The first and only FDA-approved topical gel for facial angiofibroma associated with tuberous sclerosis in adults and children 6 years and older.

my VICTORY

HYFTOR® (sirolimus topical gel) 0.2% is a clear gel that contains an mTOR inhibitor

HYFTOR® is indicated for the treatment of facial angiofibroma associated with tuberous sclerosis complex (TSC) in adults and pediatric patients 6 years of age and older. Facial angiofibroma is one of the most visible manifestations of TSC.[1,2]

HYFTOR®
(sirolimus topical gel) 0.2%

HCP.HYFTOR.com

INDICATION

HYFTOR® is an mTOR inhibitor immunosuppressant indicated for the treatment of facial angiofibroma associated with tuberous sclerosis in adults and pediatric patients 6 years of age and older.

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

HYFTOR® is contraindicated in patients with a history of hypersensitivity to sirolimus or any other component of HYFTOR®.

Please see Important Safety Information on page 5 and full Prescribing Information for additional safety information.

Not an actual patient.
Individual results may vary.

HYFTOR® (sirolimus topical gel) 0.2% Addresses an Unmet Need in the Current Treatment Landscape

Tuberous sclerosis complex (TSC) is a genetic multisystemic disease that causes noncancerous tumors, or hamartomas, to form throughout the body, including on the skin.[3]

Facial angiofibromas are pink-to-red tumors typically located on the cheeks, nose, and chin, often appearing in a butterfly pattern over the malar eminences and nasolabial folds.[2,3]

Facial angiofibroma occurs in approximately 75%–80% of TSC patients, making it one of the most predominant skin manifestations of this disease.[2,4,5]

These tumors are sometimes treated with invasive modalities (e.g., radiofrequency ablation, cryotherapy, electrocoagulation, dermabrasion, laser treatments)[6]. However, these procedures may require anesthesia. Invasive treatments can also be difficult to administer in patients with extensive angiofibroma or severe intellectual impairments.[2]

Select Important Safety Information (cont'd)
WARNINGS AND PRECAUTIONS

- Hypersensitivity Reactions: Hypersensitivity reactions, including anaphylactic/anaphylactoid reactions, angioedema, exfoliative dermatitis, and hypersensitivity vasculitis, have been associated with the oral administration of sirolimus. The concomitant use of HYFTOR® with other drugs known to cause angioedema, such as angiotensin-converting enzyme (ACE) inhibitors, may increase the risk of developing angioedema. Elevated sirolimus levels may also potentiate angioedema. Discontinue HYFTOR® immediately if symptoms occur.

Please see Important Safety Information on page 5 and full Prescribing Information for additional safety information.

Efficacy

HYFTOR® (sirolimus topical gel) 0.2%

Study Design and Details

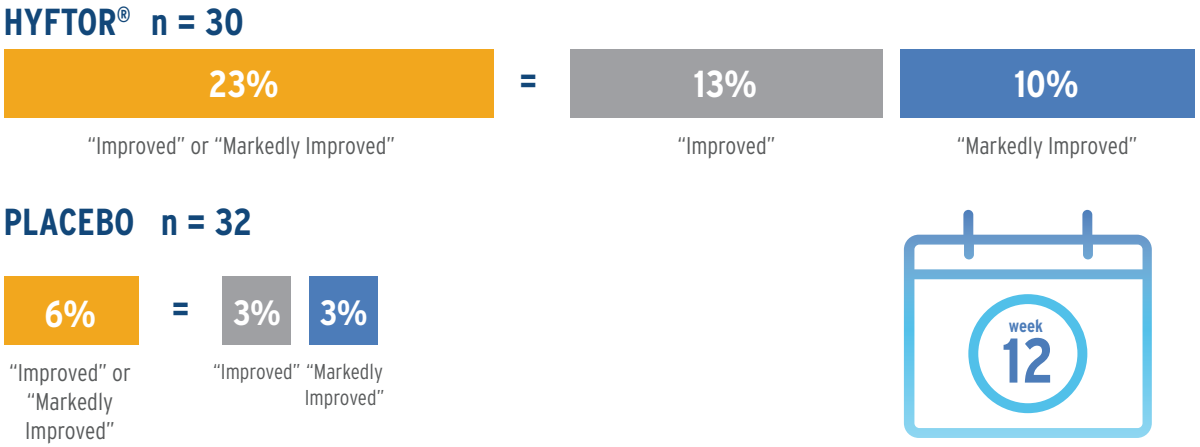
A single randomized, double-blind, placebo-controlled, multicenter phase 3 study was conducted to evaluate HYFTOR® for the treatment of adults and pediatric patients 6 years of age and older with facial angiofibroma associated with TSC[1]:

