PrescQIPP Community Interest Company

# Calcipotriol/betamethasone (Dovobet®) in psoriasis

This bulletin focuses on calcipotriol/betamethasone (Dovobet®) for the treatment of psoriasis. The annual spend on Dovobet® across England is £28.7 million (ePACT October - December 2014). QIPP projects in this area are aimed at reviewing the appropriate use and duration of treatment of Dovobet®. A 50% reduction in prescribing through stopping prolonged treatment could result in potential annual savings of £9 million across England (ePACT October - December 2014).

Support materials (briefing, aide-memoire, data collection and patient letter) are available at: http://www.prescqipp.info/resources/viewcategory/326-dovobet-in-psoriasis

## Recommendations

- Vitamin D analogue monotherapy (calcipotriol, calcitriol, tacalcitol) or corticosteroid therapy are first line treatments for the majority of patients with chronic plaque psoriasis.[1] Calcitriol ointment is the least expensive vitamin D analogue based on cost per gram. Calcipotriol ointment is the least expensive vitamin D analogue preparation if calculated using the maximum daily application over a four week period (see tables 1 and 2).
- Dovobet® is a vitamin D analogue and steroid combination product which should only be considered for poor responders.[1]
- Dovobet® is recommended as a 4th line treatment for trunk and limb psoriasis in adults but not children or adolescents.[1]
- Dovobet® gel is recommended as a 3rd line treatment for scalp psoriasis in adults and children or adolescents. Use in children is unlicensed and initiation should be restricted to secondary care.[1]
- Dovobet® should not be used for the face, flexures or genitals in adults or children.[1]
- Dovobet® should only be used **once daily** and for a **maximum duration of 4 weeks**[1] and should only be prescribed as acute treatment. It should not be routinely added to repeat prescribing lists.
- Calcipotriol scalp solution for the treatment of scalp psoriasis is expensive and should only be used in people who are intolerant of or cannot use topical corticosteroids and have mild to moderate scalp psoriasis.[1]
- Educating the patient about their condition and ensuring adherence to treatment forms a crucial part of management.[1]

## Background

Betamethasone dipropionate is a potent topical corticosteroid and calcipotriol is an active form of Vitamin D. Vitamin D preparations bind to vitamin D receptors, which inhibit keratinocyte proliferation and enhance keratinocyte differentiation.[2]

**Dovobet® ointment and gel** contain a combination of calcipotriol 50mcg and betamethasone dipropionate 0.5mg/g.

The ointment is indicated for topical treatment of stable plaque psoriasis vulgaris.[3]

The gel is indicated for topical treatment of scalp psoriasis and for mild to moderate “non-scalp” plaque psoriasis vulgaris in adults.[4]

# Psoriasis

Psoriasis is an inflammatory skin disease that typically follows a relapsing and remitting course. The prevalence of psoriasis is estimated to be around 1.3–2.2% in the UK. Psoriasis can occur at any age, although is uncommon in children (0.71%) and the majority of cases occur before 35 years. Psoriasis is associated with joint disease in a significant proportion of patients.

Plaque psoriasis is characterised by well-delineated red, scaly plaques that vary in extent from a few patches to generalised involvement. It is by far the most common form of the condition (about 90% of people with psoriasis).[1]

Other types of psoriasis include:

- Scalp psoriasis - this is usually chronic plaque psoriasis and can affect the whole scalp.
- Palmo-plantar psoriasis (pustular or hyperkeratotic) psoriasis – this can be localised involving the palms and soles or generalized, which is less common.
- Nail psoriasis – this is particularly common in individuals with psoriatic arthropathy.
- Guttate psoriasis - lesions present as small scaly papules (up to 1cm in diameter).
- Psoriatic arthropathy – this requires referral to a dermatologist.

