A.6	Calcipotriol - psoriasis
Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: 1. Psoriasis is a noncommunicable, painful, disfiguring, and disabling disease 2. It has no cure 3. Systemic medicines (e.g. methotrexate, ciclosporin, or acitretin) has significant adverse effects profile and need careful monitoring since they had to be used for long term 4. Topical treatment has value in the treatment of this difficult skin disease
Briefly summarize the role of the proposed medicine(s) relative to other therapeutic agents currently included in the Model List, or available in the market.	1. Topical therapy for psoriasis include coal tar, corticosteroids, vitamin D analogues (e.g.: Calcipotriol) and dithrinol 2. EML already lists corticosteroids and coal tar under 13.4- Medicines affecting skin differentiation and proliferation 3. Calcipotriol has not been shown to be more effective than the already listed betamethasone (with square box) 4. Applicants propose to include Calcipotriol as an “add-on” to topical corticosteroids since there can be patients for whom CS may be contra-indicated or produce AEs when used long term 5. However, for scalp psoriasis and chronic plaque psoriasis Calcipotriol is inferior to corticosteroids
Have all important studies and all relevant evidence been included in the application?	☒ Yes ☐ No ☐ Not applicable If no, please provide brief comments on any relevant studies or evidence that have not been included: 1. Application provides summary of evidence obtained from extensive search of literature including Cochrane database 2. Concern is there are very limited studies in the literature 3. Well conducted clinical trials were also scarce 4. Answer to first part is Yes, answer for second part is No (lack of relevant evidence in the literature)

Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed indication?	☐ Yes ☒ No ☐ Not applicable Briefly summarize the reported benefits (e.g. hard clinical versus surrogate outcomes) and comment, where possible on the actual magnitude and clinical relevance of benefit associated with use of the medicine(s). 1. There are no recent studies 2. There are no well conducted high quality clinical trials 3. There are no systematic reviews or meta-analyses 4. Mostly small sample studies 5. Interventions are pooled in the analysis (when pooling is removed, results are differing) 6. Placebo studies 7. Primary outcomes also varied from study to study 8. Calcipotriol vs Placebo: Not provided after pooling is removed *9.* With topical corticosteroids: *The SMD for calcipotriol against fluocinonide 0.05% ointment was -0.58 (95% CI -0.99 to -0.18; I^2 statistic = NA). Calcipotriol was statistically less effective than both diflorasone diacetate 0.05% ointment (SMD 0.27; 95% CI 0.02 to 0.52) and betamethasone dipropionate (SMD 0.43; 95% CI 0.28 to 0.58; I^2 statistic = 50.3%). But there were no statistically significant differences between calcipotriol and betamethasone valerate,* Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)? Children Yes, But low quality study as for adult ones
Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: Since safety monitoring is better done from observational studies during post marketing surveillance period, evidence of the safety and adverse effects associated with the medicine is better reported in the application than the efficacy data
Are there any adverse effects of concern, or that may require special monitoring?	☒ Yes ☐ No ☐ Not applicable Comments: Hypercalcaemia if absorbed, Skin irritation (in about 20%)
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	Favourable Reasons 1. Benefit is not supported by valid evidence on efficacy, but the product has secondary benefits like topical preparation, ease of administration, wide availability, listed in many national formularies and better acceptability by patients 2. Risk: Well known, skin irritation and hypercalcaemia (Type A adverse effect, so can be predicted and allow monitoring. Also product is very poorly absorbed to cause hypercalcaemia)

	3. Hence, I assessed the ratio to be favourable despite low quality evidence on efficacy (Patients will accept the therapy despite lack of strong evidence on efficacy) {lack of data}
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	Low
Are there any special requirements for the safe, effective and appropriate use of the medicine(s)**?** (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)	☒ Yes ☐ No ☐ Not applicable Comments: 1. Diagnosing psoriasis 2. Selecting the suitable patients 3. Anticipating and managing hypercalcaemia
Are you aware of any issues regarding the registration of the medicine by national regulatory authorities? (e.g. accelerated approval, lack of regulatory approval, off-label indication)	☐ Yes ☒ No ☐ Not applicable Comments:
Is the proposed medicine recommended for use in a current WHO Guideline approved by the Guidelines Review Committee? (refer to: https://www.who.int/publications/who-guidelines)	☐ Yes ☒ No ☐ Not applicable Comments:
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	I cannot see much issues in access, cost and affordability in different settings It is registered in many countries It is listed in NEMLs of countries like
Any additional comments	
Based on your assessment of the application, and any additional evidence / relevant information identified during the review process, briefly summarize your proposed recommendation to the Expert Committee, including the supporting rationale for your conclusions, and any doubts/concerns in relation to the listing proposal.	RECOMMEND Reasons: 1. Psoriasis is a difficult disease affecting quality of life of patients and family members 2. Topical treatment is preferred as systemic treatment have significant adverse effects and need monitoring 3. Of the documented topical treatment, steroids and coal tar are already listed in EML 4. Application of coal tar is difficult which will limit acceptance by patients 5. I have assessed benefits: risk ratio as favourable 6. Since topical corticosteroids are indicated in many other indications, stock will be fast moving and availability at “all times” would be a problem 7. Hence, I recommend adding (despite no strong evidence on efficacy) To discuss – square box To discuss – Supplementary or Core

References (if required)	