



Drug Coverage Policy

Effective Date 9/1/2024

Coverage Policy Number IP0511

Policy Title Hyftor

Dermatology – Hyftor

- Hyftor® (sirolimus 0.2% topical gel – Nobelpharma)

INSTRUCTIONS FOR USE

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Cigna Healthcare Coverage Policy

Hyftor, a topical mammalian target of rapamycin inhibitor immunosuppressant, is indicated for the treatment of **facial angiofibroma associated with tuberous sclerosis** in patients ≥ 6 years of age.¹

Disease Overview

Tuberous sclerosis complex is an autosomal dominant genetic disorder caused by mutations in two genes, tuberous sclerosis 1 and tuberous sclerosis 2.²⁻⁴ The incidence rate is approximately one in 6,000 to 10,000 births. It is characterized by non-cancerous (benign) tumors that grow in the brain, as well as in other vital organs such as the kidneys, heart, eyes, lungs, and skin. It can also impact the central nervous system causing seizures, impaired intellectual development, autism, and behavioral issues. The disease has great variability but can occur when patients are very young (around 1 year of age). Most patients (up to 80%) experience various skin conditions due to the

disease such as angiofibromas, hypomelanotic macules, and cephalic plaques. Angiofibromas in the face usually appear in young children and gradually proliferate thereafter. This manifestation can be serious as well as disfiguring.

Clinical Efficacy

The efficacy of Hyftor for its approved use was evaluated in one Phase III, randomized, double-blind, vehicle-controlled, multicenter pivotal study conducted in Japan involving 62 patients who were 6 years of age and older.^{1,2} The trial enrolled patients with tuberous sclerosis complex who had three or more facial angiofibromas that were at least 2 mm in diameter with redness present in each. Patients also had a definitive diagnosis of tuberous sclerosis complex. Use of Hyftor reduced the lesion size and redness of the facial angiofibromas after 12 weeks of use compared with vehicle.^{1,2} The assessment at 4 weeks after discontinuation of Hyftor suggests that continuation of therapy is required for benefit.² It is recommended that if symptoms do not improve within 12 weeks of Hyftor treatment, the need for continuing Hyftor should be reevaluated.¹

Medical Necessity Criteria

Hyftor is considered medically necessary when the following are met:

FDA-Approved Indication

1. Facial Angiofibroma Associated with Tuberous Sclerosis. Approve for the duration noted below if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 3 months if the patient meets ALL of the following (i, ii, iii, and iv):

- i.** Patient is ≥ 6 years of age; AND
- ii.** Patient has a definitive diagnosis of tuberous sclerosis complex by meeting ONE of the following (a or b):

- a)** There is identification of a pathogenic variant in the tuberous sclerosis complex 1 (*TSC1*) gene or tuberous sclerosis complex 2 (*TSC2*) gene by genetic testing; OR

- b)** According to the prescriber, clinical diagnostic criteria suggest a definitive diagnosis of tuberous sclerosis complex by meeting either two major features or one major feature with two minor features; AND

Note: Major feature criteria involve angiofibroma (three or more) or fibrous cephalic plaque; angiomyolipomas (two or more); cardiac rhabdomyoma; hypomelanotic macules (three or more; at least 5 mm in diameter); lymphangiomyomatosis; multiple cortical tubers and/or radial migration lines; multiple retinal hamartomas; Shagreen patch; subependymal giant cell astrocytoma; subependymal nodule (two or more); or ungula fibromas (two or more). Minor feature criteria involve "confetti" skin lesions; dental enamel pits (three or more); intraoral fibromas (two or more); multiple renal cysts; nonrenal hamartomas; retinal achromic patch; and sclerotic bone lesions.

- iii.** Patient has three or more facial angiofibromas that are at least 2 mm in diameter with redness in each; AND

- iv.** The medication is prescribed by or in consultation with a dermatologist or a physician who specializes in the management of patients with tuberous sclerosis complex; OR

B) Patient Currently Receiving Hyftor. Approve for 1 year if the patient meets ALL of the following (i, ii, iii, and iv):

- i.** Patient is ≥ 6 years of age; AND

- ii.** Patient has a definitive diagnosis of tuberous sclerosis complex by meeting ONE of the following (a or b):

- a)** There is identification of a pathogenic variant in the tuberous sclerosis complex 1 (*TSC1*) gene or tuberous sclerosis complex 2 (*TSC2*) gene by genetic testing; OR

- b) According to the prescriber, clinical diagnostic criteria suggest a definitive diagnosis of tuberous sclerosis complex by meeting either two major features or one major feature with two minor features; AND

Note: Major feature criteria involve angiofibroma (three or more) or fibrous cephalic plaque; angiomyolipomas (two or more); cardiac rhabdomyoma; hypomelanotic macules (three or more; at least 5 mm in diameter); lymphangiomyomatosis; multiple cortical tubers and/or radial migration lines; multiple retinal hamartomas; Shagreen patch; subependymal giant cell astrocytoma; subependymal nodule (two or more); or ungula fibromas (two or more). Minor feature criteria involve "confetti" skin lesions; dental enamel pits (three or more); intraoral fibromas (two or more); multiple renal cysts; nonrenal hamartomas; retinal achromic patch; and sclerotic bone lesions.

- iii. Patient has responded to Hyftor as evidenced by a reduction in the size and/or redness of the facial angiofibromas, as determined by the prescriber; AND
- iv. The medication is prescribed by or in consultation with a dermatologist or a physician who specializes in the management of patients with tuberous sclerosis complex.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

References

1. Hyftor® 0.2% topical gel [prescribing information]. Bethesda, MD: Nobelpharma; March 2022.
2. Wataya-Kaneda M, Ohno Y, Fujita Y, et al. Sirolimus gel treatment vs. placebo for facial angiofibromas in patients with tuberous sclerosis complex. A randomized clinical trial. *JAMA Dermatol.* 2018;154(7):781-788.
3. Krueger DA, Northrup H, on behalf of the International Tuberous Sclerosis Complex Consensus Group. Tuberous sclerosis complex surveillance and management: recommendations of the 2012 international tuberous sclerosis complex consensus conference. *Pediatric Neurol.* 2013;49(4):255-265.
4. Northrup H, Aronow ME, Bebin EM, et al, on behalf of the International Tuberous Sclerosis Complex Consensus Group. Updated international tuberous sclerosis complex diagnostic criteria and surveillance and management recommendations. *Pediatric Neurol.* 2021;123:50-66.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Review	Added 'Patient is currently Receiving Hyftor' criteria Updated title from Sirolimus	9/1/2024

The policy effective date is in force until updated or retired.

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