Difficult-to-treat sites encompass the face, flexures, genitalia, scalp, palms and soles and are so-called because psoriasis at these sites may have especially high impact and may result in functional impairment. These sites require particular care on prescribing topical therapy and can be resistant to treatment.[1] There is no cure for psoriasis but treatment is aimed at inducing remission or controlling symptoms.[1]

NICE recommends referring children and young people with any type of psoriasis to a specialist at presentation.[1]

# Impact and severity of psoriasis

The impact and severity of psoriasis must be assessed. Assessment tools have been associated with improved clinical outcomes in specialist setting (for example improved awareness of disease impact and ineffective treatments stopped). As a result assessment tools are recommended for use in primary care.[1,5]

# Severity

Severity is estimated by both clinician and patient using the physicians's global assessment scale, which uses the descriptions "clear", "nearly clear, "mild", "moderate", "severe" or "very severe". The Psoriasis Area and Severity Index (PASI) is also a validated tool that measures disease severity in adults with severe chronic plaque psoriasis.[1,6]

# Extent

NICE recommends measuring the extent of psoriasis by measuring body surface area (BSA). Severity is defined by how much of the body surface area is affected.

Mild psoriasis: <5% of BSA

Moderate psoriasis: 5-10% of BSA

Severe psoriasis: >10% of BSA

(Note: 1% of BSA is approximately equal to the palm of the patient's hand, excluding fingers).[1]

# Impact

Quality of life measurements across all skin disease can be carried out using the Dermatology Life Quality Index (DLQI0) validated tool for adults, or the children's dermatology life quality index (CDLQI). A score of > 10 (range 0-30) has been shown to correlate with at least a very large effect on an individual's quality of life.[1] It is available from http://www.dermatology.org.uk/quality/quality-life.html

# Patient education and adherence to treatment

The British Association of Dermatology (BAD), the Primary Care Dermatology Society (PCDS) and NICE guideline on the management of psoriasis recommended that patients be given both verbal and written information on treatment options. People must also be supported to adhere to treatment.[1,6,7] Information to facilitate discussion of risks and benefit of treatments for people with psoriasis is contained in Appendix B of the NICE guidance.[1]

Patient information leaflets are available from:

http://www.bad.org.uk/shared/get-file.ashx?id=123&itemtype=document

or
http://www.bad.org.uk/for-the-public/patient-information-leaflets scroll down for the information on topical treatments in psoriasis

http://www.patient.co.uk/health/psoriasis-leaflet

A list of patient support groups can be found in Appendix 1, page 11.

When offering topical agents take into account patient preference, cosmetic acceptability, practical aspects of application and the site(s) and extent of psoriasis to be treated. It is important to discuss the variety of formulations available. Depending on the person's preference, use:

- Cream, lotion or gel for widespread psoriasis.
- Lotion, solution or gel for the scalp or hair-bearing areas.
- Ointment to treat areas with thick adherent scale.

Psoriasis that cannot be controlled by topical treatment should be referred to secondary care for further assessment and treatment options (these include phototherapy and systemic treatment). Topical treatments alone are unlikely to be effective if the person has:

