NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Sirolimus for treating angiofibroma from tuberous sclerosis complex in people 3 years and older

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of sirolimus within its marketing authorisation for treating angiofibroma from tuberous sclerosis complex in people 3 years and older.

Background

Tuberous sclerosis or tuberous sclerosis complex is a rare genetic condition that causes mainly non-cancerous (benign) tumours to develop in different parts of the body. The tumours most often affect the brain, kidneys, heart, lungs, eyes and skin. Two disease causing genes have been identified: TSC1 and TSC2. Tuberous sclerosis complex is present from birth, although symptoms may not appear immediately. People with tuberous sclerosis complex present at different ages with a variety of clinical manifestations. The effect of tuberous sclerosis complex on the skin can cause small facial bumps known as angiofibromas, consisting of blood vessels and fibrous tissue. They generally occur centrally on the face as clusters of pink, red or brown lesions, especially focused on the nose and cheeks. These can cause recurrent bleeding, irritation and infection, eventually leading to facial scarring and disfigurement which can negatively impact quality of life. Angiofibromas normally appear at around the age of 3 to 5 and increase in size and number over a person's life. 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. Around a quarter of people with tuberous sclerosis complex inherit the disease from at least one parent.[1]

The estimated prevalence of tuberous sclerosis complex in the UK is 5.6 per 100,000.[2] Facial angiofibromas are estimated to occur in 70 to 80% of people with the condition.[3]

There is no cure for tuberous sclerosis complex and no NICE guidelines for treating the associated angiofibroma. In many people, angiofibroma lesions pose no significant morbidity, and treatment is not needed. However, in people where the condition significantly affects quality of life, the primary intervention is therapy with vascular or ablative lasers. Other techniques such as photodynamic (light) therapy, surgical excision, dermabrasion ("exfoliation"), or cryosurgery ("freezing") may also be used. Interventions are ineffective, often painful and may result in permanent scarring.[3, 4, 5]

The technology

Sirolimus (Hyftor, Nobelpharma Co) does not currently have a marketing authorisation in the UK for treating angiofibroma from tuberous sclerosis complex. It has been studied in clinical trials as a monotherapy compared with placebo gel in

people aged 2 and above with a confirmed diagnosis of tuberous sclerosis complex with visible facial angiofibromas.

Intervention(s)	Sirolimus
Population(s)	People with facial angiofibroma associated with tuberous sclerosis complex
Subgroups	If the evidence allows the following subgroups will be considered: • Subgroups by age (adults and children)
Comparators	Established clinical management without sirolimus, including: • vascular or ablative lasers • photodynamic therapy • surgical excision • dermabrasion • cryosurgery
Outcomes	The outcome measures to be considered include: • improvements in angiofibroma (including number, size and redness) • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. 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. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	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.
Related NICE recommendations	None
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 2.

	https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 Tuberous Sclerosis Association (2019) UK guidelines for managing tuberous sclerosis complex: A summary for clinicians in the NHS

Questions for consultation

Where do you consider sirolimus will fit into the existing care pathway for treating angiofibroma from tuberous sclerosis complex?

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

Would people currently receiving photodynamic therapy, surgical excision, dermabrasion and cryosurgery be eligible for sirolimus in clinical practice? If yes, when would these be used in place of laser therapy?

Would sirolimus replace current treatments, be used alongside or after them in clinical practice?

How would a response to treatment be measured in people with angiofibroma associated with tuberous sclerosis complex?

Would sirolimus be a candidate for managed access?

Do you consider sirolimus to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of sirolimus 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 will be 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.

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. We welcome comments on the appropriateness of appraising this topic through this 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. 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.

2. Hallet L, Foster T, Liu Z et al. (2011) Burden of diseases and unmet needs in tuberous sclerosis complex with neurological manifestations: systematic review. Current Medical Research and Opinion. 27: 1571-1583.

3. 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

4. TSC Alliance. Signs and Symptoms of TSC: Skin. Accessed 04 July 2022.

5. Vasani RJ. (2015) Facial angiofibromas of tuberous sclerosis treated with topical sirolimus in an Indian patient. Indian Journal of Dermatology. 60(2): 165-9.