

Tapinarof Cream 1% for Extensive Plaque Psoriasis: A Maximal Use Trial on Safety, Tolerability, and Pharmacokinetics

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Supplementary Table 1 Summary of key inclusion and exclusion criteria

Key inclusion criteria
• Men or women aged 18–75 years with clinically confirmed diagnosis of chronic psoriasis and stable disease for at least 6 months prior to the study • BSA involvement $\geq 20\%$ (scalp, palms, and soles were excluded from the %BSA calculations to determine eligibility at screening) • A PGA score ≥ 3 at screening • Presence of venous access for multiple blood draws on an area that was devoid of psoriasis
Key exclusion criteria
• Psoriasis other than plaque variant • Any sign of infection of any of the psoriatic plaques • Concurrent or history of the following conditions/diseases: ○ Immunocompromised (e.g., lymphoma, acquired immunodeficiency syndrome) or a history of malignant disease within 5 years prior to baseline ○ Chronic or acute infection requiring treatment with systemic antibiotics, antivirals, antiparasitics, antiprotozoals, or antifungals within 4 weeks prior to the baseline visit ○ Acute active bacterial, fungal, or viral (herpes simplex, herpes zoster, or chickenpox) skin infection within 1 week prior to the baseline visit ○ Significant dermatologic or inflammatory condition other than plaque psoriasis • QTcF interval >470 milliseconds • UV light therapy or prolonged exposure to natural or artificial sources of UV radiation within 4 weeks prior to baseline • Use of any prohibited medication within the indicated period before baseline: ○ Minimum of 5 half-lives for biologic agents, including rituximab, ustekinumab, secukinumab, golimumab, ixekizumab, infliximab, adalimumab, alefacept, and etanercept ○ Four weeks for systemic treatments: cyclosporin, interferon, methotrexate, apremilast, tofacitinib, mycophenolate, thioguanine, hydroxyurea, sirolimus, azathioprine, other systemic immunosuppressive or immunomodulating agents, fumaric acid derivatives, vitamin D and analogs,

retinoids (e.g., acitretin, isotretinoin), psoralens, corticosteroids, or adrenocorticotrophic hormone analogs

- Two weeks for immunizations with a live viral component
- Two weeks for drugs known to possibly worsen psoriasis, such as beta-blockers (e.g., propranolol), lithium, iodides, angiotensin-converting enzyme inhibitors, and indomethacin, unless on a stable dose for >12 weeks
- With the exception of emollients, 2 weeks for topical treatments (corticosteroids, immunomodulators, anthralin, vitamin D derivatives, retinoids, or coal tar)
- Concurrent skin lesions in the treatment area that, in the opinion of the investigator, would either interfere with study evaluations or affect the safety of the patient

BSA, body surface area; PGA, Physician Global Assessment; QTcF, QT interval corrected for heart rate using Fridericia's formula; UV, ultraviolet.

Supplementary Table 2 Grade scale for local tolerability

Score	Severity	Description
0	No irritation	No evidence of local irritation/intolerance
1	Mild	Minimal erythema and/or edema, slight glazed appearance
2	Moderate	Definite erythema and/or edema with peeling and/or cracking but does not require treatment modification
3	Severe	Erythema, edema glazing with fissures, few vesicles or papules
4	Very Severe	Strong reaction spreading beyond the treated area, bullous reaction, erosions