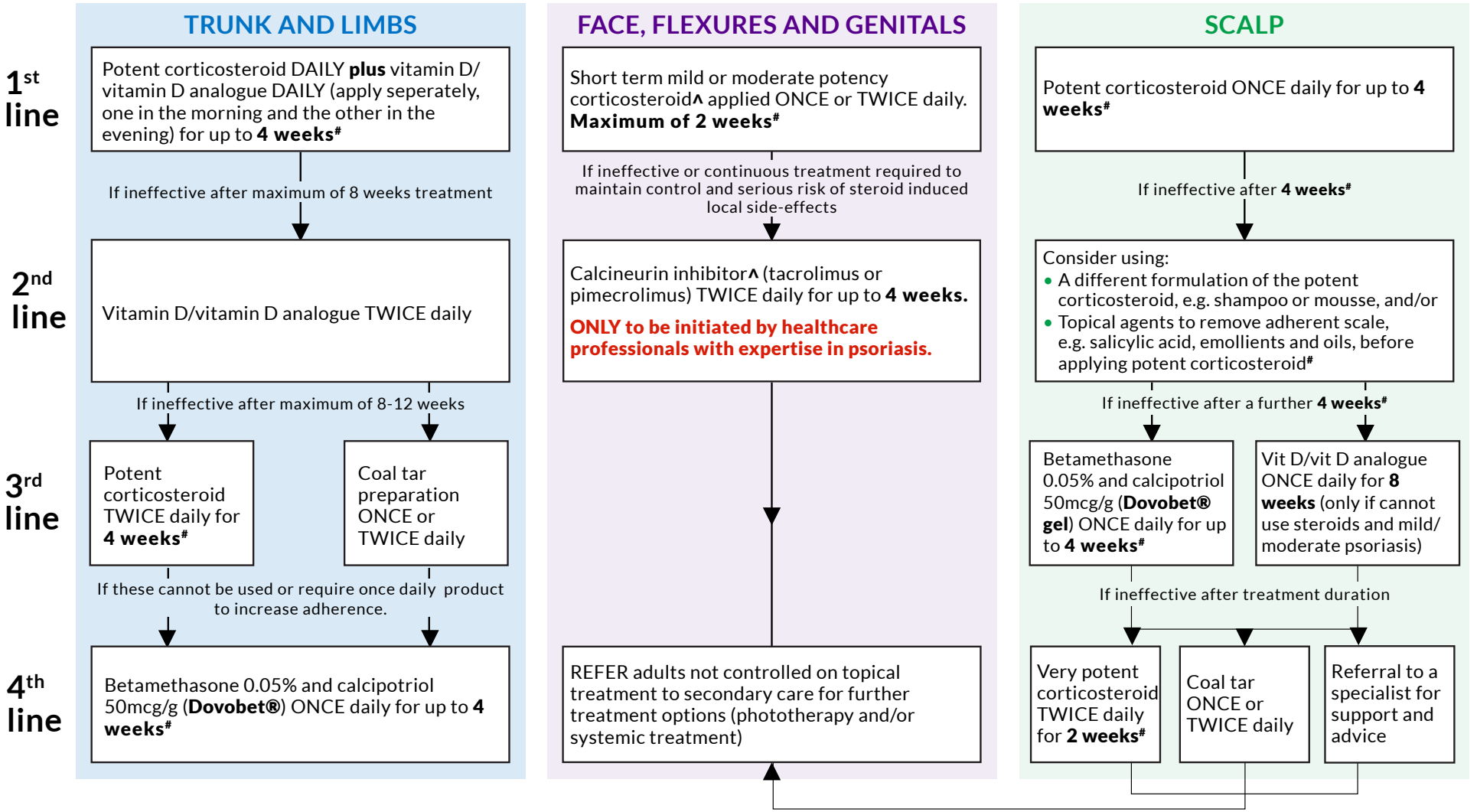
- Extensive disease (e.g. greater than 10% of body surface area affected).
- A score of at least 'moderate' on the static Physician's Global Assessment.
- Psoriasis that does not respond well to topical treatments (e.g. nail involvement).[1,5]

# Recommendations for topical therapy

Topical treatment options as recommended by NICE are summarised in the treatment algorithms 1 and 2 for adults and children.[1]

- Patients should be reviewed to assess progress and to ensure that the patient is correctly using the preparation.
- Arrange a review appointment 4 weeks after starting a new topical treatment in adults, and 2 weeks after starting a new topical treatment in children, to evaluate tolerability, toxicity, and initial response to treatment and reinforce the importance of adherence.[1] Prescribers may incorporate this into a telephone consultation.
- If there is a poor initial response after the first 4 weeks check compliance. Ask the person if they have any difficulties with application, cosmetic acceptability or tolerability. Check compliance and ask about the presence of adverse effects or any other issues to ascertain the reason for failure.
- With scalp preparations, particularly shampoos, ensure that the correct contact time of the preparation is maintained on the scalp.

