

## 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 ID3990

## Response to stakeholder organisation comments on the draft remit and draft scope

**Please note:** Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

**Comment 1: the draft remit and proposed process**

Section	Stakeholder	Comments	Action
Appropriateness of an evaluation and proposed evaluation route	Plusultra (company)	We agree with the method of evaluation ie STA	Comment noted. No action required.
	Genetic Alliance UK	None	Comment noted. No action required.
	Tuberous Sclerosis Association	Tuberous Sclerosis Association agrees with NICE that the treatment should be evaluated through its Single Technology Appraisal process.	Comment noted. No action required.
Wording	Plusultra (company)	Yes this remit reflects the clinical issues	Comment noted. No action required.
	Genetic Alliance UK	None	Comment noted. No action required.

Section	Stakeholder	Comments	Action
	Tuberous Sclerosis Association	Tuberous Sclerosis Association supports the wording of the remit as set out in the draft scope.	Comment noted. No action required.
Timing Issues	Plusultra (company)	<p>Currently no authorised medicine is available.</p> <p>Simplified patient journey as product is planned to be available from local pharmacy.</p> <p>Therefore less travel for patient, shelf life is planned to be extended over current self-made compounded products.</p> <p>As currently only option is pharmacy produced product, this new option will reduce pharmacy time / cost and also ensure product production and efficacy is standardised</p>	Comments noted. NICE aims to provide draft guidance to the NHS as close as possible to the date when the marketing authorisation for a technology is granted. NICE has scheduled this topic into its work programme. No action required.
	Genetic Alliance UK	None	Comment noted. No action required.
	Tuberous Sclerosis Association	Tuberous Sclerosis Complex (TSC) associated facial angiofibromas have been reported in up to 74.5% of paediatric TSC patients, rising to up to 88% in adults >30 years old. The facial appearance resulting from facial angiofibroma lesions is associated with high psychological and physical morbidity (for example, recurrent bleeding or nasal obstruction), as such it may be considered alongside acne vulgaris, port wine stains, atopic dermatitis, congenital melanocytic nevi and other conditions as a psychodermatological condition with both physical and psychosocial impacts. The onset of facial dermatological conditions during school-age and adolescence has been found to cause a particularly negative psychosocial impact at a time when peer relationships gain importance and self-concept	Comments noted. NICE aims to provide draft guidance to the NHS as close as possible to the date when the marketing authorisation for a technology is granted. NICE has scheduled this topic into its work programme. No action required.

Section	Stakeholder	Comments	Action
		matures. Therefore, Tuberous Sclerosis Association considers this an urgent topic that should be appraised as soon as possible	
Additional comments on the draft remit	Plusultra (company)	None	Comment noted. No action required.
	Genetic Alliance UK	None	Comment noted. No action required.
	Tuberous Sclerosis Association	No comments	Comment noted. No action required.

**Comment 2: the draft scope**

Section	Consultee/ Commentator	Comments	Action
Background information	Plusultra (company)	All information supplied is correct	Comment noted. No action required.
	Genetic Alliance UK	<p>We have been informed by the Tuberous Sclerosis Association that facial angiofibromas are one of the key diagnostic criteria for tuberous sclerosis complex (TSC) and it impacts the majority of people affected by TSC. Genetic Alliance UK believes that the burden of existing treatment options and psychosocial impact of angiofibromas is not fully captured in the background information.</p> <p>The change in facial appearance as a result of facial angiofibroma lesions significantly impacts both the individual's</p>	Comments noted. The background section has been amended to include the psychological and psychosocial impact of angiofibroma.

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		<p>psychosocial and psychological wellbeing but also that of the wider family and carers. Affected children can be bullied for appearing different to their peers, negatively impacting their education and ability to form friendships. This can cause additional worry for parents and carers.</p> <p>The current treatment options available for angiofibromas often involve laser therapies or cryosurgery, both of which are invasive, painful and not always successful. These treatments do not prevent the recurrence of lesions therefore resulting in the need for multiple treatments that can be expensive over time. These treatments are also not suitable for children therefore the psychological impact of facial angiofibromas during formative years is particularly disruptive to psychological wellbeing and education.</p>	
	Tuberous Sclerosis Association	Please include the reference that facial angiofibroma are considered one of the key diagnostic criteria for TSC (Northrup H, Aronow ME, Bebin EM, Bissler J, Darling TN, de Vries PJ, et al. Updated international tuberous sclerosis complex diagnostic criteria and surveillance and management recommendations. <i>Pediatr Neurol.</i> (2021) 123:50–66. doi: 10.1016/j.pediatrneurol.2021.07.011).	Comment noted. The scope has been updated to include the suggested information.
Population	Plusultra (company)	Yes [appropriately defined]	Comment noted. No action required.
	Genetic Alliance UK	None	Comment noted. No action required.

