

## Recommendations and Reasons

Committee to Evaluate Drugs (CED)

# Alfacalcidol intravenous injection

### Product:

ALFACALCIDOL (One-Alpha®)  
1mcg/0.5mL, 2mcg/1.0mL injection

### Class of drugs:

Vitamin D analogue

### Indication:

Treatment of secondary hyperparathyroidism in patients with chronic kidney disease

### Manufacturer:

Leo Pharma Inc.

### Highlights of Recommendation:

- ◆ Alfacalcidol (One-Alpha) intravenous injection is a synthetic vitamin D analogue indicated for the management of hyperparathyroidism caused by chronic kidney disease (i.e., secondary hyperparathyroidism).
- ◆ Alternative vitamin D analogues funded on the Ontario Drug Benefit Formulary include calcitriol (Rocatrol) oral capsule and alfacalcidol (One-Alpha) oral capsule.
- ◆ There is no good evidence that intravenous alfacalcidol (One-Alpha) injection is superior to oral vitamin D analogues in terms of efficacy or safety.
- ◆ Alfacalcidol (One-Alpha) injection costs \$7.50 per microgram, which is several times more expensive than oral vitamin D analogues.
- ◆ **Overall, the Committee noted that oral vitamin D analogues are already available on the Formulary and alfacalcidol (One-Alpha) injection has not been shown to provide superior efficacy, safety or value for money over these oral alternatives.**

### Background:

Hyperparathyroidism is the excess production of parathyroid hormone by the parathyroid glands. Parathyroid hormone controls calcium, phosphorus, and vitamin D levels within the blood and bone. Hyperparathyroidism can reduce bone density, making it easier for bones to break, as well as stiffen the arteries, creating heart problems.

Excess production of parathyroid hormone that is caused by another medical condition is known as secondary hyperparathyroidism. The most frequent cause of secondary hyperparathyroidism is chronic kidney failure.

Standard treatments for secondary hyperparathyroidism in patients with chronic kidney disease on dialysis include vitamin D therapy and phosphate binders.

## CED Recommendation

The CED recommended that alfacalcidol (One-Alpha) intravenous injection not be funded, on the basis that this product does not provide superior efficacy, safety or value for money over existing alternatives on the Formulary.

## Executive Officer Decision

Based on the CED's recommendation, the Executive Office decided not to fund alfacalcidol (One-Alpha).

## Status

Funding not available through the Ontario Public Drug Programs.

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## Detailed Discussion:

- ◆ Vitamin D therapy has been shown to reduce osteodystrophy (bone disorders) in patients with secondary hyperparathyroidism from chronic kidney disease. However, data on improvements in other important outcomes, such as heart disease, hospitalization and quality of life, are lacking. A recent meta-analysis (a synthesis of data from various studies) (*Palmer et. al. Ann Intern Med 2007.*) concluded that vitamin D therapies do not consistently reduce parathyroid hormone levels and the beneficial effects on patient outcomes are unproven.
- ◆ There are no good quality studies directly comparing the efficacy and safety of intravenous alfacalcidol (One-Alpha) injection versus oral vitamin D analogues. One study identified (*Moriniere et al. Kidney International, 1993.*) evaluated the effects of switching a treatment regimen from oral vitamin D therapy to intravenous alfacalcidol (One-Alpha) injection in dialysis patients with severe hyperparathyroidism. Seventeen patients who had previously been treated with various combinations of oral vitamin D analogues and phosphate binders were switched to receive intravenous alfacalcidol (One-Alpha) injection and calcium carbonate (a phosphate binder). After the switch in therapy, patients showed some improvements in surrogate markers of their hyperparathyroidism such as iPTH levels.
- ◆ The Committee noted that this study had many limitations. Firstly, the study was conducted in a very small number of patients. In addition, patients in the study had not yet failed oral vitamin D therapy when they were switched to intravenous alfacalcidol (One-Alpha). Most importantly, there were multiple modifications made to the patients' treatment regimen, with the switch from oral to intravenous vitamin D being only one of the changes. These deficiencies made it difficult to conclude that intravenous alfacalcidol (One-Alpha) was the sole reason for the improvements and that it is more efficacious than an oral vitamin D analogue.
- ◆ Alfacalcidol (One-Alpha) injection costs \$7.50 per microgram, while oral alfacalcidol (One-Alpha) costs \$1.22 for the 1 microgram capsule.

- ◆ Given the lack of evidence to support therapeutic superiority of intravenous alfacalcidol (One-Alpha) over oral vitamin D analogues, the higher costs, and the limited data on improvements in clinical outcomes, the Committee recommended that intravenous alfacalcidol (One-Alpha) injection not be funded.

## CEDAC Recommendation:

(<http://www.cadth.ca/index.php/en/cdr/recommendations>)

The Canadian Expert Drug Advisory Committee (CEDAC) did not review intravenous alfacalcidol (One-Alpha) injection.



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