Pharmacy Policy Bulletin: J-1232 Hyftor (sirolimus) – Commercial and Healthcare Reform	
Number: J-1232	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization:** 1. Miscellaneous Specialty Drugs Oral = Yes w/Prior Authorization **Healthcare Reform**: Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1232-004	**Original Date:** 06/01/2022
Effective Date: 07/18/2025	**Review Date:** 06/25/2025

Drugs Product(s):	• Hyftor (sirolimus)
FDA-Approved Indication(s):	• Treatment of facial angiofibroma associated with tuberous sclerosis (TSC) in adults and pediatric patients 6 years of age and older.

Background:	• The mechanism of action of Hyftor in the treatment of angiofibroma associated with TSC has not been established. TSC is associated with genetic defects in TSC1 and TSC2 which leads to the constitutive activation of mTOR. Sirolimus inhibits mTOR activation. • Tuberous sclerosis, also known as tuberous sclerosis complex (TSC) is a rare, multi-system autosomal dominant genetic disease that causes non-cancerous tumors known as hamartomas to grow in the brain and on other vital organs such as the kidneys, heart, eyes, lungs, and skin. The incidence of TSC has been estimated to be between 1:6,000 and 1:10,000 live births. TSC is a highly variable disorder; symptoms vary between individuals and range from mild to severe. Almost all patients with TSC have one or more skin lesions that are characteristic of the disorder. One of the most common lesions seen with TSC are facial angiofibromas; they are seen in approximately 75% of individuals with TSC. Facial angiofibromas are hamartomatous growths composed of blood vessels and fibrous (connective) tissue. They usually appear as small, red bumps on the face, particularly on the nose and cheeks. Facial angiofibromas can cause substantial morbidity and disfigurement as well as negatively impact quality of life. • TSC related facial angiofibromas have been treated by laser therapy, cryotherapy, and dermabrasion. These treatments can be painful, lead to scarring, and do not prevent recurrence of lesions. Hyftor may offer an advantage over other therapies since it is the only FDA-approved treatment for facial angiofibroma associated with TSC. • Prescribing Considerations:

	○ Complete all age-appropriate vaccinations as recommended by current immunization guidelines prior to Hyftor initiation. ○ The maximum recommended daily dosage is: 600 mg (2 cm) for pediatric patients 6 to 11 years of age and 800 mg (2.5 cm) for adults and pediatric patients 12 years of age and older. ○ Do not use Hyftor with occlusive dressings. ○ If symptoms do not improve within 12 weeks of treatment, reevaluate the need for continuing Hyftor.

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Hyftor may be approved when all of the following criteria are met **(A., B., and C.):**

A. The member is 6 years of age or older.

B. The member has a documented diagnosis of tuberous sclerosis complex (TSC) (ICD-10: Q85.1).

C. The member has facial angiofibromas (≥ 2 mm in diameter with redness in each) present.

II. Reauthorization

When a benefit, reauthorization of Hyftor may be approved when the following criterion is met **(A.)**:

A. The prescriber attests that the member has experienced positive clinical response to therapy, defined as a decrease in size and/or redness of facial angiofibroma.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations. .

Limitations of Coverage

None

Authorization Duration

Initial Authorization

- Commercial and HCR Plans: If approved, a 3 month authorization will be granted.

Reauthorization

- Commercial and HCR Plans: If approved, a 12 month authorization will be granted.

Automatic Approval Criteria

None

References:

1. Hyftor [package insert]. Bethesda, MD: Nobelpharma America, LLC: March 2022.
2. NORD. Tuberous Sclerosis. Available at: https://www.rare.diseases.org/rare-diseases/tuberous-sclerosis/. Accessed April 11, 2025.
3. Northrup, H, Aronow, ME, Bebin, EM, et al. Updated International Tuberous Sclerosis Complex Diagnostic Criteria and Surveillance and Management Recommendations. *Pediatric Neurology.* 123 (2021) 50-66.
4. UpToDate. Tuberous Sclerosis Complex: Genetics, Clinical Features, and Diagnosis. Available at: https://www.uptodate.com. Accessed April 11, 2025.

5. Wataya-Kaneda, M, Yuuki, O, Yasuyuki, F, et al. Sirolimus Gel Treatment vs Placebo for Facial Angiofibromas in Patients with Tuberous Sclerosis Complex. *JAMA Dermatol.* 2018 Jul; 154(7): 781-788.
6. National Institutes of Health. Angiofibroma. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/angiofibroma. Accessed April 11, 2025.
7. Koenig, MK, Bell, CS, Hebert, A, et al. Efficacy and Safety of Topical Rapamycin in Patients with Facial Angiofibromas Secondary to Tuberous Sclerosis Complex. The TREATMENT Randomized Clinical Trial. *JAMA Dermatol*. 2018; 154(7)L 773-780.