SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Alfacalcidol 0.5 microgram capsules, soft

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soft capsule contains 0.5 microgram of Alfacalcidol.

Excipients with known effect:
Each soft gelatin capsule contains 99.919 mg sesame oil and 0.026 mg soyabean oil (component of Vitamin E preparation).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsule, soft.
Reddish coloured, oval shaped, opaque, soft gelatin capsules containing oily solution and bearing the designation "A5".

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Alfacalcidol is indicated in all conditions where there is a disturbance of calcium metabolism due to impaired 1-α hydroxylation such as when there is reduced renal function. The main indications are:

a) Renal osteodystrophy
b) Hyperparathyroidism (with bone disease)
c) Hypoparathyroidism
d) Neonatal hypocalcaemia
e) Nutritional and malabsorptive rickets and osteomalacia
f) Pseudo-deficiency (D-dependent) rickets and osteomalacia
g) Hypophosphataemic vitamin D resistant rickets and osteomalacia

4.2 Posology and method of administration

Posology

Initial dose for all indications:
Adults and children over 20 kg bodyweight: 1 microgram/day

Elderly:	0.5 microgram/day
Neonates and premature infants:	0.05 - 0.1 microgram/kg/day
Children under 20 kg bodyweight:	0.05 microgram/kg/day

The dose of Alfacalcidol should be adjusted thereafter to avoid hypercalcaemia according to the biochemical response. Indices of response include plasma levels of calcium (ideally corrected for protein binding), alkaline phosphatase, parathyroid hormone, as well as radiographic and histological investigations.

Plasma levels should initially be measured at weekly intervals. The daily dose of Alfacalcidol may be increased by increments of 0.25-0.5 microgram. When the dose is stabilised, measurements may be taken every 2-4 weeks.

Most adult patients respond to doses between 1 and 3 micrograms per day. When there is biochemical or radiographic evidence of bone healing (and in hypoparathyroid patients when normal plasma calcium levels have been attained), the dose generally decreases. Maintenance doses are generally in the range of 0.25 to 1 microgram per day. If hypercalcaemia occurs, Alfacalcidol should be stopped until plasma calcium returns to normal (approximately 1 week) then restarted at half the previous dose.

a) Renal bone disease:
Patients with relatively high initial plasma calcium levels may have autonomous hyperparathyroidism, often unresponsive to Alfacalcidol. Other therapeutic measures may be indicated.

Before and during treatment with Alfacalcidol, phosphate binding agents should be considered to prevent hyperphosphataemia. It is particularly important to make frequent plasma calcium measurements in patients with chronic renal failure because prolonged hypercalcaemia may aggravate the decline of renal function.

b) Hyperparathyroidism:
In patients with primary or tertiary hyperparathyroidism about to undergo parathyroidectomy, pre-operative treatment with Alfacalcidol for 2-3 weeks alleviates bone pain and myopathy without aggravating pre-operative hypercalcaemia. In order to decrease post-operative hypocalcaemia, Alfacalcidol should be continued until plasma alkaline phosphatase levels fall to normal or hypercalcaemia occurs.

c) Hypoparathyroidism:
In contrast to the response to parent vitamin D, low plasma calcium levels are restored to normal relatively quickly with Alfacalcidol. Severe hypocalcaemia is corrected more rapidly with higher doses of Alfacalcidol (e.g. 3-5 micrograms) together with calcium supplements.

d) Neonatal hypocalcaemia:
Although the normal starting dose of Alfacalcidol is 0.05-0.1 microgram/kg/day (followed by careful titration), in severe cases doses of up to 2 microgram/kg/day may be required. Whilst ionised serum calcium levels may provide a guide to response, measurement of plasma alkaline phosphatase activity may be more useful. Levels of alkaline phosphatase approximately 7.5 times above the adult range indicate active disease.
A dose of 0.1 microgram/kg/day of Alfacalcidol has proven effective as prophylaxis against early neonatal hypocalcaemia in premature infants.

e) Nutritional and malabsorptive rickets and osteomalacia:

Nutritional rickets and osteomalacia can be cured rapidly with Alfacalcidol.Malabsorptive osteomalacia (responding to large doses of IM or IV parent vitamin D) will respond to small doses of Alfacalcidol.

f) Pseudo-deficiency (D-dependent) rickets and osteomalacia:
Although large doses of parent vitamin D would be required, effective doses of One Alfacalcidol are similar to those required to heal nutritional vitamin D deficiency rickets and osteomalacia.

g) Hypophosphataemic vitamin D-resistant rickets and osteomalacia:
Neither large doses of parent vitamin D nor phosphate supplements are entirely satisfactory. Treatment with Alfacalcidol at normal dosage rapidly relieves myopathy when present and increases calcium and phosphate retention. Phosphate supplements may also be required in some patients.

Method of administration
Oral.

