

HISTORICALLY ACCEPTED USE

Tertiary and Quaternary Committee

Executive Summary

Date: May 2022

Medicine (INN): Acitretin

Medicine (ATC): D05BB02

Indication (ICD10 code): Psoriasis (L40.1; L40.9)

Patient population: Patients with severe localized or generalized pustular psoriasis, or severe psoriasis not responding to conventional therapy.

Prevalence of condition: Prevalence of psoriasis in various countries ranges from 0.09% to 11.43%.¹ African and Asian populations have a lower frequency of between 0.4% and 0.7%.²

Level of Care: Tertiary and Quaternary

Prescriber Level: Dermatologist

Current standard of Care: Hospital level – coal tar ointment and topical corticosteroids for flares.

Efficacy estimates:

- RCT evidence has shown systemic retinoids to be effective for severe chronic plaque psoriasis, particularly when combined with photochemotherapy treatment. Generalised pustular and palmoplantar pustular psoriasis has been shown to be particularly responsive to acitretin.³
- Versus methotrexate:
 - For chronic plaque psoriasis, methotrexate was shown to be a better treatment option over acitretin in a randomized study (n=142):⁴

	Excellent response (PASI-75%)	Good response (PASI-50%)	Fair response (less than 50% reduction in PASI)	No response
Methotrexate group	38 (53.5%)	13 (18.3%)	4 (5.6%)	1(1.4%)
Acitretin group	18 (25.3%)	27 (38.0%)	8 (11.2%)	5 (7.04%)

- For significant palmoplantar psoriasis, methotrexate was proposed as the drug of choice for psoriasis with significant palmoplantar involvement in a prospective randomized trial (n=111).⁵

	Reduction of m-PPASI*		Marked improvement (m-PPASI 75)
	8 weeks	12 weeks	
Methotrexate group	15.38 ± 6.08	10.30 ± 5.97	12 (24%)
Acitretin group	17.23 ± 5.25	12.40 ± 5.31	4 (8%)
	(P = 0.04).	(P = 0.03).	(P = 0.029).

*modified palmoplantar pustular psoriasis area and severity index

Background

This agent was previously included in the Adult Hospital Level Standard Treatment Guideline and Essential Medicines List, 2006 version; for use in severe localized or generalized pustular psoriasis (prescribed by dermatologist only).

Guidelines

- The Joint American Academy of Dermatology – National Psoriasis Foundation Guidelines⁶ recommends the following regarding acitretin: (**Recommendation based on inconsistent or limited quality patient-oriented evidence**)
 - » Acitretin can be recommended as monotherapy for plaque psoriasis.
 - » Acitretin can be recommended for treatment of erythrodermic, pustular, and palmarplantar psoriasis.
 - » Acitretin can be recommended as combination therapy with PUVA for psoriasis.
 - » Acitretin can be combined with BB-UVB for plaque psoriasis.

Historically accepted use Criteria

Criteria		Comment			
1	The medicine is included in the WHO Model Essential Medicines List, either as a core or complementary item, for the indication requested.	<p>YES NO</p> <table border="1"> <tr> <td></td> <td>X</td> </tr> </table>		X	<p><i>Coal tar and corticosteroids listed under dermatological medicine. No specific psoriasis treatment outlined.</i></p>
	X				
2	The medicine is currently registered by SAHPRA for the indication.	<p>YES NO</p> <table border="1"> <tr> <td>X</td> <td></td> </tr> </table>	X		
X					
3	There is evidence of long-established (prior to 1996*) safe and effective use of the medicine for the recognised indication in the public health sector.	<p>YES NO</p> <table border="1"> <tr> <td>X</td> <td></td> </tr> </table>	X		<p>Comment:</p> <ul style="list-style-type: none"> • <i>Item previously included in the Adult Hospital Level Essential Medicines List for use in Severe localized or generalized pustular psoriasis and severe psoriasis.</i> • <i>FDA approved - 1997</i>
X					
4	There are no new safety or efficacy concerns.	<p>YES NO</p> <table border="1"> <tr> <td></td> <td>X</td> </tr> </table>		X	<p>Comment: <i>*The major side-effect of acitretin is teratogenicity. Women should be advised not to become pregnant for a least 24 months after stopping treatment with acitretin.</i></p>
	X				
5	Is budget impact expected to have an incremental increase, that a de novo review is justified?	<p>YES NO</p> <table border="1"> <tr> <td></td> <td>X</td> </tr> </table>		X	<p>Comment:</p> <p>Cost of monthly treatment at 35mg/day: R2263.16* (<i>see below actual expenditure 2021/2022– Annex 1</i>)</p> <p><i>*National Contract Price: HP09:2021SD, May 2022</i></p>
	X				
6	Equitable access across the country is essential, and is limited only by the availability of adequately trained staff and availability of equipment.	<p>YES NO</p> <table border="1"> <tr> <td>X</td> <td></td> </tr> </table>	X		<p>Comment:</p>
X					