## Algorithm 1: Topical treatment of psoriasis in adults.[1] Adapted from Herts Valley Clinical Commissioning group



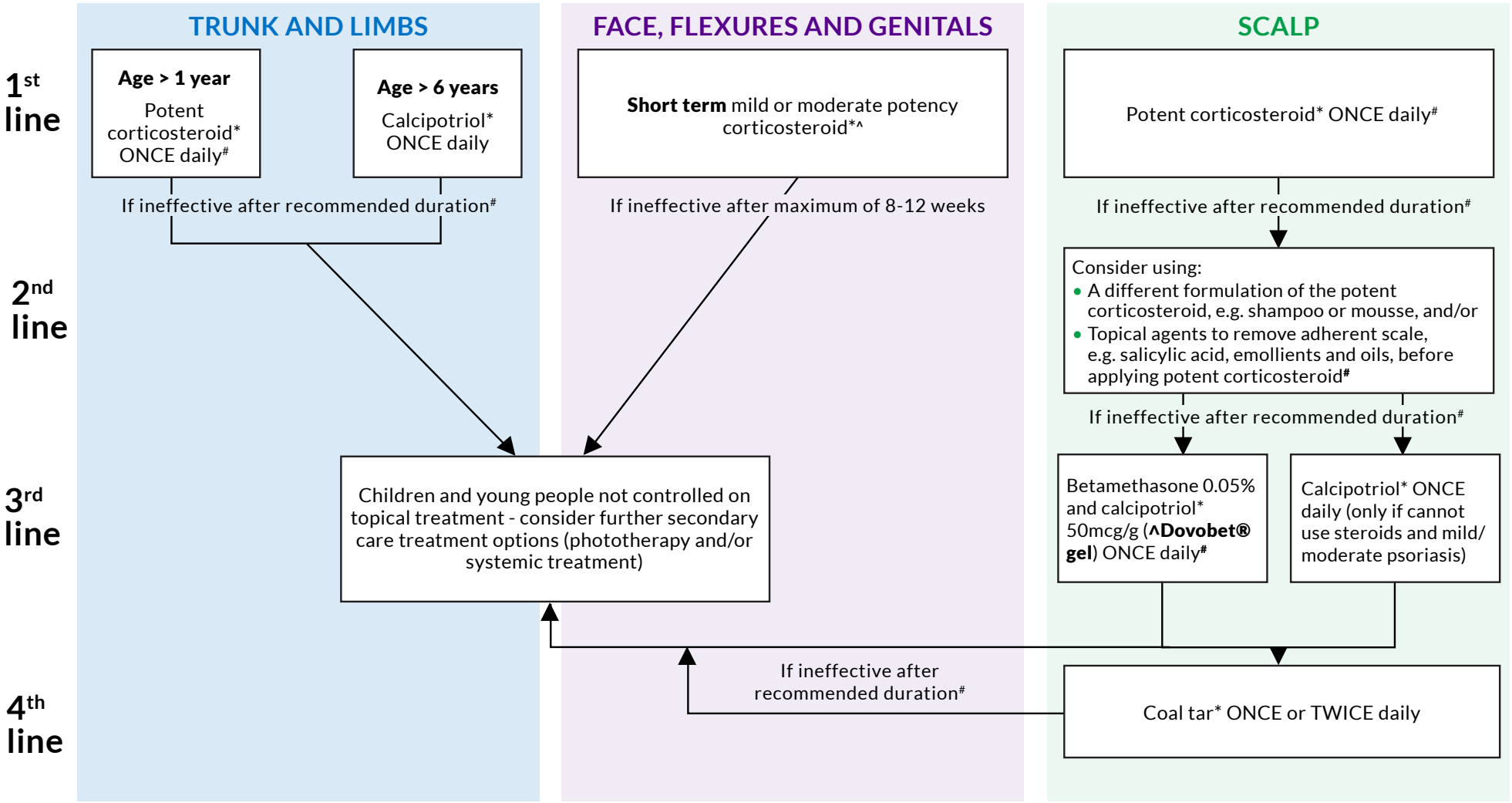

**# Aim for a break of 4 weeks between courses of treatment with potent or very potent corticosteroids.**
Consider non-steroid based products (coal tar, vit D/vit D analogues) as needed to maintain control of psoriasis during this period.

