South East London Area Prescribing Committee
Formulary recommendation

Reference:	**113**
Intervention:	**Actikerall® cutaneous solution for the topical treatment of actinic keratosis (grade I/II) in immunocompetent adult patients. Each 1 g [= 1.05 ml] of Actikerrall cutaneous solution contains 5 mg of fluorouracil and 100 mg of salicylic acid** (Fluorouracil belongs to a group of medicines known as antimetabolites, which inhibit the growth of cells (cytostatic agent). Salicylic acid is a substance to soften hard skin.)
Date of Decision:	**January 2020**
Date of Issue:	**February 2020**
Recommendation:	**GREEN – can be prescribed within agreed criteria for use in primary or secondary care**
Further Information:	• Actikerall cutaneous solution is approved for use in SEL in line with its licensed indication* and the SEL pathway for the management of actinic keratosis (AK), which forms part of the primary care dermatology guidelines. • In line with the local AK pathway, Actikerall cutaneous solution may be considered as 2nd line option in patients with palpable and moderately thick hyperkeratotic AK (grade I/II) where there are discrete, localised lesions with a thin base AND cryotherapy is **not** available or where topical therapy is preferred. • Actikerall should be applied once daily to the affected area (up to 25 cm^2) until the lesions have completely cleared or for up to a **maximum** of 12 weeks. • If severe side effects occur (e.g. inflammatory response), reduce the frequency of topical application to three times per week until the side effects improve. • The patient should be reassessed eight weeks after completion of treatment. If lesions are still present or if the AK has recurred consider referral for specialist dermatology review. • When assessing options to treat recurrent lesions, clinicians should consider that the efficacy of retreatment with Actikerall has not been formally measured in clinical trials. • Actikerall is not a suitable option if lesions are near the eye. • The total area of skin being treated with Actikerall at any one time should not exceed 25 cm^2 (5 cm x 5 cm). • The treated area should not be covered after application and the solution should be left to dry to form a film over the applied area. Each time Actikerall is reapplied the existing film should be removed beforehand by gently peeling it off. Warm water may help to remove the film. • Actikerall should not be applied to hairy skin due to sticking together of the hair in the skin area where Actikerall is applied, making it difficult to remove the film. When applied to hairy skin, a shave or other suitable methods of hair removal should be considered prior to any application. • **Patients should be counselled on the appropriate use of this topical preparation**. Please refer to the SEL primary care dermatology guidelines and supporting key messages for further information. *Actikerall cutaneous solution is licensed for the topical treatment of slightly palpable and/or moderately thick hyperkeratotic actinic keratosis (grade I/II) in immunocompetent adult patients. Grade I/II intensity is based on the 4-point scale of Olsen et al. (1991)
Shared Care/ Transfer of care required:	N/A
Cost Impact for agreed patient group	• From prevalence estimates, and predictions from the SMC review for market share of Actikerall for AK, the predicted drug costs equate to approximately £8,500 per 100,000 population. This cost is however offset by the cost of alternative treatments currently being used.

