**HERTFORDSHIRE MEDICINES MANAGEMENT COMMITTEE (HMMC):**
**CALCIPOTRIOL MONOHYDRATE AND BETAMETHASONE DIPROPIONATE CUTANEOUS FOAM (ENSTILAR®)**

**GREEN – RECOMMENDED FOR USE IN PRIMARY AND SECONDARY CARE**

<table>
<thead>
<tr>
<th>NAME: GENERIC (TRADE)</th>
<th>WHAT IT IS</th>
<th>LICENSED INDICATION</th>
<th>DATE DECISION LAST REVISED</th>
<th>DECISION STATUS</th>
<th>NICE GUIDANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcipotriol monohydrate 50mcg/g and betamethasone dipropionate 0.5mg/g (Enstilar®)</td>
<td>Cutaneous foam containing a vitamin D analogue and a potent topical steroid</td>
<td>Topical treatment of psoriasis vulgaris (plaque psoriasis) in adults</td>
<td>September 2017</td>
<td>Final</td>
<td>NICE CG153</td>
</tr>
</tbody>
</table>

**HMMC recommendation following consultation with local specialists:**
Enstilar® cutaneous foam is recommended as a fourth line topical treatment option for trunk and limb plaque psoriasis in adults as an alternative to Dovobet® ointment. The place in therapy of Enstilar® is alongside Dovobet® ointment only, offering increased patient choice. Currently the unit cost of Enstilar® is the same as that for Dovobet® ointment. Enstilar® can be initiated by primary and secondary care clinicians.

- Trunk and limb psoriasis (adults) – Recommended fourth line treatment as an alternative to Dovobet® ointment.
- Trunk and limb psoriasis (children and young people) – Not recommended.
- Face, flexures and genititals (all ages) – Not recommended.
- Scalp psoriasis (all ages) – Not recommended (not licensed). Dovobet® gel can be used.

Please also refer to psoriasis topical treatment algorithm.
HERTFORDSHIRE MEDICINES MANAGEMENT COMMITTEE

Enstilar® cutaneous foam

HMMC Recommendation
Enstilar® is suitable for the topical treatment of plaque psoriasis in adults as an alternative to Dovobet® ointment which is currently approved for use.
Enstilar® can be prescribed by any primary and secondary clinician for the treatment of plaque psoriasis in adults. It is anticipated that Enstilar® will mainly be initiated by primary care prescribers.

Prescribing Rationale
- Enstilar® had a greater treatment effect compared with the Dovobet® products as well as the separates in the same vehicle.
- It is an alternative formulation which offers patient choice.
- Although Enstilar® may be more effective than Dovobet® in the trials, amongst my psoriasis patients there is great variability with some patients preferring Enstilar®, others gaining more benefit from Dovobet®. Some older patients have found Enstilar® less easy to apply and/or difficult to use as it is in a canister spray and requires dexterity.
- Unit cost is the same as Dovobet® ointment.
- Patient choice.

Background Information
- Enstilar® would be placed in the same position as Dovobet® ointment (as per agreed HMMC psoriasis pathway) for the treatment of mild, moderate and severe psoriasis.
- The enhanced bioavailability of the active components in Enstilar® results in much quicker and greater clinical efficacy. Patients treated with Enstilar® should achieve significantly quicker results and greater clinical effects within a 4 week period, as compared to currently available options.
- The side effect profile is comparable to that for Dovobet®.
- It is anticipated that Enstilar® will mainly be initiated by primary care prescribers.
- It is proposed that patients without any diagnostic uncertainty should receive Enstilar® before the need for referral to specialist services, and that patients should receive Enstilar® before moving on to light therapy and systemic non-biologic agents such as methotrexate and ciclosporin. Hence it is anticipated that use of Enstilar® should reduce the numbers of psoriasis patients being referred to specialist services as well as prevent some patients moving on to costly and potentially more dangerous second line therapies.
- A course of treatment is 4 weeks.
- Enstilar® foam spray should be applied once-daily, directly from the container to the areas affected by psoriasis and rubbed in gently.
- A two second spray will cover an area of skin roughly equivalent to the surface area of an adult hand (inc. fingers); this is 0.5g of foam and corresponds with the 0.5g finger-tip unit used in the topical application of creams and ointments.
- The maximum daily dose of Enstilar® should not exceed 15g.
- If using other topical products containing calcipotriol in addition to Enstilar®, the total daily dose of all topical products should not exceed 15g per day.
- The total body surface area treated should not exceed 30%.
- Enstilar® contains a potent group 3 steroid; concurrent treatment with other steroids on the same treatment area must be avoided.
- Place in therapy – an alternative to currently available formulations (gel, ointment currently available) as an option for patients. No additional cost pressure. Increased choice and potential patient benefit as one product may be more acceptable than another.
Evidence of Clinical Effectiveness

The efficacy and safety of Enstilar® has been evaluated in:

- Two randomised, controlled phase 3 studies (PSO-FAST and PSO-ABLE [patients with mild to moderate psoriasis])(Leonardi et al., 2015, LEO Pharma UK, 2016b)
- Two randomised, controlled phase 2 studies(Koo et al., 2015, Lebwohl et al., 2016)
- Two single-arm phase 2 studies(Quelle-Roussel et al., 2015, Taraska et al., 2014)