Psoriasis that cannot be controlled by topical treatment should be referred to secondary care for further assessment and treatment options (these include phototherapy and systemic treatment).

^ Unlicensed indication, i.e. off-label use.

## Algorithm 2: Topical treatment of psoriasis in children and young people[1] Adapted from Herts Valley Clinical Commissioning group

Children and young people with any type of psoriasis should be referred to secondary care at presentation. Most topical treatments to be initiated by specialist. Duration of treatment course to be clearly stated when requesting GP to continue prescribing or repeat courses.




**# Aim for a break of 4 weeks between courses of treatment with potent or very potent corticosteroids.**
Consider non-steroid based products (coal tar, vit D/vit D analogues) as needed to maintain control of psoriasis during this period.

* Refer to BNF for Children for information on appropriate dosing and duration of treatment.

^ Unlicensed indication, i.e. off-label use.

## Vitamin D analogues

- The vitamin D analogues available are calcipotriol, calcitriol and tacalcitol. These are used for most types of psoriasis and are the preferred choice for maintenance treatment.
- NICE assumed a class effect for these medicines and have not recommended one preparation over another. Published expert opinion suggests that calcitriol (active metabolite of vitamin D) and tacalcitol are less irritant than calcipotriol.[5]
- Vitamin D and vitamin D analogues are generally safe to use, however when used at high doses there is a potential risk of systemic side-effects (hypercalcaemia and hypercalciuria). For this reason a maximum dose application is specified in the summary of product characteristics (SPC).
- Calcipotriol ointment is the least expensive of the vitamin D preparations if used at the maximum daily application for 4 weeks.
- Calcipotriol is also the only vitamin D analogue licensed in children over 6 years.[8]
- Calcipotriol scalp solution for the treatment of scalp psoriasis is expensive and should only be used in people who are intolerant of or cannot use topical corticosteroids at this site or have mild to moderate scalp psoriasis.[1] It should be applied daily for 8 weeks.

## Corticosteroids

- These are an effective and acceptable and effective in treating psoriasis but with prolonged usage may cause skin atrophy, telangiectasia, hypopigmentation and rarely systemic absorption. There may be a risk of generalised pustular psoriasis or of rebound effects when discontinuing treatment.[1]
- Do not use continuously at any site for more than 8 weeks (potent corticosteroids) or more than 4 weeks (very potent corticosteroids).[1]
- Aim for a break of 4 weeks between courses of treatment with potent or very potent corticosteroids. Consider non-steroid based products (coal tar, calcipotriol/ vitamin D analogues) as needed to maintain control of psoriasis during this period.[1]
- Only mild to moderate topical steroids can be used on the face and flexural areas, and in children. For very thick plaques or on certain areas like scalp, palms and soles, a stronger topical steroid is needed.

## Calcipotriol/betamethasone combination therapy (Dovobet®)

- NICE found that when treatments were compared with each other, very few trials showed a statistically significant difference between treatments. However once daily combined calcipotriol monohydrate and betamethasone dipropionate was found to be more effective than once-daily vitamin D preparations, once-daily potent corticosteroid and once-daily retinoid therapy.[1]
- The NICE guideline development group (GDG) noted that in studies that compared various treatment sequences (e.g. combined calcipotriol/betamethasone products with vitamin D alone or alternating vitamin D for the full trial period) if the combined product was present anywhere in the sequence, even just for the first 4 weeks, the efficacy was improved compared with vitamin D alone. The GDG stated that the data suggested that this increased efficacy could be maintained by subsequent use of vitamin D analogue alone.[1]
- The NICE cost effectiveness analysis, showed that although combined calcipotriol monohydrate/ betamethasone dipropionate was found to be the most effective treatment, it was not cost effective. NICE demonstrated that separate application of a vitamin D and potent corticosteroid represents the most cost-effective first-line option for trunk and limb psoriasis. The NICE GDG felt that the modest additional benefits it produced were insufficient to justify the extra cost of this product; hence the reason for it being placed as a 3rd or 4th line option.[1]

## Trunk and limbs: Adults[1]

Adults: Dovobet® is recommended as a 4th line option if a twice-daily potent corticosteroid or coal tar preparation cannot be used or a once-daily preparation would improve adherence in adults. It should be applied once daily for up to 4 weeks. If necessary, treatment periods may be continued beyond 4 weeks or repeated on the advice of a specialist. Ointment and gel formulations are available. Consider non-steroid based products (coal tar, calcipotriol/vitamin D analogues) as needed to maintain control of psoriasis during this period.