Cost Impact for agreed patient group cont'd	• It is expected that diclofenac 3% gel is currently used frequently for AK and drug acquisition costs are equivalent to Actikerall. However, fluorouracil 5% cream is less costly (depending on the amount of tubes used). • Availability of Actikerall cutaneous solution within primary is, however, expected to reduce referrals for treatment with cryotherapy within the secondary care setting, which will also result in service related savings.
Usage Monitoring & Impact Assessment	**Trusts/Community dermatology clinics** • Monitor and submit usage and audit data on request to the APC (community clinics to submit through their borough based leads).
	Borough based teams: • Monitor primary care prescribing data. • Audit locally (including locally commissioned dermatology services) to ensure use in line with this recommendation and the local pathway. • Exception reports from GPs if inappropriate prescribing requests are made to primary care.
Evidence reviewed	**References (from evidence evaluation prepared December 2018)** 1. Berker D et al. British Association of Dermatologists' guidelines for the care of patients with actinic keratosis 2017. British Journal of Dermatology (2017); 176: pages 20-43. 2. Marks R, Rennie G, Selwood T. Malignant transformation of solar keratoses to squamous cell carcinoma. Lancet (1988); 331 (8589): pages 795–797 3. Bavinck J et al. Treatments for common and plantar warts. British Medical Journal (2011); 342: d3119. 4. NICE Clinical Knowledge Summaries 2014. Warts and verrucae. Accessed online here (08.11.18) 5. Up to date (online recourse). Cutaneous warts (common, plantar, and flat warts). Accessed here (12/11/2018). 6. Scottish Medicines Consortium. Fluorouracil 0.5% / salicylic acid 10% cutaneous solution (Actikerall®) SMC No. (728/11) 09 September 2011. Accessed via here (02.11.18). 7. Actikerall 5mg/g + 100mg/g Cutaneous Solution. Summary product of characteristics. Accessed via https://www.medicines.org.uk. Last accessed 12/11/2018. 8. Primary Care Dermatology Society Actinic Keratoses Treatment Pathway. Accessed here (06.11.18). 9. Sterling JC et al. British Association of Dermatologists' guidelines for the management of cutaneous warts 2014. British Journal of Dermatology (2014); 171: pages 696 – 712. 10. Primary Care Dermatology Society Warts pathway. Accessed here (12/11/2018) 11. Kwok CS et al. Topical Treatments for cutaneous warts (Review). Cochrane Database of Systematic Reviews (2012); Issue 9. Art. No.: CD001781. DOI: 10.1002/14651858.CD001781.pub3 12. Stockfelth E, Kerl H, Zwingers T, Willers C. Low-dose 5-flourouracil in combination with salicylic acid as a new lesion-directed option to treat topically actinic keratosis: histological and clinical study results. British Journal of Dermatology (2011); 165: pages 1101-1108. 13. Stockfleth E, Zwingers T, Willers C et al. Recurrence rates and patient assessed outcomes of 0.5% 5-fluorouracil in combination with salicylic acid treating actinic keratoses. Eur J Dermatol (2012); 22: pages 370–4. 14. Stockfleth E, von Kiedrowski R, Dominicus R, Ryan J, Ellery A, Falques M, et al. Efficacy and safety of 5-fluorouracil 0.5%/salicylic acid 10% in the field-directed treatment of actinic keratosis: a phase III, randomized, double-blind, vehicle-controlled trial. Dermatol Ther (2011);7: pages 81–96 15. Szeimies R, Dirschka T, Prechtl A, Melzer A. Efficacy of lowdose 5-FU/salicylic acid in AK in relation to treatment duration. JDDG Journal der Deutschen Dermatologischen Gesellschaft (2015);13: pages 430–8 16. Zschocke I et al. Efficacy and benefit of a 5-FU/SA preparation in the therapy of common and plantar warts – systematic literature review and meta-analysis. Journal der Deutschen Dermatologischen Gesellschaft (2004); 2: pages 187-193. 17. Jetter et al. Field Cancerization Therapies for Management of Actinic Keratosis: A Narrative Review. Am J Clin Dermatol (2018); 19: pages 543-557. 18. Verrumal® Physician Leaflet 2010. Accessed online via here (12/11/2018). 19. Leon S et al. A highly effective topical compound medication for the treatment of cutaneous warts. Practical Dermatology (2017). Accessed via here (12/11/2018)

NOTES:

a) Area Prescribing Committee recommendations and minutes are available publicly via the APC website.

b) This Area Prescribing Committee recommendation has been made on the cost effectiveness, patient outcome and safety data available at the time. The recommendation will be subject to review if new data becomes available, costs are higher than expected or new NICE guidelines or technology appraisals are issued.

c) Not to be used for commercial or marketing purposes. Strictly for use within the NHS