4.3 Contraindications

Hypersensitivity to the active substance, soya or to any of the excipients listed in section 6.1.

Hypercalcaemia, metastatic calcification.

4.4 Special warnings and precautions for use

During treatment with Alfacalcidol, serum calcium and serum phosphate levels should be monitored regularly especially in children, patients with renal impairment and patients receiving high doses. PTH, alkaline phosphatase and calcium phosphates should be monitored as clinically indicated.

Hypercalcaemia might appear in patients treated with Alfacalcidol. For this reason, patients should be informed about the clinical symptoms connected with hypercalcaemia. Signs of hypercalcaemia are muscle and bone pain, muscle weakness, confusion, dehydration, anorexia, fatigue, nausea and vomiting, constipation, polyuria, sweating, headache, polydipsia, hypertension and somnolence.

Hypercalcaemia can be rapidly corrected by stopping treatment until plasma calcium levels return to normal (in about one week). Alfacalcidol may then be restarted at a reduced dose (half the previous dose) with monitoring of calcium.

Prolonged hypercalcaemia may aggravate arteriosclerosis, cardiac valve sclerosis or nephrolithiasis and therefore prolonged hypercalcaemia should be avoided when Alfacalcidol is used in these patients. Transient or even long-lasting deterioration of kidney function has been observed. Alfacalcidol should also be used with caution in patients with calcification of pulmonary tissue as this may result in cardiac disease.

In patients with renal bone disease or severely reduced renal function, a phosphate binding agent could be used simultaneously with alfacalcidol to prevent increased serum phosphate and potential metastatic calcification.

Alfacalcidol should be used with caution in patients with granulomatous diseases such as sarcoidosis where the sensitivity to vitamin D is increased due to increased hydroxylation activity.

Concurrent use of digitalis glycosides in the presence of hypercalcaemia due to vitamin D administration increases the potential for cardiac arrhythmias.
Alfacalcidol capsules contain sesame oil as an excipient. Sesame oil may rarely cause severe allergic reactions.
Alfacalcidol capsules contain soyabean oil. If you are allergic to peanut or soya, do not use this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction

Thiazide diuretics and calcium containing preparations
Concurrent use of thiazide diuretics or calcium containing preparations may enhance the risk of hypercalcaemia. Calcium levels should be monitored.

Other vitamin D containing preparations
Concurrent use of other vitamin D containing preparations may enhance the risk of hypercalcaemia. Use of multiple vitamin D analogues should be avoided.

Anticonvulsants
Anticonvulsants (e.g. barbiturates, phenytoin, carbamazepine or primidone) have enzyme-inducing effects resulting in an increased metabolism of alfacalcidol. Patients taking anticonvulsants may require larger doses of Alfacalcidol

Magnesium-containing antacids
Absorption of magnesium-containing antacids may be enhanced by Alfacalcidol, increasing the risk of hypermagnesaemia.

Aluminium-containing preparations
Alfacalcidol may increase the serum concentration of aluminium. Patients taking aluminium-containing preparations (e.g. aluminium hydroxide, sucralfate) should be monitored for signs of aluminium related toxicities.

Bile acid sequestrants
Concomitant oral administration of bile acid sequestrants such as cholestyramine may impair the intestinal absorption of oral Alfacalcidol formulations. Alfacalcidol should be administered at least 1 hour before, or 4 to 6 hours after the intake of the bile acid sequestrant in order to minimise the potential risk of interaction.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is a limited amount of data from the use of alfacalcidol in pregnant women. Studies in animals have shown reproductive toxicity at high doses. (see Section 5.3) Therefore, Alfacalcidol is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breast-feeding

Although it has not been established, it is likely that increased amounts of 1,25-dihydroxyvitamin D will be found in the milk of lactating mothers treated with Alfacalcidol. This may influence calcium metabolism in the infant.
Consequently, breast-fed infants of alfacalcidol-using mothers should be monitored closely for hypercalcaemia.

Fertility
There are no clinical studies on the effect of Alfacalcidol on fertility. A pre-clinical study did not show an effect on fertility in rats.

4.7 Effects on ability to drive and use machines

Alfacalcidol has no or negligible direct influence on the ability to drive and use machines. However, the patient should be informed that dizziness may occur during treatment and take this into account while driving or using machines.

4.8 Undesirable effects

The estimation of the frequency of undesirable effects is based on a pooled analysis of data from clinical studies and spontaneous reporting.

The most frequently reported undesirable effects are various skin reactions such as pruritus and rash, hypercalcaemia, gastrointestinal pain/discomfort and hyperphosphataemia.

Renal failure has been reported post-marketing.

Undesirable effects are listed by MedDRA system organ class (SOC) and the individual undesirable effects are listed starting with the most frequently reported one. Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.

