tirbanibulin (Klisyri®)

EOCCO POLICY

Policy Type: PA Pharmacy Coverage Policy: EOCCO229

Description

Tirbanibulin (Klisyri) is a topical microtubule inhibitor.

Length of Authorization

- Initial: One-time fill
- Renewal: Not eligible/Cannot be renewed

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
tirbanibulin (Klisyri)	2.5 mg/250 mg (1%) ointment in a single-dose packet	actinic keratosis (AK)	5 packets/5 days

Initial Evaluation

I. Tirbanibulin (Klisyri) may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, a dermatologist; **AND**
   C. Member has not been treated with tirbanibulin (Klisyri) before; **AND**
   D. A diagnosis of **actinic keratosis (AK)** when the following are met:
      1. Member will treat lesions on the face or scalp; **AND**
      2. Treatment with at least **TWO** of the following have been ineffective, not tolerated, or all are contraindicated:
         i. 5-fluorouracil (5-FU) cream
         ii. Imiquimod cream
         iii. Diclofenac gel

II. Tirbanibulin (Klisyri) is considered investigational when used for all other conditions, including but not limited to:
   A. Patients with recurrent AK previously treated with tirbanibulin (Klisyri)
   B. Treatment of AK on other body parts (e.g. hands, legs, neck, etc.) other than the face or scalp

Supporting Evidence

I. The safety and efficacy of tirbanibulin (Klisyri) has been studied in adult patients, with no clinical trial data to support the use in pediatric patients; however, AK is a skin condition generally seen in the older population.

II. AK is the most common precancer that forms on skin damaged by chronic exposure to ultraviolet (UV) rays from the sun or indoor tanning. Most AKs do not progress to squamous cell carcinoma (SCC), but majority of cutaneous SCCs progress from AKs. Given AK may progress to SCC, dermatologist involvement in the patient's care is recommended.

III. Patients previously treated with tirbanibulin (Klisyri) were excluded from the clinical trials. The patients in the clinical trial only received one five-day treatment of tirbanibulin (Klisyri). The safety and efficacy of treating with a second application (i.e., treating AK that has recurred after treatment with tirbanibulin [Klisyri]) is unknown.

IV. The safety and efficacy of tirbanibulin (Klisyri) was studied in two identically designed Phase 3, double-blind, vehicle-controlled, randomized, parallel-group, multicenter studies in 702 patients with AK of the face or scalp.

- The majority of patients were white and male, with a Fitzpatrick skin type of I (pale white skin, blue/green eyes, blond/red hair) or II (fair skin, blue eyes) and a median of six lesions.
- The primary efficacy outcome was complete response rate and the main secondary outcome was partial response.

Outcomes	Trial 1 (N=351)		Trial 2 (N=351)		Pooled data (N=702)	
	tirbanibulin (N=175)	vehicle (N=176)	tirbanibulin (N=178)	vehicle (N=173)	tirbanibulin (N=353)	vehicle (N=349)
Complete response rate*	77 (44%)	8 (5%)	97 (54%)	22 (13%)	174 (49%)	30 (9%)
Difference	40% 95% CI (32-47); p <0.001		42% 95% CI (33-51); p <0.001		41% 95% CI (35-47); p <0.001	
Partial Response rate**	119 (68%)	29 (16%)	136 (76%)	34 (20%)	255 (72%)	63 (18%)
Difference	52% 95% CI (43-60); p <0.001		57% 95% CI (48-65); p <0.001		54% 95% CI (48-60); p <0.0001	

* Proportion of subjects achieving complete clearance of all AK in the selected area

** Proportion of subjects achieving reduction of at least 75% in the number of lesions within the application area

- Tirbanibulin (Klisyri) treated patients who achieved CR (N=174) were included in a one year follow up; of those, 124 (73%) patients developed lesions within the area treated with tirbanibulin (Klisyri). Out of the 124 patents, 72 (58%) had recurrent lesions and 52 (42%) had new lesions. The sustained complete clearance is 27%.
- The most common local reactions were erythema (91% of the patients) and flaking or scaling (82%). Although generally mild, crusting, swelling, vesiculation or pustulation, erosion, and ulceration were also seen.

V. Longstanding therapies for the treatment of AK include destructive therapies [e.g., surgery, cryotherapy, dermabrasion, photodynamic therapy (PDT)], field ablation treatments (e.g.,

chemical peels, laser resurfacing), and topical medications (e.g., fluorouracil, imiquimod, diclofenac).

- Topical medications including fluorouracil, imiquimod and diclofenac are used as first-line therapy with a well-established long-term efficacy and safety profile.
- In a randomized controlled trial comparing the recurrence of AKs after treatment with fluorouracil 5%, imiquimod 5%, or PDT, fluorouracil had the highest cumulative probability of remaining free from treatment failure (defined as <75% reduction in AK lesions) 12 months after treatment. For fluorouracil, 75% of patients were free from treatment failure, followed by imiquimod at 54%, PDT at 38%.
- Tirbanibulin (Klisyri) is a topical ointment applied once daily for five consecutive days. Patients who were previously treated with tirbanibulin (Klisyri) were excluded from the clinical trials. The patients in the clinical trial only received one five-day treatment cycle of tirbanibulin (Klisyri) and had a high recurrence rate (73%) one year after treatment. There is limited data on long-term safety and efficacy.

Investigational or Not Medically Necessary Uses

I. Tirbanibulin (Klisyri) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Patients previously treated with tirbanibulin (Klisyri): Patients previously treated with tirbanibulin (Klisyri) were excluded from the clinical trials. The patients in the clinical trial only received one five-day treatment cycle of tirbanibulin (Klisyri). The safety and efficacy of treating more than one 25cm^2 area at a time or as a second application in an area with recurrence is unknown. There is no clinical trial data to support the use in patients previously treated.
   B. Treatment of AK on other body parts (e.g. hands, legs, neck, etc.) other than the face or scalp: The safety and efficacy of tirbanibulin (Klisyri) was studied in patients with AK of the face or scalp. No patients with lesions on other body parts were included in the clinical trial. There is no clinical trial data to support the use on other parts of the body.

References

1. Blauvelt A, Kempers S, Lain E, et al. Phase 3 Trials of Tirbanibulin Ointment for Actinic Keratosis. *N Engl J Med*. 2021;384(6):512-520. doi:10.1056/NEJMoa2024040.
2. R.N. Werner, et al. Evidence- and consensus-based (S3) Guidelines for the Treatment of Actinic Keratosis – International League of Dermatological Societies in cooperation with the European Dermatology Forum. EADV 2015, 29, 2069–2079 DOI: 10.1111/jdv.13180
3. Maud H.E. Jansen, M.D., et al. Randomized Trial of Four Treatment Approaches for Actinic Keratosis. N Engl J Med 2019; 380:935-946 DOI: 10.1056/NEJMoa1811850

4. Actinic keratosis: Diagnosis and treatment. Retrieved February, 2021, from https://www.aad.org/public/diseases/skin-cancer/actinic-keratosis-treatment
5. de Oliveira ECV, et al. Actinic keratosis - review for clinical practice. Int J Dermatol. 2019;58(4):400-407.

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	05/2021