Cheshire and Merseyside

TIRBANIBULIN 10mg/g ointment (Klisyri® ▼) for actinic keratosis

The Cheshire and Merseyside Area Prescribing Group recommends the prescribing of TIRBANIBULIN 10mg/g ointment (Klisyri® ▼), following specialist initiation, for field treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis (Olsen grade 1) of the face or scalp.

AMBER following specialist initiation

Tirbanibulin ointment (Klisyri®) is recommended, within its licensed indication[1], for the field treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis (Olsen grade 1) of the face or scalp.

It is recommended as a second line option for patients who do not tolerate topical fluorouracil (Efudix®).

It is recommended as a first line option for patients:

- who are likely to have poor or no compliance with other first line treatment
- who requires assistance with application of the product

Tirbanibulin ointment must be initiated by a specialist clinician competent and experienced in the assessment and diagnosis of actinic keratosis. The specialist clinician may be situated in either primary or secondary care.

Since it is a single 5-day course of treatment the initiating prescriber (specialist) will prescribe the complete course.

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

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Effectiveness[1]

Mechanism of Action

Tirbanibulin disrupts microtubules by direct binding to tubulin, which induces cell cycle arrest and apoptotic death of proliferating cells, and is associated with disruption of Src tyrosine kinase signalling.

Clinical Efficacy

Study Design: The efficacy and safety of tirbanibulin applied on the face or scalp for 5 consecutive days was studied in 2 randomised, double-blind, vehicle-controlled Phase III studies including 702 adult patients (353 patients treated with tirbanibulin and 349 patients treated with vehicle).

Participants: Patients had 4 to 8 clinically typical, visible, discrete, non-hyperkeratotic, non-hypertrophic, actinic keratosis lesions within a contiguous 25 cm^2 treatment field on the face or scalp. In the tirbanibulin group, the mean age was 69 years (range 46 to 90 years) and 96% of patients had Fitzpatrick skin type I, II, or III.

Intervention: On each of the 5 scheduled dosing days, the ointment was applied once to the entire 25cm^2 maximum treatment field. Efficacy, measured as complete (primary endpoint) and partial clearance rate, was assessed at day 57.

Outcomes: At day 57 (pooled data from two RCTs)

Primary endpoint: Complete clearance rate - tirbanibulin 49%, vehicle 9% (p<0.0001), complete clearance rate (face, n=238) - tirbanibulin 56%, vehicle 10% (p<0.0001), complete clearance rate (scalp, n=115) - tirbanibulin 36%, vehicle 6% (p<0.0001)

Secondary endpoint: Partial clearance rate (≥75%) - tirbanibulin 72%, vehicle 18% (p<0.0001), partial clearance rate (face, n=238) - tirbanibulin 78%, vehicle 21% (p<0.0001), partial clearance rate (scalp, n=115) - tirbanibulin 61%, vehicle 13% (p<0.0001).

Long term efficacy

A total of 204 patients achieved complete clearance of actinic keratosis lesions in the treatment field at day 57 (174 treated with tirbanibulin and 30 treated with vehicle) and were eligible for a one year follow-up period for safety monitoring and to evaluate sustained efficacy. After one year, the recurrence rate in patients treated with tirbanibulin was 73%. There was a higher recurrence rate for scalp lesions compared to facial lesions. Of the patients who developed recurrences, 86% had either 1 or 2 lesions. Furthermore, 48% of patients developing recurrences reported at least 1 lesion that was not identified at the time of the initial treatment (i.e., newly occurring lesions counted as recurrences).

Safety

Contraindications

> Hypersensitivity to the active substance or to any of the excipients (see SPC for full list of excipients).[1]

Special Warnings and Precautions for Use

> Avoid contact with eyes - may cause eye irritation. In the event of accidental contact rinse immediately with large amounts of water and seek medical advice as soon as possible.[1]
> Do not use on the inside of the nostrils, on the inside of the ears, or on the lips.[1]
> Application not recommended until the skin has healed from treatment with any previous medicinal product, procedure or surgical treatment.[1]
> Do not apply to open wounds or broken skin where the skin barrier is compromised.[1]
> Changes in the appearance of actinic keratosis could suggest progression to invasive squamous cell carcinoma. Clinically atypical lesions for actinic keratosis or suspicious for malignancy should be appropriately managed.[1]
> Propylene glycol may cause skin irritation.[1]
> Patients and carers should be advised that excessive exposure to direct sunlight, including the use of sunlamps and sunbeds, are to be avoided. If sun exposure is unavoidable, protective clothing should be worn.[2]

Adverse effects

The most frequently reported adverse reactions are local skin reactions , including erythema (91%), flaking/scaling (82%), crusting (46%), swelling (39%), erosion/ulceration (12%), and vesiculation/pustulation (8%) at the application site. Application site pruritus (9.1%) and pain (9.9%) have been reported in the treatment area. Treatment effect may not be adequately assessed until resolution of local skin reactions.[1]

Cost[3]

The cost per treatment course (5 sachet pack) is £59.00 (excluding VAT).
Estimate 1200 patients per year across Cheshire & Mersey ICB. Use would be in place of either the current second line treatment option (Imiquimod 5% cream (Aldara®); £48.60 per course) or the current first line treatment (fluorouracil 5% cream (Efudix®); £32.90 per course).

Patient factors

- Not recommended during pregnancy and in women of childbearing potential not using contraception.[1]
- Unknown whether tirbanibulin/metabolites are excreted in human milk. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from tirbanibulin ointment therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.[1]
- Do not apply to breast or nipple and avoid contact with infant's skin.[2]
- Use with caution in immunocompromised patients.[1]

Prescribing information

- Apply to the affected field on the face or scalp once daily for 5 consecutive days.[1]

Treatment application[1] (see also Special Warnings and Precautions for Use)

- Each sachet is for single use only and should be discarded after use.
- Hands should be washed with soap and water before and immediately after application of the ointment.
- Before application the treatment field should be washed with mild soap and water and then dried. A thin layer should be applied evenly over the entire treatment field; maximum treatment area 25 cm^2.
- Tirbanibulin should be applied at approximately the same time each day. The treatment area should not be bandaged or otherwise occluded. The treated area should not be touched or washed for approximately 8 hours after application. After this period, the treated area may be washed with mild soap and water.
- If a dose is missed, apply the ointment as soon as remembered and continue with the regular schedule. Tirbanibulin should not be applied more than once a day.

Implementation notes

- Tirbanibulin ointment must be initiated by a specialist clinician competent and experienced in the assessment and diagnosis of actinic keratosis, and may be situated in either primary or secondary care.
- Not recommended during pregnancy and in women of childbearing potential not using contraception.[1]
- It is the responsibility of the initiating prescriber (the specialist) to ensure that the patient is using contraception prior to commencing treatment, advised of the need to continue use during treatment, and is counselled appropriately. Confirmation that benefits, risks and contraception have been discussed and details of any action taken should be provided to primary care. Primary care prescribing of contraception may need to be requested.

Assessment of therapeutic effect

The initiating prescriber (specialist) will assess therapeutic effect approximately 8 weeks after treatment start. If the treated area does not show complete clearance, alternative treatment options should be considered. There are no clinical data on more than one treatment course. If recurrence occurs, or new lesions develop within the treatment area, other treatment options should be considered.

References

1. Almirall Limited. Summary of Product Characteristics; Klisyri 10 mg/g ointment, 28 January 2022. Accessed 16 March 2023.
2. British National Formulary (2023); Tirbanibulin. Accessed 17 March 2023.
3. NHS Business Services Authority. Dictionary of Medicine and Devices, dm+d Browser. Accessed 16 June 2023.