- 62 patients enrolled in the study, including 25 between 6 and 18 years of age
- Patients applied either HYFTOR® or a placebo vehicle gel twice daily to the skin of their face affected with angiofibroma for 12 weeks.
- The efficacy was assessed by the investigator (live assessment) based on the composite improvement from baseline in size and redness of facial angiofibromas, using subjects' baseline photographs as reference
- An assessment of "improved" was defined as at least a 50% reduction in size and a 2-level reduction in redness, and an assessment of "markedly improved" was defined as at least a 75% reduction in size and a 3-level reduction in redness

Composite Improvements in Facial Angiofibromas at Week 12

- 23% of patients were assessed as "improved" or "markedly improved" at 12 weeks in the pivotal trial.[1]

Improvement in Facial Angiofibroma Associated with Tuberous Sclerosis at Week 12



Safety

The most common adverse reactions (≥1%) are[1]:

- Dry skin
- Application site irritation
- Pruritus
- Acne
- Acneiform dermatitis
- Ocular hyperemia
- Skin hemorrhage
- Skin irritation

These are not all the possible side effects of HYFTOR®

Select Important Safety Information (cont'd)

WARNINGS AND PRECAUTIONS

- Serious Infection: Serious infections, including opportunistic infections, have been reported after oral administration of sirolimus. Cases of progressive multifocal leukoencephalopathy (PML), sometimes fatal, have been reported in patients treated with oral sirolimus. Discontinue HYFTOR® immediately if symptoms of infection occur.

Please see Important Safety Information on page 5 and full Prescribing Information for additional safety information.

HYFTOR®
(sirolimus topical gel) 0.2%

Dosage And Administration

HYFTOR® should be applied to the skin of the face affected with angiofibroma twice daily, in the morning and at bedtime. The maximum recommended daily dosage is[1]:

- 600 mg (2 cm/~.75 in) for pediatric patients 6 to 11 years of age
- 800 mg (2.5 cm/~1 in) for adults and pediatric patients 12 years of age and older
  - Complete all age-appropriate vaccinations as recommended by current immunization guidelines prior to HYFTOR® initiation
  - If symptoms do not improve within 12 weeks of treatment, reevaluate the need for continuing HYFTOR®
  - Do not use HYFTOR® with occlusive dressings
  - For topical use only. Not for oral, ophthalmic, or intravaginal use

Store refrigerated at 2° to 8°C (36° to 46°F).
Protect from light.

Patient Access And Support

FDA-approved, cGMP-manufactured HYFTOR® is available through specialty pharmacies equipped to handle cold storage requirements and meet the unique needs of the small population of tuberous sclerosis complex (TSC) patients with facial angiofibroma and their providers. Nobelpharma is committed to making access as simple and seamless as possible. Subject to patient eligibility, this may include expediting the initiation of patient therapy through:

- Benefit/insurance verification
- Prescription/prior authorization
- Adherence support/refill reminders
- Access to reimbursement services
- Information on meeting cold storage requirements

Please see Important Safety Information on page 5 and full Prescribing Information for additional safety information.

1. HYFTOR® Gel 0.2% Prescribing Information. Nobelpharma America, LLC; 2025
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. doi:10.1001/jamadermatol.2018.1408
3. Curatolo P, Bombardieri R, Jozwiak S. Tuberous sclerosis. *Lancet*. 2008;372(9639):657-668. doi:10.1016/S0140-6736(08)61279-9
4. Cinar SL, Kartal D, Bayram AK, et al. Topical sirolimus for the treatment of angiofibromas in tuberous sclerosis. *Indian J Dermatol Venereol Leprol*. 2017;83(1):27-32. doi:10.4103/0378-6323.190844
5. Northrup H, Koenig MK, Pearson DA, Au KS. Tuberous sclerosis complex. July 13, 1999. Updated April 16, 2020. Accessed April 21, 2021. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. *GeneReviews*. University of Washington, Seattle; 1993-2021.
6. Salido-Vallejo R, Garnacho-Saucedo G, Moreno-Giménez JC. Current options for the treatment of facial angiofibromas. *Actas Dermosifiliogr*. 2014;105(6):558-568. doi:10.1016/j.ad.2012.11.020
7. Data on file. Nobelpharma America, LLC, 2021.

