National Institute for Health and Care Excellence

Health Technology Evaluation

Vibegron for treating symptoms of overactive bladder [ID6300]
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	Pierre Fabre	We believe the most appropriate route for this topic is the NICE fast track process given that vibegron demonstrates overall at least comparable efficacy and safety to its comparator mirabegron at a similar cost. Further details on this will be provided in the comments throughout this document.	Thank you for your comment. The population in the scope has been kept broad. A cost-comparison is not appropriate for the full population in the scope. However, the company can choose to submit for a narrower population using the cost-comparison process.
	Astellas Pharma Ltd	Appropriate single technology appraisal route.	Thank you for your comment.

Section	Stakeholder	Comments [sic]	Action
Wording	Pierre Fabre	The licence wording is anticipated to be [redacted] Therefore, we consider the wording of the remit to be appropriate.	Thank you for your comment. Vibegron will be considered within its marketing authorisation.
	Astellas Pharma Ltd	*Does the wording of the remit reflect the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider? If not, please suggest alternative wording.* Yes	Thank you for your comment. No action required.
Timing issues	Pierre Fabre	OAB syndrome is associated with physical, emotional, and financial burden (1). After failed conservative measures, such as behavioural changes and lifestyle therapies, antimuscarinic drugs are most commonly prescribed, but these have systemic side effects that can lead to poor compliance. (1) β3-adrenergic receptor (β3AR) agonists, including mirabegron and vibegron, are effective treatment options with a manageable safety profile for people with OAB. (2) Mirabegron is a first-generation β3AR agonist that is effective in the treatment of reducing urination frequency and episodes of urgency urinary incontinence (UUI). However, the drawbacks of this drug include potential interactions with cytochrome P450 enzymes (CYPs) and cardiovascular sequelae due to a lack of specificity to β3AR. In contrast, vibegron is a second-generation β3AR agonist offering patients an important new treatment option that is highly selective for β3AR and has been shown to not inhibit or induce a number of major human cytochrome P450 enzymes. It is effective for reducing UUI episodes and daily micturition number and has a favourable side effect profile (1).	Comment noted. NICE aims to publish final guidance for all new technologies within 90 days of receiving marketing authorisation.

Section	Stakeholder	Comments [sic]	Action
	Astellas Pharma Ltd	No comment	No action required.
Additional comments on the draft remit	Pierre Fabre	None	No action required.
	Astellas Pharma Ltd	None	No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Pierre Fabre	We consider this section to be accurate and complete.	Thank you for your comment. No action required.
	Astellas Pharma Ltd	No additional comments.	No action required.
Population	Pierre Fabre	The population stated, “Adults with symptoms of overactive bladder”, is correct and in line with the anticipated Marketing Authorisation for vibegron. As vibegron is intended to be positioned in the existing NICE pathway (NICE guideline 123) at the same place in therapy as mirabegron (please see **Error! Reference source not found.**), it is anticipated vibegron will be used in the same patient population recommended by NICE for mirabegron of “treatment of the symptoms of overactive bladder only for people in whom antimuscarinic drugs are contraindicated or clinically ineffective, or have unacceptable side effect” (NICE technology appraisal TA290)	Thank you for your comment. Vibegron will be considered within its marketing authorisation. The company can narrow the population for consideration within its submission.

Section	Consultee/ Commentator	Comments [sic]	Action
	Astellas Pharma Ltd	*Is the population defined appropriately?* Yes	Thank you for your comment. No action required.
Subgroups	Pierre Fabre	The subgroups are appropriate. It is not anticipated there are any subgroups in which vibegron is expected to be more clinically or economically beneficial.	Comment noted. Where evidence allows, the cost-effectiveness of the technology in relevant subgroups will be considered by the committee during appraisal.
	Astellas Pharma Ltd	Sub-groups suggested are appropriate.	Thank you for your comment. No action required.
Comparators	Pierre Fabre	The current comparator described in the draft scope includes mirabegron and antimuscarinic drugs. We believe that mirabegron is the only appropriate comparator to vibegron within the existing NICE pathway. Vibegron and mirabegron are both small molecule agonists which target β_3ARs expressed in the bladder, the primary function of which is to aid in detrusor smooth muscle relaxation during the filling stage of the micturition cycle (3). Vibegron is intended to be positioned alongside mirabegron, as a third line therapy (following behavioural changes and lifestyle therapies, and anti-muscarinic drugs), Vibegron has demonstrated at least similar efficacy and safety profiles in a recent published ITC (4). We consider vibegron to be a direct alternative to mirabegron and therefore mirabegron would be the most appropriate and only comparator in the current NICE pathway (NICE guideline 123).	Thank you for your comment. The population in the scope has been kept broad in line with the marketing authorisation. Therefore, the comparators appropriate for the broad population have been included in the scope. The company can choose to submit evidence for a narrower