Section	Consultee/ Commentator	Comments	Action
	Tuberous Sclerosis Association	Tuberous Sclerosis Association considers the population to be defined correctly.	Comment noted. No action required.
Subgroups	Plusultra (company)	The sub-groups of patients with AF is appropriate	Comment noted. No action required.
	Genetic Alliance UK	None	Comment noted. No action required.
	Tuberous Sclerosis Association	Tuberous Sclerosis Association agrees that subgroups by age should be considered.	Comment noted. No action required.
Comparators	Plusultra (company)	No current comparators are available apart from those mentioned	Comment noted. <b>December 2023:</b> During the scoping workshop at the last round of consultation (November 2022), the clinical experts explained 'off-label sirolimus (tablet formulation)' is a treatment for facial angiofibroma. However, it was decided that the off-label sirolimus (tablet formulation) was not an appropriate comparator for this appraisal.
	Genetic Alliance UK	None	Comment noted. <b>December 2023:</b> During the scoping workshop at the last round of consultation (November 2022), the

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			clinical experts explained 'off-label sirolimus (tablet formulation)' is a treatment for facial angiofibroma. However, it was decided that the off-label sirolimus (tablet formulation) was not an appropriate comparator for this appraisal.
	Tuberous Sclerosis Association	Tuberous Sclerosis Association believes all relevant comparators have been included in the draft scope.	Comment noted. <b>December 2023:</b> During the scoping workshop at the last round of consultation (November 2022), the clinical experts explained 'off-label sirolimus (tablet formulation)' is a treatment for facial angiofibroma. However, it was decided that the off-label sirolimus (tablet formulation) was not an appropriate comparator for this appraisal.
Outcomes	Plusultra (company)	Yes [appropriate]	Comment noted.
	Genetic Alliance UK	None	Comment noted. No action required.
	Tuberous Sclerosis Association	Tuberous Sclerosis Association suggest that the following relevant outcome measure is added to the scope to differentiate it from the health-related quality of life of the patient: • Caregiver health-related quality of life	Comment noted. 'Caregiver health-related quality of life' is covered by the outcome 'health-related quality of life'

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			included in the scope. No action required.
Equality	Plusultra (company)	We believe that this product will enable patients with AF to achieve a better quality of life with the addition of this therapeutic option as highlighted in this recently published paper. See attached link below.  <a href="http://journal.frontiersin.org/article/10.3389/fmed.2022.967971/full?utm_source=Email_to_authors_&amp;utm_medium=Email&amp;utm_content=T1_11.5e1_author&amp;utm_campaign=Email_publication&amp;field=&amp;journalName=Frontiers_in_Medicine&amp;id=967971">http://journal.frontiersin.org/article/10.3389/fmed.2022.967971/full?utm_source=Email_to_authors_&amp;utm_medium=Email&amp;utm_content=T1_11.5e1_author&amp;utm_campaign=Email_publication&amp;field=&amp;journalName=Frontiers_in_Medicine&amp;id=967971</a>	Comment noted. No action required.
	Genetic Alliance UK	None	Comment noted. No action required.
	Tuberous Sclerosis Association	No comments	Comment noted. No action required.
Other considerations	Plusultra (company)	No additional comments	Comment noted. No action required.
	Genetic Alliance UK	None	Comment noted. No action required.
	Tuberous Sclerosis Association	No comments	Comment noted. No action required.

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Questions for consultation	Nobelpharma (company)	None	Comment noted. No action required.
	Genetic Alliance UK	None	Comment noted. No action required.
	Tuberous Sclerosis Association	No comments	Comment noted. No action required.
Additional comments on the draft scope	Plusultra (company)	No comments	Comment noted. No action required.
	Genetic Alliance UK	None	Comment noted. No action required.
	Tuberous Sclerosis Association	No comments	Comment noted. No action required.

**The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope**

Neonatal & Paediatric Pharmacists Group