National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Relugolix with oestradiol and norethindrone acetate for treating uterine fibroids

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

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

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	Gedeon Richter (UK)	Yes, the draft remit is appropriate.	Thank you for your comment. No action required.
Wording	Gedeon Richter (UK)	Relugolix combination therapy (CT) contains 40 mg relugolix, 1 mg estradiol (E2) (as hemihydrate), and 0.5 mg norethisterone acetate (NETA). We suggest the remit should reflect the licensed indication for Relugolix CT: [redacted]	Thank you for your comments. The wording of the remit has been updated.
Timing Issues	Gedeon Richter (UK)	The timing is appropriate.	Thank you for your comment. No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Gedeon Richter (UK)	The focus of the background information should be on all symptoms of uterine fibroids, which would include heavy menstrual bleeding. Multiple sources show the presence of uterine fibroids adversely affect quality of life due to pain, discomfort, urinary frequency, fatigue, energy/mood, and sexual function – as well as heavy menstrual bleeding.	Thank you for your comments. The background section has been updated to include other relevant symptoms.
The technology/ intervention	Gedeon Richter (UK)	We suggest the following additions to the first paragraph: -The brand name submitted in the UK is 'Ryeqo', Relumina will not be used. -'Relugolix CT contains relugolix, a GnRH receptor antagonist which binds to and blocks the GnRH receptor (GnRHR) in the anterior pituitary gland. E2 and NETA add-back therapy counteract the detrimental side effects associated with reduced oestrogen levels, such as vasomotor symptoms and reduction in bone mineral density.' Second paragraph: 'Relugolix CT does not currently have a marketing authorisation in the UK for the treatment of uterine fibroids. It has been studied in clinical trials as a combination product containing relugolix, E2 and NETA compared with placebo in premenopausal women aged 18 to 50 years old with symptoms of uterine fibroids.'	Thank you for your comments. The brand name described in the scope has been updated. The description of the technology has been updated to explain that it is administered in combination with oestradiol and norethindrone acetate.

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Population	Gedeon Richter (UK)	We suggest including [redacted] as per the proposed licensed indication.	Thank you for your comment. The population in the scope has been updated.
Comparators	Gedeon Richter (UK)	Relugolix CT will be the only oral pharmacological treatment option available for the long-term management of symptoms of uterine fibroids, as such there are no direct comparators. Furthermore, the novel combination of add-back therapy in Relugolix CT maintains patient bone mineral density levels, which is not currently available in alternative pharmacological treatments for the management of uterine fibroid symptoms.	Thank you for your comments. The comparators in the scope have been updated to include only hormonal treatments.
Outcomes	Gedeon Richter (UK)	We would propose including: - Change in bone mineral density - Uterine fibroid volume - Uterine volume - Vasomotor symptoms We do not believe 'rates of bladder infection' is a relevant outcome measure for Relugolix CT.	Thank you for your comments. The outcomes listed in the scope have been updated. Uterine fibroid volume and vasomotor symptoms (as an example of an adverse effect) have been added and rates of bladder infection has been removed. The outcomes listed are not intended to be exhaustive.

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Other considerations	Gedeon Richter (UK)	Patients with fibroids < 2cm in diameter were excluded from the Relugolix CT clinical trials. Therefore, we have substantial evidence to support treating women with uterine fibroids > 3cm, but less data for women with fibroids < 3cm in diameter, as per the suggested subgroups.	Thank you for your comments. The reference to subgroups has been removed from the scope.
Innovation	Gedeon Richter (UK)	There is a significant unmet patient need for a non-surgical treatment option for the long-term management of the multiple symptoms associated with uterine fibroids. Relugolix CT is the first once-daily oral GnRH antagonist combined with add-back therapy to be licensed in Europe for treatment of uterine fibroid symptoms. Relugolix CT is a novel combination of active ingredients, with relugolix blocking GnRH from binding to GnRH receptors in the anterior pituitary, which results in suppressed secretion of FSH and LH. The resulting decrease in endogenous production of E2 and progesterone caused by a reduction in follicular growth and ovulation inhibits the growth and symptoms of uterine fibroids. The addition of exogenous E2 leads to systemic oestrogen concentrations consistent with those in the early follicular phase of the menstrual cycle, which enables minimisation of bone mineral density loss and vasomotor symptoms. The addition of NETA serves to prevent endometrial hyperplasia. NICE guidance supports shared decision making between health professionals and patients, and we believe Relugolix CT offers patients suffering with symptoms of uterine fibroids a long-term pharmacological treatment option not currently available to them.	Thank you for your comments. The appraisal committee will consider the innovative nature of this technology during the appraisal. No action required.

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Questions for consultation	Gedeon Richter (UK)	Q. Will relugolix with oestradiol and norethisterone acetate be used as an addition to current standard care, or would it replace current standard care options? A. Relugolix CT will be the only long-term pharmacological treatment suitable for most women with symptoms of uterine fibroids. It will also be an alternative, long-term, treatment option to surgery. Q. Where do you consider relugolix with oestradiol and norethindrone acetate will fit into the existing NICE pathway: heavy menstrual bleeding? A. Relugolix CT will be a first-line pharmacological treatment option for symptoms of uterine fibroids > 2cm. As per the expected licensed indication, Relugolix CT should be positioned as the only long-term pharmacological treatment option to manage symptoms of uterine fibroids.	Thank you for your comments. No action required.

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

Takeda UK

Ipsen