Calcipotriol
A Review of its Pharmacological Properties and Therapeutic Efficacy in the Management of Psoriasis

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Synopsis

Calcipotriol (calcipotriene) is a vitamin D₃ analogue which inhibits cell proliferation, enhances cell differentiation and appears to influence immunological factors which may play a role in the origins of psoriasis. In patients with chronic
plaque psoriasis, twice-daily topical calcipotriol 50 μg/g is more effective than unmedicated vehicle, betamethasone (betamethasone valerate), fluocinonide, dithranol (anthralin) and coal tar in patients with nonscalp psoriasis; however, patients with scalp psoriasis respond better to betamethasone than calcipotriol.

In the treatment of patients with severe psoriasis, calcipotriol used together with cyclosporin or psoralen ultraviolet A yields superior results to those achieved with either regimen alone. The efficacy of calcipotriol demonstrated in short term trials is sustained in noncomparative studies of up to 1 year in duration.

Data from several clinical trials involving nearly 2000 patients show that calcipotriol is well tolerated, the most common adverse events being mild and transient irritation of lesions or perilesional skin which occur in 15.1 to 25.8% of patients. At recommended dosages hypercalcaemia and hypercalciuria are very rare. Calcipotriol is better tolerated than short-contact dithranol, but causes more adverse events than betamethasone particularly in patients with scalp psoriasis.

In conclusion, wide clinical trial experience has established calcipotriol as an effective and well tolerated topical therapy for the management of psoriasis. Calcipotriol can thus be considered to be an important option in the treatment of this difficult disorder.

In various in vitro and ex vivo models, calcipotriol at concentrations greater than $1.0 \times 10^{-10}$ mol/L, markedly inhibits cell proliferation and enhances cell differentiation. In patients with psoriasis, calcipotriol 50 μg/g reduces cell proliferation and increases cell differentiation of psoriatic skin.

Both in vitro and in patients with psoriasis, calcipotriol, has been shown to influence several immunological and inflammatory mediators, which may be linked to the cause of psoriasis, including the down-regulation of various interleukins, T cells, cell adhesion molecules and the plasminogen system, and up-regulation of nerve growth factor, transforming growth factor-β and calcitriol receptors. Furthermore, the drug binds to calcitriol receptors with an affinity similar to that of calcitriol.

In patients with psoriasis, 1 to 6% of topically applied calcipotriol is systemically absorbed. The drug is rapidly metabolised by a variety of cell types, including hepatocytes and human keratinocytes, to less active metabolites.

In patients with nonscalp psoriasis, twice-daily calcipotriol 50 μg/g ointment or cream was superior to vehicle alone in reducing the severity of psoriasis and was associated with a larger percentage of responders. After 2 weeks of treatment, severity scores for erythema, infiltration and desquamation were reduced in comparison with vehicle. This short term improvement was continued in long term noncomparative studies which lasted for up to 12 months.

Calcipotriol 50 μg/g ointment applied twice daily for 4 to 8 weeks was more effective in the treatment of nonscalp psoriasis, than twice daily topical applications of ointments containing either betamethasone 0.1%, fluocinonide 0.05%, short-contact dithranol 0.1 to 2%, or coal tar 15%. However, betamethasone 0.1% solution was superior to calcipotriol 50 μg/g solution in the treatment of scalp psoriasis in a short term study. Calcipotriol 50 μg/g was better accepted cosmetically than short-contact dithranol. In patients with severe psoriasis, calcipotriol in combination with oral cyclosporin or psoralen ultraviolet A (PUVA) yielded greater results than each regimen alone. In combination, the percentages of patients responding were 84 and 87%, whereas cyclosporin and PUVA alone pro-