be administered where necessary.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.

Hypercalcaemia, evidence of vitamin D toxicity, hypervitaminosis D, decreased renal function, metastatic calcification.

4.4 Special warnings and precautions for use

Adequate dietary calcium is necessary for clinical response to Ergocalciferol therapy.

Caution should be used when the injectable forms are used in patients with vitamin D resistant rickets as the range between the toxic and therapeutic dosage is narrow.

Vitamin D should be administered with caution to infants and patients who may have an increased sensitivity to its effects. Use with care in patients with renal impairment, renal calculi or heart disease or arteriosclerosis who might be at increased risk of organ damage if hypercalcaemia were to occur.

Ergocalciferol is not recommended for use in hypoparathyroidism. In the event of hypoparathyroidism when Ergocalciferol is used, calcium, parathyroid hormone or dihydrotachysterol may be required.

Dosage should be individualised. Frequent serum and urinary calcium, phosphate and urea nitrogen determinations should be carried out. Adequate fluid intake should be maintained.

Should hyperglycaemia develop, Ergocalciferol should be discontinued immediately.

Because of the effect on serum calcium, Ergocalciferol should only be administered to patients with renal stones when potential benefits outweigh possible hazards.

4.5 Interaction with other medicinal products and other forms of interaction

Ergocalciferol and:-

i) Magnesium-containing antacids : hypermagnesaemia may develop in patients on chronic renal dialysis.

ii) Digitalis glycosides : hypercalcaemia in patients on digitalis may precipitate cardiac arrhythmias.

iii) Verapamil atrial fibrillation has recurred when supplemental calcium and Ergocalciferol have induced hypercalcaemia.

iv) Anti-convulsants: vitamin D requirements may be increased in patients taking anti-convulsants (e.g. carbamazepine, phenobarbital, phenytoin and primidone).

v) Thiazide diuretics : hypoparathyroid patients on Ergocalciferol may develop hypercalcaemia due to increased Ergocalciferol (although Ergocalciferol is not recommended for use in hypoparathyroidism).

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of ergocalciferol in pregnant women. Ergocalciferol Injection should not be used in pregnancy unless the potential benefit outweighs the potential hazards to the foetus.

Animal studies have shown foetal abnormalities associated with hypervitaminosis D. Calcifediol and calcitriol are teratogenic in animals when given in doses several times the human dose. The offspring of a woman administered 17-144 times the recommended dose of calcitriol during pregnancy manifested mild hypercalcaemia in the first 2 days of life, which returned to normal at day 3.

Breast-feeding

Ergocalciferol is excreted in human milk in limited amounts and effects have been shown in infants of treated women. In a mother given large doses of Ergocalciferol, 25-hydroxycholecalciferol appeared in the milk and caused hypercalcaemia in the child. Monitoring of the infants serum calcium is required in such cases. Ergocalciferol should not be administered to breast-feeding mothers.

Fertility

None stated.

4.7 Effects on ability to drive and use machines

Ergocalciferol may cause drowsiness and can affect the ability to drive and use machines. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

Adverse events are generally associated with excessive intake of ergocalciferol leading to the development of hypercalcaemia.

The following convention has been used for the classification of frequency:
Very common (≥ 1/10)
Common (≥ 1/100 to < 1/10)

Uncommon (≥ 1/1,000 to < 1/100)
Rare (≥ 1/10,000 to < 1/1,000)
Very rare (<1/10,000)
Not known (cannot be estimated from the available data)

System Organ Class	Adverse event	Frequency
Metabolism and nutrition disorders	Hypercalcaemia *	Very common
	Hypercholesterolaemia†	Not known
	Muscle weakness§	Not known
	Muscle pain§	Not known
	Mild acidosis†	Not known
	Polydipsia†	Not known
	Anorexia†	Not known
Psychiatric disorders	Overt psychosis†	Rare
	Somnolence§	Not known
Nervous system disorders	Headache§	Not known
Endocrine disorders	Hypoparathyroidism* pseudohypopathyroidism*	Very common
Eye disorders	Conjunctivitis (calcific)	Not known
	Photophobia	Not known
Cardiac disorders	Cardiac arrhythmias	Not known
Rebal disorders	Elevated serum creatinine levels*	Very common
Vascular disorders	Generalised vascular calcification†	Not known
	Hypertension†	Not known
Respiratory, thoracic and mediastinal disorders	Rhinorrhoea†	Not known
Gastrointestinal disorders	Pancreatitis†	Not known
	Nausea§	Not known
	Vomiting§	Not known
	Dry mouth§	Not known
	Constipation§	Not known
	Diarrhoea§	Not known
	Abdominal pain§	Not known
Skin and subcutaneous tissue disorders	Pruritus†	Not known
Musculoskeletal and connective tissue disorders	Bone pain§	Not known
	Ectopic calcification†	Not known
Renal and urinary disorders	Polyuria†	Not known
	Nocturia†	Not known
	Nephrocalcinosis†	Not known
	Albuminuria†	Not known
	Reversible azotemia†	Not known
Reproductive system and breast disorders	Decreased libido†	Not known

