

HISTORICALLY ACCEPTED USE
Tertiary and Quaternary Committee

Executive Summary

Date: March 2020

Medicine (INN): 5-fluorouracil topical ointment

Medicine (ATC): L01BC02

Indication (ICD10 code): L57.0 Actinic Keratosis

Patient population: Patients with actinic keratosis – field directed treatment

Prevalence of condition: The National Cancer Registry (2014) does not provide any information regarding the incidence of Actinic Keratosis (AK) as it is a pre-cancerous condition. AK prevalence in a Turkish study was found to be 2.50% among patients of all ages.¹ Prevalence higher in European countries at 19-24% (Fair skin is a risk factor) in those older than 60 years.²

Level of Care: Tertiary and Quaternary

Prescriber Level: Dermatologist

Current standard of Care: 5-fluorouracil

Search: "Keratosis, Actinic"[Mesh] AND "Fluorouracil"[Mesh] AND (Meta-Analysis[ptyp] OR Randomized Controlled Trial[ptyp] OR systematic[sb])

Efficacy estimates: A network meta-analysis (2013)³ evaluated eight treatments (fluorouracil 0.5% and 5%, ALA-photodynamic therapy, cryotherapy, diclofenac 3%, hyaluronic acid 2.5%, imiquimod 5%, ingenol mebutate 0.015-0.05%, MAL-photodynamic therapy, and placebo) for actinic keratosis. The efficacy ranking of ‘participant complete clearance’ was highest in those treated with 5-FU. It must be noted that data is weak with selective reporting.

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.	YES <input checked="" type="checkbox"/>	NO <input type="checkbox"/>
2	The medicine is currently registered by SAHPRA for the indication.	YES <input checked="" type="checkbox"/>	NO <input type="checkbox"/>
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.	YES <input checked="" type="checkbox"/>	NO <input type="checkbox"/>
		Comment: initial studies from the early 1970s ^{4, 5, 6}	
4	No new safety or efficacy concerns.	YES <input checked="" type="checkbox"/>	NO <input type="checkbox"/>
		Comment: Women of childbearing age should be on contraception.	

5	Budget impact is not expected to have an incremental increase, that a de novo review is justified.	<table border="1"> <tr> <td data-bbox="943 199 1127 231">YES</td> <td data-bbox="1131 199 1312 231">NO</td> </tr> <tr> <td data-bbox="943 237 1127 275">X</td> <td data-bbox="1131 237 1312 275"></td> </tr> </table> <p data-bbox="873 281 1477 352">Comment: Price per course: R1220.10 (twice daily applications for 2-4 weeks)</p>	YES	NO	X	
YES	NO					
X						
6	Equitable access across the country is essential, and is limited only by the availability of adequately trained staff and availability of equipment.	<table border="1"> <tr> <td data-bbox="943 371 1127 403">YES</td> <td data-bbox="1131 371 1312 403">NO</td> </tr> <tr> <td data-bbox="943 409 1127 447">X</td> <td data-bbox="1131 409 1312 447"></td> </tr> </table> <p data-bbox="873 453 998 485">Comment:</p>	YES	NO	X	
YES	NO					
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

It is recommended that 5-fluorouracil ointment be included on the Essential Medicines List for the management of actinic keratosis.

References

¹ Yaldiz, Mahizer MD. Prevalence of actinic keratosis in patients attending the dermatology outpatient clinic Medicine: July 2019 - Volume 98 - Issue 28 - p e16465.

² de Berker D, McGregor JM, Mohd Mustapa MF, Exton LS, Hughes BR. British Association of Dermatologists' guidelines for the care of patients with actinic keratosis. 2017. British Journal of Dermatology (2017)176: 20–43.

³ Gupta AK, Paquet M. Network meta-analysis of the outcome 'participant complete clearance' in nonimmunosuppressed patients of eight interventions for actinic keratosis: a follow-up on a Cochrance review. British Journal of Dermatology. 2013, 169: 250-259.

⁴ Hodge SJ, Schrodt GR, Owen LG. Effect of topical 5-fluorouracil treatment on actinic keratosis: a light and electron microscopic study. J Cutan Pathol. 1974;1 (6):238-48.

⁵ Breza T, Taylor JR, Eaglstein WH. Noninflammatory Destruction of Actinic Keratoses by Fluorouracil. Arch Dermatol. 1976;112(9):1256–1258. doi:10.1001/archderm.1976.01630330026006.

⁶ Dillaha CJ, Jansen GT, Honeycutt WM, Bradford AC. Selective Cytotoxic Effect of Topical 5-Fluorouracil. Arch Dermatol. 1983;119(9):774–783. doi:10.1001/archderm.1983.01650330066015

Appendix

Safe application of 5-fluorouracil topical ointment

Always apply according to doctors instructions

The following application principles should be taken into account:

- Applied once or twice daily.
- Best to apply mornings and evenings (try not to apply at bedtime- contact with pillows may cause undesirable spread).
- Apply a thin layer on affected area. Avoid contact with eyes, nostrils, and lips.
- Do not apply to broken skin or open cuts.
- Can be applied with a finger, however be sure to wash hands after applying.
- Moisturizers and makeup should only be applied 20 minutes after application of 5-fluorouracil topical ointment.
- Always apply sunscreen (high sun protection factor) to those areas exposed to the sun (apply 20 min after application of 5-fluorouracil topical ointment).
- Limit exposure to the sunshine and wear appropriate clothing to cover exposed areas.