Tube not shown at actual size

For more information visit HCP.HYFTOR.com

Nobelpharma

INDICATION

HYFTOR® is an mTOR inhibitor immunosuppressant indicated for the treatment of facial angiofibroma associated with tuberous sclerosis in adults and pediatric patients 6 years of age and older.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

HYFTOR® is contraindicated in patients with a history of hypersensitivity to sirolimus or any other component of HYFTOR®.

WARNINGS AND PRECAUTIONS

- **Hypersensitivity Reactions:** Hypersensitivity reactions, including anaphylactic/anaphylactoid reactions, angioedema, exfoliative dermatitis, and hypersensitivity vasculitis, have been associated with the oral administration of sirolimus. The concomitant use of HYFTOR® with other drugs known to cause angioedema, such as angiotensin-converting enzyme (ACE) inhibitors, may increase the risk of developing angioedema. Elevated sirolimus levels may also potentiate angioedema. Discontinue HYFTOR® immediately if symptoms occur.
- **Serious Infection:** Serious infections, including opportunistic infections, have been reported after oral administration of sirolimus. Cases of progressive multifocal leukoencephalopathy (PML), sometimes fatal, have been reported in patients treated with oral sirolimus. Discontinue HYFTOR® immediately if symptoms of infection occur.
- **Malignancy:** Lymphoma and other malignancies, particularly of the skin, have been observed after oral administration of sirolimus. Patients should minimize or avoid exposure to natural or artificial sunlight (tanning beds or UVA/B treatment) while using HYFTOR®. If patients need to be outdoors, they should wear protective clothing and discuss other sun protection measures with their physician.
- **Hyperlipidemia:** Increased serum cholesterol and triglycerides requiring treatment have been observed with oral administration of sirolimus. Monitor for hyperlipidemia during treatment.
- **Interstitial Lung Disease/Non-Infectious Pneumonitis:** Cases of interstitial lung disease (ILD) (including pneumonitis, bronchiolitis obliterans organizing pneumonia [BOOP], and pulmonary fibrosis), some fatal, with no identified infectious etiology have occurred in patients receiving oral sirolimus. Discontinue HYFTOR® immediately if symptoms of ILD occur.
- **Immunizations:** During treatment with HYFTOR®, vaccinations may be less effective. Complete all age-appropriate vaccinations as recommended by current immunization guidelines prior to initiating treatment with HYFTOR®. The use of live vaccines should be avoided during treatment with HYFTOR®.
- **Embryo-Fetal Toxicity:** Based on animal studies and the mechanism of action, oral sirolimus can cause fetal harm when administered to a pregnant woman. In animal studies, oral sirolimus caused embryo-fetal toxicity when administered during the period of organogenesis at maternal exposures that were equal to or less than human exposures at the recommended lowest starting dose. HYFTOR® is systemically absorbed after topical administration and may result in fetal exposure. Advise pregnant women of the potential risk to a fetus. Advise female patients of reproductive potential to avoid becoming pregnant. They should use effective contraception prior to, throughout treatment and for 12 weeks after the final dose of HYFTOR®.
- **Male Infertility:** Azoospermia or oligospermia has been observed after oral administration of sirolimus. Advise males that HYFTOR® may impair fertility.

ADVERSE REACTIONS

The most common adverse reactions (≥ 1%) are dry skin, application site irritation, pruritus, acne, acneiform dermatitis, ocular hyperemia, skin hemorrhage, and skin irritation.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** Based on animal studies and mechanism of action, oral sirolimus can cause fetal harm when administered to a pregnant woman. HYFTOR® is systemically absorbed after topical administration and may result in fetal exposure.
- **Lactation:** Breastfeeding is not recommended during treatment with HYFTOR®.
- **Infertility:** Based on clinical findings and animal studies, male and female fertility may be compromised by the treatment with sirolimus.

Please see full Prescribing Information for additional safety information.

Nobelpharma