

National Institute for Health and Care Excellence

Health Technology Evaluation

Linzagolix for treating symptoms of endometriosis ID6357

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 [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Theramex	No additional comments.	Thank you
	Endometriosis UK	Endometriosis UK are pleased that alternative options of treatment for endometriosis pain are being considered and we feel it is appropriate to evaluate this topic.	Thank you for your comments
Wording	Theramex	No additional comments.	Thank you
	Endometriosis UK	Yes	Thank you
Timing issues	Theramex	The Company recognises the need for additional treatment options for pain associated with endometriosis. However, after careful consideration, a request for delay regarding the initiation of the NICE process has been made. The main reason for this request is that the EMA feedback is expected around May/June 2024, and this is anticipated to impact the capacity to plan	Thank you for your comments

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		and prepare for a NICE submission deadline in mid-August, as communicated by NICE on 14 th March 2024. The NICE scheduling team have since responded to say that the next available submission date would be April 2025 - with an ITP of February 2025.	
	Endometriosis UK	With increased diagnosis times, delays in access to treatment with members of the endometriosis community feeling though their symptoms are dismissed (Endometriosis UK, 2024). Endometriosis welcome a timely and urgent evaluation of this topic.	Thank you for your comments
Additional comments on the draft remit	Theramex	N/A	No response needed
	Endometriosis UK	None	No response needed

Comment 2: the draft scope

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Background information	Theramex	No additional comments.	Thank you
	Endometriosis UK	In regards to the statement: 'Approximately 1 in 10 women of reproductive age in the UK suffers from endometriosis. Endometriosis can be a chronic condition affecting people throughout their reproductive lives (and sometimes beyond). It needs to be made clear that alot of people suffer from endometriosis symptoms post menopause. The bracket at the end of the sentence is	Thanks for your comments. The background condition is meant to be a summary of the condition. The brackets at the end of the sentence have been

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		inadequate to those who are still suffering and they need be offered the same level of care of those who are in their reproductive years.	removed so it now says '...and beyond.'
Intervention (s)	Theramex	For endometriosis, the linzagolix treatment regimen will be 200mg with hormonal add-back therapy. The current scope lists the intervention "with or without hormone-based therapy". This is incorrect, it should read: "Linzagolix (with hormone-based therapy)".	Thank you. This has not been changed because the final license wording is not yet known.
Population	Theramex	Population defined as: "Adults with symptoms of endometriosis".	Thank you for your comment. This has been changed.
	Endometriosis UK	Would treatment be available for those with both suspected and confirmed diagnosis. Considering increasing diagnosis times, average of 8 years and 10 months within the UK (Endometriosis UK, 2024), we hope treatment will be available for people with suspected endometriosis. This will prevent delays in accessing treatment, managing endometriosis pain, preventing more complex chronic pain issues in the future.	Thank you for your comment. This can be considered by the committee during the appraisal based on the evidence provided. The committee will assess the technology in line with its marketing authorisation.
Subgroups	Theramex	There are no subgroups for this technology.	Thanks for your comment. As other stakeholders consider the subgroups appropriate, these have been retained. The company will have the opportunity to justify

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			their considerations of the relevance of subgroups in their submission.
	Endometriosis UK	<p>Yes, these subgroups are appropriate.</p> <p>Please also consider further sub-group: People having short-term treatment for 6 months or less, with hormone-based therapy.</p> <p>To support those people having short-course treatment, who may be experiencing vaso-motor symptoms, to improve treatment compliance.</p>	Thanks for your comment. The subgroups have been amended.
Comparators	Theramex	<p>Where hormone-based therapy is suitable</p> <p>Linzagolix is intended to be a second-line therapy. Based on the NICE draft guidance of relugolix,</p> <ul style="list-style-type: none"> • analgesics or non-steroidal anti-inflammatory drug (NSAID) alone or in combination with each other • neuromodulators and • hormonal treatments <p>are first-line treatment options (paragraph 3.3.) and therefore not considered appropriate comparators.</p> <p>Instead, relevant comparators considered:</p> <ul style="list-style-type: none"> • gonadotropin-releasing hormone (GnRH) agonists • relugolix-estradiol-norethisterone acetate (subject to NICE evaluation) • surgery <p>Where hormone-based therapy is not suitable</p> <p>As linzagolix will only be used with hormone-based therapy, this section should be removed.</p>	Thanks for your comments. Surgery has been added as a comparator but the other comparators have been retained as comparators listed in the scope tend to be broad. The most appropriate comparator(s) will be discussed in more detail during the appraisal and by the committee, with input from the company submission and clinical experts. Furthermore, the draft guidance for relugolix CT (ID3982) is still subject to

