PRIOR AUTHORIZATION POLICY

POLICY: Dermatology – Hyftor Prior Authorization Policy
- Hyftor® (sirolimus 0.2% topical gel – Nobelpharma)

REVIEW DATE: 06/05/2024

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 AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. 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.

CIGNA NATIONAL FORMULARY COVERAGE:

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 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 reevalauted.[1]

POLICY STATEMENT

Prior Authorization is recommended for prescription 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.

- **Hyftor® (sirolimus 0.2% topical gel (Nobelpharma) is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):**

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.

CONDITIONS NOT COVERED

- **Hyftor® (sirolimus 0.2% topical gel (Nobelpharma) is(are) considered experimental, investigational or unproven for ANY other use(s); 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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	05/24/2023
Annual Revision	No criteria changes.	06/05/2024