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		The inclusion of antimuscarinic drugs as a comparator would not be appropriate by precedent, as the NICE recommended indication for mirabegron is for treatment of the symptoms of overactive bladder only for people in whom antimuscarinic drugs are contraindicated or clinically ineffective, or have unacceptable side effects" (NICE technology appraisal TA290)".	population for whom mirabegron is the appropriate comparator.
	Astellas Pharma Ltd	*Are the comparators listed considered to be the standard treatments currently used in the NHS with which the technology should be compared? Have all relevant comparators been included?* Yes	Thank you for your comment. No action required.
Outcomes	Pierre Fabre	We consider the outcomes included in the scope to be appropriate.	Thank you for your comment. No action required.
	Astellas Pharma Ltd	*Are the outcomes listed appropriate? Will these outcome measures capture the most important health related benefits (and harms) of the technology?* Yes	Thank you for your comment. No action required.
Equality	Pierre Fabre	There are no equality considerations concerning protected characteristics.	Thank you for your comment. No action required.
	Astellas Pharma Ltd	*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 draft remit and scope may need changing in order to meet these aims. In particular, please tell us if the draft remit and scope:* • *could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/will be licensed;*	Thank you for your comment. No action required.

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		• *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.* No	
Other considerations	Pierre Fabre	None	No action required.
	Astellas Pharma Ltd	None	No action required.
Questions for consultation	Pierre Fabre	***1) Are invasive treatment options (such as botulinum toxin type A, percutaneous sacral nerve stimulation, urinary diversion and laparoscopic augmentation cystoplasty [including clam cystoplasty]) expected to be considered comparators to vibegron? Would Axonics sacral neuromodulation system be considered as a comparator to vibegron?*** The third-line positioning in the NICE pathway of vibegron and mirabegron means that invasive treatment options, such as botulinum toxin type A, percutaneous sacral nerve stimulation, urinary diversion and laparoscopic augmentation cystoplasty [including clam cystoplasty]) and the Axonics sacral neuromodulation system would not be considered comparators, as these treatments are placed fourth line. According to NICE guideline 123), invasive treatment options are considered for:	Thank you for your comment. No action required.

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		"women with overactive bladder that has not responded to non-surgical management or treatment with medicine and who wish to discuss further treatment options" According to the same guidance percutaneous sacral nerve stimulation is recommended for: *"women after local or regional MDT review if their overactive bladder has not responded to non-surgical management including medicines and for those where a) symptoms have not responded to botulinum toxin type A, or b) they are not prepared to accept the risks of needing catheterisation associated with botulinum toxin type A"* For these reasons, it should be made clear in the scope that mirabegron is the principal comparator of interest. Based on the intended third line placement of vibegron (in line with the positioning of mirabegron), invasive treatment/ percutaneous sacral nerve stimulation (fourth line) should not be considered comparators to vibegron.	
		2) Would vibegron be a candidate for managed access? No	Thank you for your comment. No action required.
		3) Do you consider that the use of vibegron can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? We do not expect any substantial difference in health benefits based on the current published ITC.	Thank you for your comment. No action required.
		4) Is the technology likely to be similar in its clinical effectiveness and resource use to any of the comparators? Or in what way is it different to the comparators?	

Section	Consultee/ Commentator	Comments [sic]	Action
		Yes, vibegron is anticipated to be relatively similar to mirabegron in its clinical effectiveness and resource use. No head-to-head trial has been carried out to compare vibegron and mirabegron in the treatment of OAB, however, based on results from a published indirect treatment comparison (ITC) study, which included nine phase 3 randomised controlled trials of vibegron or mirabegron in patients with OAB, the clinical effectiveness of vibegron is similar to that of mirabegron (4) The ITC demonstrated that vibegron is associated with a significant improvement in total incontinence episodes at 4 and 52 weeks, and volume voided at 12 and 52 weeks, compared to mirabegron. Improvement in micturitions is similar between vibegron and mirabegron. Incidence of adverse events is also generally comparable between vibegron and mirabegron. Resource use is expected to be similar between vibegron and mirabegron due to similar clinical effectiveness and safety profile, and identical drug administration method. **5)** ***Will the intervention be used in the same place in the treatment pathway as the comparator(s)? Have there been any major changes to the treatment pathway since NICE technology appraisal 290 (2013) was published? If so, please describe.*** Vibegron is intended to be positioned in the same place in the treatment pathway as mirabegron (See Figure 1). Mirabegron is recommended by NICE in TA290 as an option for treating OAB in patients for whom antimuscarinic drugs are contraindicated or clinically ineffective or have unacceptable side effects. To the best our knowledge, we are not aware of any major changes to the treatment pathway since NICE TA290 was published. *6)* ***Will the intervention be used to treat the same population as the comparator(s)?***	Thank you for your comment. No action required. Thank you for your comment. No action required.