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)

Metabolism and nutrition disorders	
Common:	Hypercalcaemia Hyperphosphataemia
Psychiatric disorders	
Not known:	Confusional state
Nervous system disorders	
Uncommon:	Headache

Rare:	Dizziness
Gastrointestinal disorders	
Common:	Abdominal pain and discomfort
Uncommon:	Diarrhoea Vomiting Constipation Nausea
Skin and subcutaneous tissue disorders	
Common:	Rash Pruritus Various types of rash such as erythematous, maculopapular and pustular have been reported
Not known:	Urticaria
Musculoskeletal and connective tissue disorders	
Uncommon:	Myalgia
Renal and urinary disorders	
Common:	Hypercalciuria
Uncommon:	Nephrolithiasis/ Nephrocalcinosis
Not known	Renal impairment (including acute renal failure)
General disorders and administration site conditions	
Uncommon:	Fatigue/asthenia/malaise Calcinosis

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Excessive intake of Alfacalcidol may lead to the development of hypercalcaemia, however, the effect is reversed rapidly on withdrawal.

In severe cases of hypercalcaemia general supportive measures should be undertaken: Keep the patient well hydrated by i.v. infusion of saline (force diuresis), measure electrolytes, calcium and renal function indices, assess electrocardiographic abnormalities, especially in patients using digitalis. More specifically, treatment with glucocorticosteroids, loop diuretics, bisphosphonates, calcitonin and eventually haemodialysis with low calcium content should be considered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vitamin D and analogues, ATC code A11CC03.

Clinical efficacy and safety

Alfacalcidol is converted rapidly in the liver to 1,25-dihydroxyvitamin D. This is the metabolite of vitamin D which acts as a regulator of calcium and phosphate metabolism. Since this conversion is rapid, the clinical effects of Alfacalcidol and 1,25-dihydroxyvitamin D are very similar.

Impaired 1α-hydroxylation by the kidneys reduces endogenous 1,25-dihydroxyvitamin D production. This contributes to the disturbances in mineral metabolism found in several disorders, including renal bone disease, hypoparathyroidism, neonatal hypocalcaemia and vitamin D dependent rickets. These disorders, which require high doses of parent vitamin D for their correction, will respond to small doses of Alfacalcidol.

The delay in response and high dosage required in treating these disorders with parent vitamin D makes dosage adjustment difficult. This can result in unpredictable hypercalcaemia which may take weeks or months to reverse. The major advantage of Alfacalcidol is the more rapid onset of response, which allows a more accurate titration of dosage. Should inadvertent hypercalcaemia occur it can be reversed within days of stopping treatment.

5.2 Pharmacokinetic properties

In patients with renal failure, 1-5 μg/day of lα-hydroxyvitamin D (1α-OHD3) increased intestinal calcium and phosphorus absorption in a dose-related manner. This effect was observed within 3 days of starting the drug and conversely, it was reversed within 3 days of its discontinuation.

In patients with nutritional osteomalacia, increases in calcium absorption were noted within 6 hours of giving 1 μg 1α-OHD3 orally and usually peaked at 24 hours. 1α-OHD3 also produced increases in plasma inorganic phosphorus due to increased intestinal absorption and renal tubular re-absorption. This latter effect is a result of PTH suppression by 1α-OHD3. The effect of the drug on calcium was about double its effect on phosphorous absorption.

Patients with chronic renal failure have shown increased serum calcium levels within 5 days of receiving 1α-OHD3 in a dose of 0.5 - 1.0 μg/day. As serum calcium rose, PTH levels and alkaline phosphatase decreased toward normal.

5.3 Preclinical safety data

The non-clinical toxicity of alfacalcidol is attributed to the known vitamin D-effect of calcitriol on calcium homeostasis, which is characterised by hypercalcaemia, hypercalciuria and eventually soft tissue calcification.
Alfacalcidol is not genotoxic.

No specific effects of alfacalcidol on fertility or behaviour of the offspring were noted in rats and rabbits. In terms of embryo-fetal development, fetal toxicity (postimplantation loss, lower litter size and lower pup weight) was observed at doses high enough to cause toxicity in the dams. High doses of vitamin D are known to be teratogenic in experimental animals.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Sesame oil Refined
- Vitamin E Preparation (D-Alpha-tocopherol and Soyabean oil)
- Gelatin
- Glycerol
- Potassium Sorbate
- Titanium dioxide
- Red iron oxide
- Purified Water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions

6.5 Nature and contents of container

Packed in PVC/PVDC-Aluminium blisters.
They are subsequently packed into pouch (30 capsules packed in 3 blister strips) and carton boxes.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

Euro-Link Pharma Ltd
110 Butterfield,
Great Marlings, Luton,
Bedfordshire, LU2 8DL,
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 43542/0229

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

04/03/2026

10 DATE OF REVISION OF THE TEXT

04/03/2026