* The Essential Drugs Programme (EDP) of South Africa was established in terms of the National Drug Policy (NDP) which was implemented in 1996

Recommendation

Acitretin is recommended for inclusion on the Tertiary and Quaternary Level Essential Medicine List for the management of Patients with severe localized or generalized pustular psoriasis, or severe psoriasis not responding to conventional therapy under the care of a dermatologist. This item is currently being procured on contract (annexure 1) and it is not expected this formal approval on the Essential Medicine List will increase this use.

**The major side-effect of acitretin is teratogenicity. Women should be advised not to become pregnant for a least 24 months after stopping treatment with acitretin. Similar consent and pregnancy processes to be adopted as for isotretinoin oral usage.*

Annexure 1

Actual annual expenditure (May 2021 – May 2022):

Product	Contract price*	Average usage/month**	Average monthly budget impact	Average usage/year	Average annual budget impact
Acitretin; 10mg; Capsule; 30 Capsules	R728.42	116	R84,557.42	1,393	R1,014,689.06
Acitretin; 25mg; Capsule; 30 Capsules	R1696.39	257	R436,820.43	3,090	R5,241,845.10
				TOTAL	R6,256,534.16

*MHPL: May 2022

** RSA Pharma: actual usage data May 2020 - May 2022 averaged by months over the period

Acitretin usage of past 3 calendar years:

	2019	2020	2021
	Annual usage	Annual usage	Annual usage
Acitretin 10mg 28's	1676	1614	666
Acitretin 25mg 28's	2959	3022	1302

RSA Pharma data

References

¹ World Health Organisation. Global report on Psoriasis. WHO Library, 2016. https://apps.who.int/iris/bitstream/handle/10665/204417/9789241565189_eng.pdf.psoriasis;jsessionid=54912784D28C9F36ECCD45471AC5775B?sequence=1

² Engler D, Chezuba HP, Masuku P. Psoriasis – Review. South African Pharmacy Journal. 2017, 84(5):38-42.

³ Griffiths CEM, Clark CM, Chalmers RJG, Li Wan Po A, Williams HC. A Systematic review of treatment for severe psoriasis. Health Technology Assessment. 2000, 4 (40).

⁴ Noor SM, Ayub N, Paracha MM. Efficacy and safety of methotrexate versus acitretin in chronic plaque psoriasis. J Postgrad Med Inst. 2017, 31(1):4-7

⁵ Janagond AB, Kanwar AJ, Handa S. Efficacy and safety of systemic methotrexate vs. acitretin in psoriasis patients with significant palmoplantar involvement: a prospective, randomized study. JEADV. 2013, 27: e384-e389.

⁶ Menter A, Gelfand JM, Connor C, Armstrong AW, Cordoro KM, Davis DM, et.al. Joint American Academy of Dermatology – National Psoriasis Foundation guidelines of care for management of psoriasis with systemic nonbiologic therapies. *J Am Acad Dermatol.* 2020, 82: 1445-1486.