## Trunk and limb: Children and young people[1]

Dovobet® is not recommended for prescribing. NICE recommends to refer children with any form of psoriasis to a specialist at presentation.

## Scalp psoriasis: Adults[1]

Dovobet® is recommended as a 3rd line option if the response to treatment with a potent corticosteroid for scalp psoriasis remains unsatisfactory. Dovobet® is available as a gel for scalp psoriasis. It should be applied once daily for 4 weeks. If necessary, treatment periods may be continued beyond 4 weeks or repeated on the advice of a specialist. There is no data on the long-term use of Dovobet although the licence for gel does state use for 8 weeks for non-scalp areas.

## Scalp psoriasis: Children and young people[1]

Dovobet® is recommended as a 3rd line option if the response to treatment with a potent corticosteroid for scalp psoriasis remains unsatisfactory (as above in adults). Use of Dovobet® gel in children and adolescents is unlicensed and should be initiated by specialists. NICE guidance also reinforces this and states that he prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. It advises to refer to the General Medical Councils Good practice in prescribing medicines – guidance for doctors, for further information.[9]

## Face, flexures* and genitals: All ages[1]

### *(Skin folds/creases i.e. armpits, groin and under the breasts)

Not recommended.

Prescribing information on managing psoriasis and specific indications on Dovobet® is available in an aide-memoire (attachment 1). Tables 1 and 2 on page  provide a comparison of licensed indication and cost of Dovobet® and vitamin D preparations in adults and children.

**Table 1: Comparison of licensed indications, dosage and cost of calcipotriol/betamethasone and vitamin D preparations in adults**

| Product | Licensed indication in adults | | Dosage[10] | Maximum recommended daily quantity[10] | Cost/g or mL (using most cost effective sized tube)[11,12] | Cost/4 weeks at maximum recommended doses for licensed indications (using the most cost effective tube sizes)[11,12] |
|---|---|---|---|---|---|---|
| | Mild to moderate "non scalp" plaque psoriasis | Scalp psoriasis | | | | |
| Calcipotriol/ Betamethasone Ointment 0.005%/0.05% (Dovobet®) | Yes | No | Daily | 15g | 63p/g | £266.28 |
| Calcipotriol/ Betamethasone Gel 0.005%/0.05% (Dovobet®) | Yes | Yes | Daily | Stable plaque psoriasis: 15g Scalp: 1-4g | 55p/g | Plaque- £231.56<br>Scalp - £61.75 |
| Calcipotriol 50 microgram/g ointment (Dovonex®) | Yes | No | Once or twice daily | 100g/week | 22p/g | £88.67 |
| Calcipotriol 50micrograms/ mL scalp solution | No | Yes | Twice daily | 60mL/weekly* | 90p/mL | £215.42 |
| Calcitriol 3 microgram/g ointment (Silkis®) | Yes | No | Twice daily | 30g | 18p/g | £151.70 |
| Tacalcitol 4 microgram/g ointment (Curatoderm®) | Yes | No | Daily | 10g | 31p/g | £86.41 |
| Tacalcitol 4 microgram/g lotion (Curatoderm®) | Yes | No | Daily | 10mL | 43p/mL | £118.81 |

*If calcipotriol scalp solution and ointments are used together, the maximum dose of calcipotriol is 5mg each week, 60mL calcipotriol scalp solution with 30g cream/ointment OR 30mL scalp solution with 60g cream/ointment.