The primary outcomes of the phase 3 studies are detailed below:

- PSO-FAST study. Patients with 2%-30% of their body surface area affected by psoriasis, an Investigators (physicians) Global Assessment of disease (PGA) of at least mild and a modified PASI (mPASI) score of ≥2 on the trunk/limbs were randomised to daily treatment with either Enstilar® (n=323), or vehicle (n=103) for 4 weeks. Significantly more patients treated with Enstilar® than with foam spray vehicle achieved treatment success at week 4: 53.3% vs. 4.8% respectively (Odds Ratio 30.3, 95% CI; 9.7 to 94.3, p<0.001, number need to treat [NNT] with Enstilar® to get one treatment success = 2)(Leonardi et al., 2015).
- PSO-ABLE study. Physician's Global Assessment (PGA) rated plaque psoriasis of mild-to- moderate severity, with 2–30% BSA affected (trunk and/or limbs) and a modified (excluding the head) Psoriasis Area and Severity Index (mPASI) score ≥2 on the trunk/limbs were randomised to treatment with once-daily Enstilar® (n=185), calcipotriol/BDP gel (n=188), foam spray vehicle (n=47) or gel vehicle (n=43) for up to 4 weeks and 8 weeks respectively. Significantly more patients using Enstilar® compared with calcipotriol/BDP gel had treatment success (clear/almost clear with at least a two-step improvement in disease severity from baseline according to PGA): 36.2% at week 4 vs. 22.5% at week 8 respectively, (OR; 2.42, 95% CI; 1.34 to 4.37, p=0.003, NNT=7) (LEO Pharma UK, 2016b). The different endpoints reflect the differences in the maximum licensed duration of treatment: 4 weeks for Enstilar® (LEO Pharma UK) and 8 weeks for Dovobet Gel (LEO Laboratories Ltd., 2015a).

The primary outcomes of the two randomised, controlled phase 2 trials are detailed below:

- Comparison with calcipotriol/BDP ointment (Dovobet ointment) (n=376): At Week 4, a significantly larger proportion of patients using Enstilar® met the primary outcome of treatment success according to the PGA (‘clear’ or ‘almost clear’ with at least a two-step improvement according to the PGA) compared with those using calcipotriol/BDP ointment: 54.6% vs. 43.0%; mean difference 11.6%; OR; 1.7, 95% CI; 1.1 to 2.8; p=0.025, NNT=9. A greater proportion of patients using Enstilar® had achieved ‘treatment success’ as early as week 2 than those using calcipotriol/BDP ointment (29.7% vs. 20.9%) (Koo et al., 2015).
- Comparison with calcipotriol and with betamethasone (n=302): After 4 weeks of treatment, Enstilar® was significantly more effective on the body than its individual active components. Significantly more patients treated with Enstilar® than with calcipotriol or betamethasone alone met the primary outcome of treatment success (‘clear’ or ‘almost clear’ for patients with at least moderate disease at baseline, ‘clear’ for patients with mild disease at baseline) according to the PGA at week 4. Enstilar® vs. calcipotriol: 45.0% vs. 15.0% (p<0.001), NNT=3. Enstilar® vs. betamethasone; 45.0% vs. 31.0% (p=0.047), NNT=7. Enstilar® was superior to calcipotriol cutaneous foam (OR; 4.34, 95% CI; 2.16 to 8.72, p<0.001) and betamethasone cutaneous foam (OR; 1.81, 95% CI; 1.00 to 3.26, p=0.047) (Lebwohl et al., 2016).

Cost Effectiveness

- The drug acquisition cost of Enstilar® is £39.68 for a 60g pressurised container. The budget impact per patient (weighted average 117g Enstilar® used over the recommended treatment period of 4 weeks (Koo et al., 2015, Lebwohl et al., 2016, Leonardi et al., 2015, LEO Pharma A/S, 2015) is £77.38.
- As a comparison, Dovobet® ointment is also £39.68 per 60g tube.
- Enstilar® is not listed as a high cost drug. It will be reimbursed through the National Tariff in England (Monitor and NHS England 2016) with prescribing mainly in primary care.

The needs of the population

2-3% of population will have psoriasis. 80% will not present for medical diagnosis/care (self-managed). Of those treated Dovobet® would be currently used in all presented cases and Enstilar® foam would be an alternative in this group (alternative not an addition).

The needs of the community

Psoriasis patients have limited product choice – this increases choice/possibility of effective treatment with no cost pressure. Psoriasis is a chronic long term debilitating disease with psychological impact on lives. If patients are offered a treatment that they are able to use and find effective this impact can be reduced.
## Policy Drivers
This product fits within NICE guidance NICE Psoriasis. The assessment and management of psoriasis. NICE CG 153. Issued October 2012.

## Equity
Patients should have equal access to Enstilar® regardless of their location.

## Implementability
No additional training would be required by GPs as they currently prescribe Dovobet® ointment.

## References
Please see Leo Pharma UK formulary pack where much of this information has been sourced from.