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			consultation comments and is not final guidance. The section 'Where hormone-based therapy is not suitable' has been retained as the scope has been left broad, since the final license wording is not known.
	Endometriosis UK	<p>As the scope is for treating pain caused by endometriosis surgical management options should also be included as a comparator as this is an alternative treatment options for endometriosis symptoms management. Although this should be deemed as an alternative option and not grouped with medical options as listed within scope.</p> <p>Surgical management options:</p> <ul style="list-style-type: none"> • Excision / ablation of endometriosis. • Excision /ablation of endometriosis with hysterectomy with or without oophorectomy. 	Thanks for your comments. Surgery has been added as a comparator and as a separate bullet from medical options.
Outcomes	Theramex	<p>It is proposed that the outcome measures below should be excluded:</p> <ul style="list-style-type: none"> • recurrence of endometriosis • admission to hospital • subsequent surgical treatment • fertility • complications of treatment <p>as these are not part of the clinical trials program</p>	Thanks for your comments. As outlined in NICE's health technology evaluation manual (section 2.2.18 – 2.2.21), outcomes listed in the scope are selected on the basis of their importance to

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		<p>The outcome measures to be included are:</p> <ul style="list-style-type: none"> • pain • opioid use • analgesic use • adverse effects of treatment • health-related quality of life 	patients and carers rather than on their availability in the clinical studies.
	Endometriosis UK	As well as measuring recurrence of endometriosis, progression and regression of endometriosis should also be captured as an outcome.	Thanks for your comments. The scope has been amended.
Equality	Theramex	No additional comments.	Thank you
	Endometriosis UK	<ul style="list-style-type: none"> • At the moment, what treatments and drugs are offered are based on the knowledge of individual medical professionals as well as what is currently available in certain areas and different NHS Trusts. This means the choices of treatments can vary across the UK. We would like to know if patients will be able to access this medication, regardless of where they are living and whether this medication could be initiated within primary, secondary or tertiary care settings. 	Thank you. NICE guidance would apply nationally. The setting of care for this technology will be considered in the appraisal with input from experts.
Other considerations	Theramex	<p>Economic analysis: We acknowledge that there is an ongoing evaluation of relugolix in the same indication.</p> <p>Cost comparison route to be considered as reference case if relugolix has been launched and shown to be cost-effective prior to evaluation of linzagolix.</p>	As the appraisal on relugolix combination therapy is still ongoing, it is not appropriate to consider this appraisal as a cost comparison at the moment. However, the appropriateness of a cost comparison

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			could be re-considered if relugolix combination therapy is recommended. This could occur at the progression decision point, or a cost-comparison could be considered as a scenario analysis within the appraisal.
	Endometriosis UK	<ul style="list-style-type: none"> • It needs to be considered that most of the options available as treatments for endometriosis at the moment can all have considerable side effects. Patients have expressed how they were often being prescribed a type of contraceptive for their pain without any real investigation as to what the pain might be or were not given enough information about the potential side effects of hormonal contraceptives. • We would like to understand more about the drug including potential side effects, and how these would be properly assessed and looked into. Effective patient information will be key. There is also a concern about the perceived lack of information about the long-term side effects of this drug, especially for those who may have already have had several years of taking prescribed GnRH Analogues/Agonists. Concerns include potential conditions such as cardiovascular disease and osteoporosis. Patients have spoken about their want of treatments or drugs that are not hormonal and with less potential side effects. • All medical treatment options are also currently all hormonal which are not suitable for those wishing to conceive. 	Thank you for your comments. The submissions from the company, patient and professional organisations should include current concerns and considerations about current treatment options and for linzagolix.

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		<ul style="list-style-type: none"> Whilst we are keen to see this drug made available for those for whom it is appropriate, we would like to add that the treatment and management options for those with endometriosis are limited due to historic lack of research. We would urge NICE to look to identify further possible ways to identify and provide new technologies to endometriosis patients 	
Questions for consultation	Theramex	No additional comments.	Thank you
	Endometriosis UK	<ol style="list-style-type: none"> Where do you consider linzagolix will fit into the existing care pathway for symptoms of endometriosis? <ul style="list-style-type: none"> As a second line treatment, when first line treatments such as contraceptives, progestagens, analgesics and non-steroidal anti-inflammatory drugs (NSAID) alone or in combination have not been successful. Would there be circumstances where you would have linzagolix for a short period of time? (i.e. for 6 months or less) <ul style="list-style-type: none"> For short-term symptom management in wait for surgical management. For those who are contraindicated for add-back HRT and requiring short-term symptom relief. Have all relevant comparators for linzagolix been included in the scope? Are surgical options (endometrial ablation, excision and hysterectomy, with or without oophorectomy) relevant as comparators for linzagolix? <ul style="list-style-type: none"> Answered above. Are the outcomes listed appropriate? <ul style="list-style-type: none"> Answered above. 	<p>Thank you for your comments. The submissions from the company, patient and professional organisations should include current concerns and considerations about endometriosis and its impact on people with the condition, with current treatment options and for linzagolix.</p> <p>Taking into consideration the submissions and input from clinical experts, the committee will consider suitability for managed access,</p>

