

## Data Sheet

### Name of Medicine

### One-Alpha

**Alfacalcidol      Leo**

### Presentation

One-Alpha capsules 0.25 mcg are white oval capsules with a joining seam around the middle and 8 mm in length. One-Alpha capsules 1.0 mcg are smooth, brown oval capsules of 8 mm in length. One-Alpha drops 2.0 mcg/ml are a clear colourless solution. One-Alpha solution 0.2 mcg/ml is a clear or slightly opalescent colourless solution of low viscosity. One-Alpha injection 2 mcg/ml is a clear and colourless solution.

### Uses

#### Action

Alfacalcidol (1 $\alpha$ -OHD<sub>3</sub>) is rapidly converted in the liver to 1,25-dihydroxyvitamin D<sub>3</sub> (1,25-(OH)<sub>2</sub>D<sub>3</sub>), the metabolite of vitamin D which acts as a regulator of calcium and phosphate homeostasis.

Impaired endogenous production of 1,25-dihydroxyvitamin D<sub>3</sub> by the kidneys appears to contribute to the disturbances in mineral metabolism found in several disorders, including renal bone disease, hypoparathyroidism, and vitamin D-dependent rickets. These disorders, which require high doses of vitamin D for their correction will respond to small doses of One-Alpha.

As compared to vitamin D, the main advantage of One-Alpha is more rapid onset and offset of action. This allows a more accurate titration of dosage and decreases the risk of prolonged hypercalcaemia.

#### Pharmacokinetics

Serum levels of 1,25-(OH)<sub>2</sub> D<sub>3</sub> peak approximately 12 hours after a single dose of One-Alpha and remain at measurable levels for at least 48 hours. The effect of 1 mcg of One-Alpha on calcium absorption has been observed within 6 hours and was maximal at 24 hours. The biological half-life is approximately 35 hours.

#### Indications

Disease caused by disturbances in the calcium metabolism in consequence of reduced endogenous production of 1,25-dihydroxyvitamin D<sub>3</sub>. Renal osteodystrophy. Postoperative or idiopathic hypoparathyroidism. Pseudohypoparathyroidism. As an adjunct to the management of tertiary hyperparathyroidism. Vitamin D-resistant rickets or osteomalacia. Vitamin D-dependent rickets, neonatal hypocalcaemia or rickets. Malabsorption of calcium. Malabsorptive and nutritional rickets and osteomalacia. Postmenopausal osteoporosis.

## **Dosage and Administration**

Initial dose:

Adults and children above 20 kg body weight: 1 mcg daily

Children under 20 kg body weight: 0.05 mcg/kg/day

Neonates: 0.1 mcg/kg/day

Dosage in the elderly: 0.5 mcg/day

It is important to adjust dosage thereafter according to the biochemical responses and to avoid hypercalcaemia. Indices of response include levels of serum calcium, alkaline phosphatase, parathyroid hormone, urinary calcium excretion as well as radiographic and histological investigations. Patients with marked bone disease (other than those with renal failure) may tolerate higher doses without developing hypercalcaemia. However, failure of the serum calcium to rise promptly in osteomalacia patients does not necessarily mean that a higher dose is required since calcium from increased intestinal calcium absorption may be incorporated into demineralized bone. Most patients will respond to doses between 1 and 3 mcg daily.

The dose requirements generally decrease in patients with bone disease when there is biochemical or radiographic evidence of bone healing and in hypoparathyroid patients after normal serum calcium levels have been attained. Maintenance doses are generally in the range of 0.25 to 1 mcg daily.

In patients with osteoporosis receiving One-Alpha, the recommended dosage for One-Alpha for postmenopausal osteoporosis patients is 1 mcg daily. The dose should be titrated according to the individual needs. Calcium supplementation should not be required if the normal dietary intake is in region of 1500 mg per day. However, many postmenopausal patients have dietary intake as little as 600 mg per day and calcium supplementation of 0.5 – 1 g per day could be required.