System Organ Class	Adverse event	Frequency
General disorders and administration site conditions	Hyperthermia†	Not known
	Fatigue§	Not known
	Irritability†	Not known
	Weakness§	Not known
Investigations	Elevated AST †	Not known
	Elevated ALT†	Not known
	Elevated BUN†	Not known
	Weight loss†	Not known
Surgical and medical procedures	Metallic taste§	Not known

*In clinical studies on hypoparathyroidism and pseudohypopathyroidism, hypercalcaemia was noted on at least one occasion in about 1 in 3 patients and hypercalciuria in about 1 in 7. Elevated serum creatinine levels were observed in about 1 in 6 patients (approximately one half of whom had normal levels at baseline).

§ Possible early symptoms of hypercalcaemia
†Possible late symptoms of hypercalcaemia

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms
Administration to patients in excess of their daily requirement can cause hypercalcaemia (see section 4.8), hypercalciuria and hyperphosphataemia. Concomitant high intake of calcium and phosphate may lead to similar abnormalities.

Management
Treatment of chronic overdose with resulting hypercalcaemia consists of immediate withdrawal of the vitamin, a low calcium diet and generous fluid intake. Severe cases may require hydration with intravenous saline together with symptomatic and supportive treatment as indicated by the patient's clinical condition. Plasma calcium U & E's should be monitored.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vitamin D and analogues, ATC Code: A11CC01

Mechanism of action and Pharmacodynamic effects
Ergocalciferol (vitamin D) is a fat soluble vitamin. In conjunction with parathyroid hormone and calcitonin, it regulates calcium haemostasis. Ergocalciferol metabolites promote active absorption of calcium and phosphorous by the small intestine, increase rate of excretion and resorption of minerals in bone and promote resorption of minerals in bone and promote resorption of phosphate by renal tubules.

Ergocalciferol deficiency leads to rickets in children and osteomalacia in adults. Ergocalciferol reverses symptoms of nutritional rickets or osteomalacia unless permanent deformities have occurred.

5.2 Pharmacokinetic properties

Distribution
Stored chiefly in the liver, ergocalciferol is also found in fat, muscle, skin and bones. In plasma, it is bound to alpha globulins and albumin.

Biotransformation
There is a lag of 10 to 24 hours between administration of ergocalciferol and initiation of its action in the body. Maximal hypercalcaemic effects occur about 4 weeks after daily administration of a fixed dose and the duration of action can be ≥ 2 months. Ergocalciferol is hydroxylated in the liver and further metabolism occurs in the kidney.

Elimination
The primary route of excretion of Ergocalciferol is in the bile. Additionally, some is excreted in the urine and faeces. There is also enterohepatic re-cycling.

5.3 Preclinical safety data
None stated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethyl oleate

6.2 Incompatibilities
None stated.

6.3 Shelf life
36 months

6.4 Special precautions for storage

Store below 25°C.
Keep the ampoules in the outer carton in order to protect from light.

6.5 Nature and contents of container

1ml clear, one-point cut (OPC) glass Type 1 Ph Eur ampoules packed in cartons of 5 or 10 ampoules. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Plastic syringes should not be used to administer Ergocalciferol 300,000 IU solution for injection.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

RPH Pharmaceuticals AB
Box 603
101 32 Stockholm
Sweden

8 MARKETING AUTHORISATION NUMBER(S)

PL 36301/0008

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

04/04/2006

10 DATE OF REVISION OF THE TEXT

09/12/2022