



Drug Coverage Policy

Effective Date 8/15/2025

Coverage Policy NumberIP0511

Policy Title.....Hyftor

Dermatology – Hyftor

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

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

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 in terms of onset and 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

Coverage Policy

POLICY STATEMENT

Prior Authorization is required for benefit coverage of Hyftor. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Hyftor as well as the monitoring required for adverse events and long-term efficacy, approval requires Hyftor to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required for use of Hyftor as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, medical test results, claims records, prescription receipts, and/or other information.

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 \geq 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 **[Documentation Required]**; OR
 - b)** 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 **[Documentation Required]**; AND

Note: Examples of documentation include a chart note, laboratory or medical test results, etc. 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 **[Documentation Required]**; AND

Note: Examples of documentation include a chart note, laboratory or medical test results, etc.

- 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 **[Documentation Required]**; OR

- b) 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 **[Documentation Required]**; AND

Note: Examples of documentation include a chart note, laboratory or medical test results, etc. 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 **[Documentation Required]**; AND

Note: Examples of documentation include a chart note, laboratory or medical test results, etc.

- 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

Hyftor for any other use is considered not medically necessary. 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
Annual Review	Added "[documentation required]" throughout policy.	8/15/2025

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

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