

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

**Sirolimus for treating facial angiofibroma from tuberous sclerosis complex in people 6 years and older**

**Draft scope**

**Draft remit/evaluation objective**

To appraise the clinical and cost effectiveness of sirolimus gel within its marketing authorisation for treating facial angiofibroma associated with tuberous sclerosis complex in people 6 years and older.

**Background**

Tuberous sclerosis or tuberous sclerosis complex is a rare genetic condition that causes non-cancerous (benign) tumours to develop in different parts of the body.<sup>1</sup> The tumours most often affect the brain, kidneys, heart, lungs, eyes and skin. Two disease causing genes have been identified: TSC1 and TSC2. Around 1 in 3 people with tuberous sclerosis complex inherit the disease from a parent who also has the condition.<sup>2</sup>

The effect of tuberous sclerosis complex on the skin can cause small facial bumps known as angiofibromas, consisting of blood vessels and fibrous tissue.<sup>3,4</sup> Most people with tuberous sclerosis complex will develop facial angiofibromas<sup>3</sup>, and they are considered one of the key diagnostic criteria for tuberous sclerosis complex.<sup>5</sup> They usually develop from around the age of 5 and may increase in size and number over a person's life.<sup>3,4</sup> They generally occur centrally on the face as clusters of pink, red or brown lesions, often on the nose, cheeks and chin. These can cause recurrent bleeding, irritation and infection, eventually leading to facial scarring and disfigurement. This can negatively impact quality of life, affecting psychological and psychosocial wellbeing.<sup>3,4</sup> The severity of the condition varies amongst individuals, and, in rare cases, lesions may become large enough to block vision or breathing through the nose.<sup>6</sup>

The estimated number of people with tuberous sclerosis complex in the UK is between 3,700 and 11,000.<sup>1</sup> Facial angiofibromas are estimated to occur up to 75% of children with the condition, rising to 88% of adults aged over 30.<sup>4</sup>

There is no cure for tuberous sclerosis complex and no NICE guidelines for treating the associated facial angiofibroma. In people where the condition significantly affects quality of life, treatment options include vascular or ablative lasers, photodynamic (light) therapy, surgical excision, dermabrasion ("exfoliation"), or cryosurgery ("freezing"). These procedures are often painful and may result in permanent scarring.<sup>3,5</sup>

**The technology**

Sirolimus gel (Hyftor, Plusultra) has a marketing authorisation in the UK for the treatment of facial angiofibroma associated with tuberous sclerosis complex in adults and children aged 6 years and older.

<b>Intervention(s)</b>	Sirolimus gel
<b>Population(s)</b>	People aged 6 and older with facial angiofibroma associated with tuberous sclerosis complex
<b>Comparators</b>	Established clinical management including, but not limited to: <ul style="list-style-type: none"> <li>• vascular or ablative lasers</li> <li>• photodynamic therapy</li> <li>• surgical excision</li> <li>• dermabrasion</li> <li>• cryosurgery</li> </ul>
<b>Outcomes</b>	The outcome measures to be considered include: <ul style="list-style-type: none"> <li>• improvements in facial angiofibroma (including number and size)</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>
<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p>
<b>Other considerations</b>	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
<b>Related NICE recommendations</b>	None.
<b>Related National Policy</b>	The NHS Long Term Plan (2019) <a href="#">NHS Long Term Plan</a> NHS England (2023) <a href="#">Manual for prescribed specialist services (2023/2024)</a>

	Tuberous Sclerosis Association (2019) <a href="#">UK guidelines for managing tuberous sclerosis complex: A summary for clinicians in the NHS</a>
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### Questions for consultation

What treatments are currently available for treating facial angiofibroma associated with tuberous sclerosis complex in the NHS? Please clarify the sequencing of treatments for facial angiofibroma associated with tuberous sclerosis complex.

How often do people have treatment for facial angiofibroma? What factors determine the need for treatment?

Have all relevant comparators been included in the scope?

Are there relevant subgroups for this population that should be considered?

Where do you consider sirolimus gel will fit into the existing care pathway treating facial angiofibroma caused by tuberous sclerosis complex?

Please select from the following, will sirolimus gel be:

- A. Prescribed in primary care with routine follow-up in primary care
- B. Prescribed in secondary care with routine follow-up in primary care
- C. Prescribed in secondary care with routine follow-up in secondary care
- D. Other (please give details):

For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would sirolimus gel be a candidate for managed access?

Do you consider that the use of sirolimus gel can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which sirolimus gel is licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Draft scope for the evaluation of Sirolimus for treating facial angiofibroma from tuberous sclerosis complex in people 6 years and older

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Page 3 of 4

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Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at <https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation>).

### References

1. Tuberous Sclerosis Association (2022) [What is TSC?](#) Accessed September 2024.
2. Caban C, Khan N, Hasbani DM, et al. (2016) [Genetics of tuberous sclerosis complex: implications for clinical practice](#). The Application of Clinical Genetics 10:1-8.
3. TSC Alliance (2023) [Clinical manifestations: Skin](#). Accessed September 2024.
4. Monaghan M, Takhar P, Langlands L, et al. (2022). [Impact of facial angiofibromas in tuberous sclerosis complex and reported efficacy of available treatments](#). Frontiers in Medicine 9:967971.
5. Northrup H, Aronow ME, Bebin EM, et al. (2021) [Updated international tuberous sclerosis complex diagnostic criteria and surveillance and management recommendations](#). Pediatric Neurology 123:50-66.
6. Quartier J, Lapteva M, Boulaguiem Y, et al. (2021) [Polymeric micelle formulations for the cutaneous delivery of sirolimus: A new approach for the treatment of facial angiofibromas in tuberous sclerosis complex](#). International Journal of Pharmaceutics 604:120736.
7. Amin S, Lux A, Khan A, et al. (2017) [Sirolimus Ointment for Facial Angiofibromas in Individuals with Tuberous Sclerosis Complex](#). International Scholarly Research Notices 8404378.