**Table 2: Comparison of indications, dosage and cost of calcipotriol/betamethasone and vitamin D preparations in children**

| Product | BNF recommendations in children (age range stated)[13] | | Dose[13] | Maximum recommended daily dose quantity (unless stated)[13] | Cost/g or mL[11,12] | Cost/4 weeks at maximum recommended doses for licensed indications (using the most cost effective tube sizes)[11,12] |
|---|---|---|---|---|---|---|
| | Mild to moderate "non scalp" plaque psoriasis | Scalp psoriasis | | | | |
| Calcipotriol/ Betamethasone Ointment 0.005%/0.05% (Dovobet®) unlicensed | 12-18 years (specialist use only) | No | Daily | 75g weekly | 63p/g | £190.20 |
| Calcipotriol/ Betamethasone Gel 0.005%/0.05% (Dovobet®) unlicensed | 12-18 years (specialist use only) | 12-18 years (specialist use only) | Daily | Stable plaque psoriasis: 75g weekly<br>Scalp: 1-4g | 55p/g | Plaque- £165.40<br>Scalp - £61.75 |
| Calcipotriol 50 microgram/g ointment (Dovonex®) | > 6 years only | No | Once or twice daily | 6-12 years maximum 50g weekly; over 12 years max 75g weekly. | 22p/g | £66.50 at 75g max weekly |
| Calcipotriol 50micrograms/ mL scalp solution unlicensed | no | 6-18 years (specialist use only) | Twice daily | 6-12 years: max 30mL weekly^<br>12-18 years: max 45mL weekly^ | 90p/mL | £161.56 at 45mL max weekly |
| Calcitriol 3 microgram/g ointment (Silkis®) unlicensed | >12 years only | No | Twice daily | 30g | 18p/g | £151.70 |
| Talcalcitol 4 microgram/g ointment (Curatoderm®) unlicensed | >12 years only | No | Daily | 10g | 31p/g | £86.41 |
| Talcacitol 4 microgram/g lotion unlicensed | >12 years only | No | Daily | 10mL | 43p/mL | £118.81 |

unlicensed – refer to summary of product characteristics available at www.medicines.org.uk

^In children if calcipotriol scalp solutions (specialist prescribed) are also used the maximum total calcipotriol is 2.5mg in any one week for child 6–12 years (e.g. 20mL scalp solution with 30g ointment); max. 3.75mg in any one week for child 12–18 years (e.g. 30 mL scalp solution with ointment 45g).

## Savings

Across England, £28.7 million is spent annually on Dovobet® preparations (ePACT October - December 2014). NICE states that Dovobet® should only be used for up to 4 weeks. A 50% reduction in prescribing across England **could result in potential annual savings of £9 million or £15,987 per 100,000 patients**. Patient education and adherence to treatment is a crucial part of management.

The annual spend on calcipotriol scalp solution across England is £4.1 million (ePACT October - December 2014). It is important to ensure that it is only used for people who cannot use corticosteroids and have mild to moderate scalp psoriasis.[1]

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## Additional PrescQIPP resources

Briefing | Data pack | Implementation resources

Available here: http://www.prescqipp.info/resources/viewcategory/326-dovobet-in-psoriasis

**Information compiled by Anita Hunjan, PrescQIPP Programme, January 2015 and reviewed by Katie Smith, East Anglia Medicines Information Service, February 2015.**

**Non-subscriber publication June 2015.**

At the time of publication the PrescQIPP NHS Programme was hosted by Papworth NHS Trust and the Eastern Academic Health Science Network.

**Contact** help@prescqipp.info **with any queries or comments related to the content of this document.**

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The use and application of this guidance does not override the individual responsibility of health and social care professionals to make decisions appropriate to local need and the circumstances of individual patients (in consultation with the patient and/or guardian or carer). Terms and conditions

# Appendix 1

| Support groups | Web link |
|---|---|
| The Psoriasis Association | www.psoriasis-association.org.uk |
| Psoriasis and Psoriatic Arthritis Alliance | www.papaa.org |
| DermNETnz | www.dermnetnz.org |
| British Association of Dermatologists (BAD) | www.bad.org.uk |
| British Skin Foundation | www.britishskinfoundation.org.uk |