NEW DRUGS

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Calcifediol high-strength formulation for vitamin D deficiency

Keywords
calcifediol, Vistella, vitamin D deficiency

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Active ingredient: calcifediol

Brand name (sponsor): Vistella (Aspen Pharmacare)

Presentation: 255-microgram soft gelatin capsules

Route of administration: oral

Approved indication: treatment of vitamin D deficiency in adults, and maintenance treatment as required

Background: Vitamin D3 (colecalciferol) promotes absorption of calcium and phosphate in the gut and plays an important role in bone health. It is primarily synthesised in the skin through exposure to sunlight, with a smaller contribution from dietary sources. To become active, vitamin D3 is first converted in the liver to calcifediol (25-hydroxyvitamin D), the form of vitamin D that is measured in the serum, before being converted in the kidneys to calcitriol, the biologically active form.

Calcifediol is available over the counter as a 10-microgram capsule. Vistella, a prescription-only product, is the first high-strength calcifediol preparation, for intermittent administration (usually monthly), to be approved in Australia.

Clinical trials: Two clinical studies have evaluated the efficacy and safety of oral calcifediol using the same dosage regimen approved in Australia (255 micrograms once monthly or sometimes fortnightly).

Postmenopausal women with vitamin D deficiency: In a double-blind, randomised controlled trial in postmenopausal women with vitamin D deficiency (25-hydroxyvitamin D concentrations below 50 nanomol/L), participants (n=303) were randomised to one of three groups: oral calcifediol 255 micrograms monthly for 12 months, oral calcifediol 255 micrograms monthly for 4 months followed by placebo for 8 months, or oral colecalciferol 25,000 units (625 micrograms) monthly for 12 months.[1] The primary efficacy endpoint was the percentage of participants achieving serum 25-hydroxyvitamin D concentrations above 75 nanomol/L at 4 months.[1,2] At month 4, 35% of participants who received calcifediol achieved target 25-hydroxyvitamin D concentrations versus 8.2% of participants who received colecalciferol.[2]

After 12 months of continuous treatment, the proportions of participants who achieved target 25-hydroxyvitamin D concentrations were 21.6% with calcifediol 255 micrograms once a month, versus 9.2% with colecalciferol 625 micrograms once a month. In participants who had calcifediol withdrawn after 4 months, a significant decrease in 25-hydroxyvitamin D was observed, with 86.7% falling below 50 nanomol/L by month 12.[1]

Younger adults with no comorbidities: Calcifediol was also studied in younger adults aged 18 to 50 years in a phase 1 clinical trial (n=101, 66% female).[3] The study comprised a 4-month open-label treatment phase followed by a 5-month double-blind, placebo-controlled phase.

During the open-label phase, participants with 25-hydroxyvitamin D concentrations below 25 nanomol/L (n=7) received fortnightly calcifediol, while those with concentrations between 25 and 50 nanomol/L (n=94) received monthly calcifediol. After 1 month of treatment, 57% of participants achieved target 25-hydroxyvitamin D concentrations (above 50 nanomol/L), increasing to 83% after 4 months.

At the end of the open-label phase, participants with target 25-hydroxyvitamin D concentrations were randomised to receive either calcifediol or placebo, taken monthly for 5 months. At the end of the study, 89% of those who received calcifediol maintained target concentrations compared with 49% on placebo.[3]

Adverse effects: The main adverse effects of calcifediol are those associated with excessive vitamin D supplementation and hypercalcaemia. When taken at the approved dose and frequency, calcifediol is usually well tolerated.[4] A serum 25-hydroxyvitamin D concentration above 375 nanomol/L is associated with an increased incidence of adverse effects.[5]

Dosage and administration: The standard dosage of calcifediol is 255 micrograms (one capsule) once a month, taken orally. More frequent doses may be

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Report all suspected adverse reactions to new drugs to enable continued monitoring of their benefit–harm balance.

needed for severe vitamin D deficiency; however, the dose should not exceed one capsule every 2 weeks and the frequency should be lowered once vitamin D concentrations have stabilised.[5]

Precautions: In patients with severe renal impairment (creatinine clearance less than 30 mL/min), there may be a significant reduction in efficacy because calcifediol is activated in the kidneys.

In patients with prolonged immobilisation, a dose reduction may be needed to avoid hypercalcaemia.[5]

Vistella capsules contain the colouring agent sunset yellow, which can cause allergic reactions and asthma, especially in patients allergic to acetylsalicylic acid.[5]

Calcifediol concentrations may be reduced if administered with drugs that induce cytochrome P450 3A4 (e.g. phenytoin). Other drugs that can interact with calcifediol include orlistat, digoxin, verapamil and corticosteroids.[5]

Use in pregnancy and breastfeeding: Calcifediol is classified as Therapeutic Goods Administration pregnancy category B3 and should not be used during pregnancy. It is excreted into breastmilk and should not be used during breastfeeding.[5]

Place in therapy: Calcifediol 255-microgram (Vistella) capsules provide another option for the treatment of vitamin D deficiency in adults. There is some evidence that calcifediol may increase vitamin D concentrations more rapidly than colecalciferol; however, no clinical trials to date have compared the approved calcifediol dosage regimen with colecalciferol dosage regimens commonly used in Australia for the initial treatment of vitamin D deficiency (e.g. 75 to 125 micrograms daily for 6 to 12 weeks[6]). It is important to note that colecalciferol and calcifediol cannot be therapeutically compared microgram to microgram.[7] Pharmacokinetic studies and a 2024 international consensus statement suggest calcifediol may have an advantage over colecalciferol in certain groups, such as people with vitamin D malabsorption or obesity,[8,9] and it may be beneficial in patients requiring rapid correction of deficiency.[9] Monthly (or in some cases fortnightly) dosing may be more convenient than daily supplementation for some people, but may be prone to dosing errors and over-supplementation if taken more frequently than recommended. Vistella is not listed on the Pharmaceutical Benefits Scheme and is more expensive than colecalciferol.

Practice points: Monitor 25-hydroxyvitamin D concentrations while on treatment and monitor for hypercalcaemia. Patients should be advised on the importance of adhering to the recommended treatment frequency, and recommendations around diet and co-administration of calcium supplements to minimise risk of toxicity. Patients should also be educated on the signs and symptoms of hypercalcaemia (e.g. weakness, fatigue, drowsiness, headache, nausea, vomiting, abdominal cramps).

This new drug comment was finalised on 27 October 2025.

At the time this new drug comment was prepared, the Australian Public Assessment Report was available from the Therapeutic Goods Administration. The sponsor did not provide the Clinical Evaluation Report.

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