One-Alpha injection can be given as an IV injection following each haemodialysis. The injection should be administered into the return line from the haemodialysis machine at the end of each dialysis. The initial dosage for adults is 1 mcg per dialysis. The maximum dose recommended is 6 mcg per dialysis and not more than 12 mcg per week.

Patients currently taking barbiturates or other anticonvulsants may need larger doses of One-Alpha to produce the desired effect.

## **Contraindications**

Hypercalcaemia

## **Warnings and Precautions**

One-Alpha should be used in pregnancy and lactation only if considered necessary by a physician.

Throughout the treatment with One-Alpha, regular serum calcium determinations are essential. Indeed, One-Alpha should be used only when adequate facilities are available for monitoring of serum calcium and other appropriate biochemical parameters on a regular basis.

If hypercalcaemia occurs, One-Alpha medication should be stopped immediately until serum calcium levels return to normal (in about one week) and then re-started at half the previous dose. The risk of hypercalcaemia depends on such factors as the degree of any mineralization defect, renal function, and the dose of One-Alpha. Hypercalcaemia will occur when there is biochemical evidence of bone healing (e.g. a return towards normal in the level of plasma alkaline phosphatase) and the dose of 1alpha-OHD<sub>3</sub> is not reduced appropriately. Prolonged hypercalcaemia should be avoided, particularly in chronic renal failure.

Frequency of monitoring: Plasma calcium levels should be measured at weekly to monthly intervals depending on the progress of the patient. Frequent estimations are necessary in the early stages of treatment (particularly when the plasma calcium is already relatively high) and later when there is evidence of bone healing.

Plasma calcium levels should be estimated regularly during the initial treatment of disorders without significant bone involvement, e.g. hypoparathyroidism. In patients with renal bone disease One-Alpha should be given in combination with a phosphate binding agent to prevent hyperphosphataemia, which is known to increase the risk of metastatic calcification.

One-Alpha injection should be avoided in patients with known sensitivity to injections containing propylene glycol and used with caution in small premature infants.

### **Adverse effects**

Apart from hypercalcaemia, no other side effects have been reported.

### **Interactions**

Barbiturates and other anticonvulsants may reduce the effectiveness of One-Alpha so that the dose needs to be increased.

### **Overdosage**

Hypercalcaemia is treated by stopping treatment with One-Alpha. Severe hypercalcaemia may require additional treatment with a "loop" diuretic and intravenous fluids or with corticosteroids.

### **Pharmaceutical Precautions**

Capsules: Do not store above 25°C  
Injection, solution and drops: Store at 2-8°C

One-Alpha should be protected from light.

### **Medicine Classification**

Prescription medicine.

## **Package Quantities**

100	Capsules 0.25 mcg
100	Capsules 1.0 mcg
10 ml & 20 ml	Oral drops 2 mcg/ml
60 ml	Solution 0.2 mcg/ml
0.5 ml/1 ml (Packs of 10 ampoules)	Injection 2 mcg/ml

## **Further Information**

### ***List of Excipients***

One-Alpha capsules 0.25 mcg: sesame oil,  $\alpha$ -tocopherol, gelatin, glycerol (85 per cent), potassium sorbate, titanium dioxide.

One-Alpha capsules 1 mcg: sesame oil,  $\alpha$ -tocopherol, gelatin, glycerol (85 per cent), potassium sorbate, red iron oxide (E172), black iron oxide (E172).

One-Alpha oral drops/solution: macrogolglycerol hydroxylstearate, citric acid monohydrate, sodium citrate, sorbitol,  $\alpha$ -tocopherol, methyl parahydroxybenzoate, anhydrous ethanol, purified water.

One-Alpha injection: citric acid monohydrate, anhydrous ethanol, sodium citrate, propylene glycol and water for injection.

## **Name and Address**

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## **Date of Preparation**

April 1992 (Revised July 1993 and December 2001)