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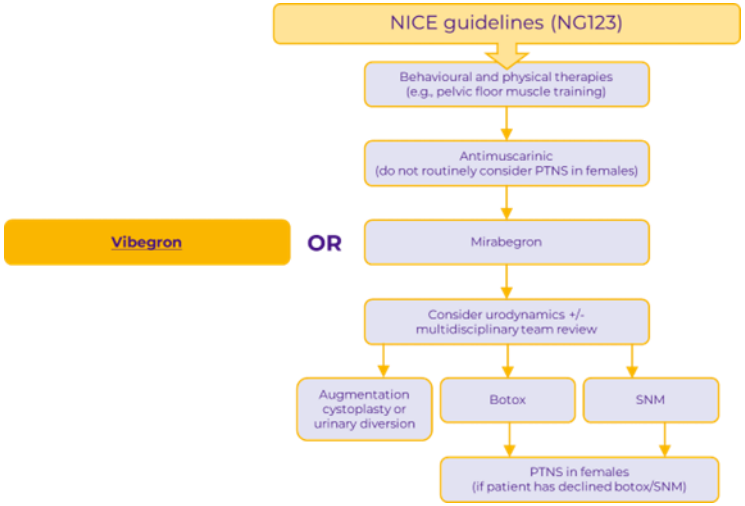
		Yes	Thank you for your comment. No action required.
		7) Overall is the technology likely to offer similar or improved health benefits compared with the comparators? Yes. As demonstrated in the ITC study (4) vibegron is associated with a significant improvement in total incontinence episodes at 4 and 52 weeks, and volume voided at 12 and 52 weeks, compared to mirabegron. Improvement in micturitions is similar between vibegron and mirabegron. Vibegron is therefore likely to have at least comparable efficacy to mirabegron. Incidence of adverse events is also generally comparable between vibegron and mirabegron.	Thank you for your comment. No action required.
		8) Would it be appropriate to use the cost-comparison methodology for this topic? Yes, a cost-comparison methodology is appropriate for this topic. As per NICE's method guide on cost-comparison, if the technology provides similar or greater benefits at a similar or lower overall cost than the comparator, the cost-comparison method should be recommended as an option. As highlighted in an ITC study (4), vibegron has demonstrated improvements in total incontinence episodes at weeks 4 and 52, and in volume voided at weeks 12 and 52, compared to mirabegron. Additionally, the improvement in micturitions and the safety profile were similar between vibegron and mirabegron. As at least similar efficacy and safety are expected, resource use is also anticipated to be similar. A cost-comparison case is therefore recommended based on similar efficacy profiles and anticipated similar costs of treatment.	Thank you for your comment. The population in the scope has been kept broad. A cost-comparison is not appropriate for the full population in the scope. However, the company can choose to submit for a narrower population using the cost-comparison process.

Section	Consultee/ Commentator	Comments [sic]	Action
	Astellas Pharma Ltd	See below.	Comment noted. Please see responses to comments below.
Additional comments on the draft scope	Pierre Fabre	Figure 1. Vibegron intended place in therapy according to current NICE patient pathway for management of urinary incontinence and pelvis organ prolapse in women (NICE guideline 123, last updated 24 June 2019)  **References** 1. Vibegron for the treatment of overactive bladder: a comprehensive update. Stephanie Gleicher, Elisabeth M. Sebesta, W. Stuart Reynolds & Roger	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		Dmochowski. 13, 2022, Expert Opinion on Pharmacotherapy, Vol. 23, pp. 1479-1484. 2. An Evaluation of the Efficacy and Safety of Vibegron in the Treatment of Overactive Bladder. Frankel J, Staskin D, Varano S, Kennelly MJ, Jankowich RA, Haag-Molkenteller C. 3, 2022, Ther Clin Risk Manag, Vol. 18, pp. 171-182. 3. Selectivity and Maximum Response of Vibegron and Mirabegron for β3-Adrenergic Receptors. Brucker B, King J, Mudd PN and McHale K. 2022, Current Therapeutic Research, Vol. 96, p. 100674. 4. Efficacy of Vibegron and Mirabegron for Overactive Bladder: A Systematic Literature Review and Indirect Treatment Comparison. ., Michael J. Kennelly . Thomas Rhodes . Cynthia J. Girman. 11, 2021, Vol. 38, pp. 5452–5464. 5. Vibegron: First Global Approval. Keam, Susan. 17, 2018, Drugs, Vol. 78, pp. 835-1839. 6. Administration, US Food and Drug. Drug Trials Snapshot: GEMTESA. US Food and Drug Administration. [Online] 2023. [Cited: 20 September 2023.] https://www.fda.gov/drugs/drug-approvals-and-databases/drug-trials-snapshot-gemtesa.	
	Astellas Pharma Ltd	Invasive surgical treatment options (such as botulinum toxin type A, percutaneous sacral nerve stimulation, urinary diversion and laparoscopic augmentation cystoplasty [including clam cystoplasty]) are not direct comparators to pharmacological treatments, including Vibegron.	Thank you for your comment. No action required.

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		Invasive surgical options are considered for patients who have not responded to non-surgical options. Recommendations | Urinary incontinence and pelvic organ prolapse in women: management | Guidance | NICE 1.4.43 Invasive Surgical options vary slightly between men and women. Cystoscopy and Botulinum Toxin A injections are considered for female patients with OAB due to the potential requirement for clean intermittent self-catheterisation. Recommendations | Urinary incontinence and pelvic organ prolapse in women: management | Guidance | NICE 1.4.26 Axonics sacral neuromodulation system would not be considered as a comparator to vibegron.	

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

None