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		<p>5. Are there any subgroups of people in whom linzagolix is expected to be more clinically effective and cost effective or other groups that should be examined separately? (for example, with or without add-back hormonal therapy)</p> <ul style="list-style-type: none"> • Answered above. <p>6. Would linzagolix be a candidate for managed access?</p> <ul style="list-style-type: none"> • There may be an option for medication to be accessed prior to licence. However we understanding that this is usually an option for treatments that required starting urgently such as cancer treatments or chemotherapy, which we recognise may not be appropriate for our community. <p>7. Do you consider that the use of linzagolix can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?</p> <ul style="list-style-type: none"> • Many patients describe endometriosis as debilitating, with daily pain and an overall lower quality of life. Those we interviewed for the submission said they often feel like their life is on hold, and struggle with daily tasks especially when they have a high pain day. • In the Endometriosis APPG Report which was published in 2020, 10,000 patients were asked about their quality of life living with endometriosis and 95% of respondents said endometriosis symptoms have had a negative or very negative impact on their wellbeing. • Respondents that we interviewed for a previous submission on the for the drug Relugolix–estradiol–norethisterone acetate also described living with endometriosis as extremely challenging and the detrimental impact that the condition's symptoms can have 	benefits not included in the QALY and the impact of any potential equality issues.

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		<p>upon their day-to-day lives both logistically and in terms of quality of life and general physical and mental wellbeing requires exhaustive resilience.</p> <p>8. Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.</p> <ul style="list-style-type: none"> • We regularly gather information on experience of patients about the diagnosis and treatment of endometrioses. In the last 3 years this has included 4 surveys, receiving between 2,000 and 10,000 responses. In addition to surveys, we regularly consult the endometriosis community, analyse information gathered through our support services such as Helpline enquiries, and undertake qualitative and focus group research. <p>9. 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:</p> <ul style="list-style-type: none"> • could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which linzagolix 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. 	

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		<p>10. Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.</p> <ul style="list-style-type: none"> • There is a risk of osteoporosis from these use of this drug. We want to know what recommendation NICE will provide regarding any management, including dosing of HRT and imaging including DEXA bone scans to assess bone mineral density. It needs to be clear how frequently these should be obtained alongside treatments, as well as the duration of treatments. 	
Additional comments on the draft scope	Theramex	No additional comments.	Thank you.
	Endometriosis UK	<ul style="list-style-type: none"> • Endometriosis UK believe that the consideration of Linzagolix being used as a potential drug to treat endometriosis is positive, especially with it being a GnRH antagonist which has a quicker onset of action when compared to GnRH agonists and hope that it will be accepted as a new form of treatment. We believe that Linzagolix will be able to provide benefits and relief to those suffering with endometriosis. • It is positive that patient would have a tablet which can be taken daily so if there were concerns about side effects, then the patient would be able to stop taking the drug, rather than as at present, being on similar drugs which may require a 1 month or 3 month injection dose. GnRH agonist treatments initiate a flare response with commencement of treatment, this isn't the case with GnRH antagonist which is beneficial to the patient group • Another benefit is that the tablet is available in different doses, therefore dosing can be modified for patient suitability. • It is positive that the drug can be used for a much longer period of time compared to GnRH agonists as these treatments are licensed for a maximum of 6 months. 	Thank you for your comments. The submissions from the company, patient and professional organisations should include current concerns and considerations about current treatment options and for linzagolix.

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		<ul style="list-style-type: none">• It can be considered positive that HRT is not included in this drug due to some adverse side effects that HRT can cause. There is also flexibility in add-back HRT prescribing alongside treatment.• Bone density is a concern for people who will be undergoing this type of treatment, especially as it does not have HRT as an additional component. It would be important to have bone density scans to monitor bone mineral density alongside treatment. If osteopenia is recognised this would contraindicate treatment.	