

Dr Mark Chakravarty

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Please reply to -

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Dear Dr Chakravarty,

# Final appraisal document - Relugolix–estradiol–norethisterone acetate for treating moderate to severe symptoms of uterine fibroids ID3842

FEmISA submitted comprehensive evidence to this Technology Appraisal, which also included concerns over the safety, efficacy and side effects of this medicine. While FEmISA does not appeal against the use of this medicine we understand a positive Technology Appraisal is supposed to be mandatory to CCGs and now ICSs to implement and there should be safeguards and monitoring of the use of this medicine.

We appeal on the grounds that: The recommendation is unreasonable in the light of the evidence submitted to NICE.

**Efficacy** – The NICE appraisal document states – Relugolix *“is an effective non-surgical treatment*”. There was no evidence submitted or considered that it is as effective as hospital treatment for symptomatic fibroids e.g. uterine artery/fibroid embolisation [UAE/UFE], myomectomy, hysterectomy, MR guided focused ultrasound and endometrial ablation for fibroids <3cm, which are proven long-term treatments for symptomatic fibroids. (Both hysterectomy and myomectomy have never been formally reviewed for safety or efficacy and there is a paucity of evidence on morbidity and mortality for myomectomy.)

There is serious concern that women will be denied access to these effective hospital treatments by CCGs/ICSs as this medicine is so much cheaper.

The only clinical evidence submitted was for treatment duration of 1 year, so efficacy beyond this is not established.

As per FEmISA’s submission, fibroids cause a large number of symptoms and the medicine has only been shown to be effective at reducing some symptoms for the maximum of 1 year.

There were no comparative studies between Relugolix and other GNRH agonists, even though superiority was claimed that side-effects were fewer and less severe.

GNRH agonists should not be administered to women immediately before UAE/UFE, as the reduced blood supply to the fibroids compromises the outcome.

**Safety** – “*can be used long term, which could mean improved and sustained symptom relief”* The only clinical evidence on Relugolix submitted had a treatment duration of 1 year. The safety beyond 12 months has not been established. Other GNRH agonists can normally only be given for a maximum duration of 6 months.

*“preserves the uterus and fertility”* – There was no evidence submitted on the effect of Relugolix on fertility. It is unknown. There was also no mention that Afro-Caribbean women and other women with darker skins suffer from fibroids much younger than others and will require treatment at an early age, sometimes in their 20s and 30s. The effect of Relugolix on fertility is even more important to them than older women.

* 1. *“Treatment pathway and comparator*” - The information summary is incorrect. Women seek treatment from the symptoms of fibroids and they may also be a cause of infertility. The commonest symptom is heavy menstrual bleeding, but there are many other including severe pain. Anaemia can be the outcome of poor or inadequate management of heavy menstrual bleeding symptoms.

There are so many factual inaccuracies in this section that they are not all commented upon here, but this section needs rewriting. It appears that RCOG was not a stakeholder and did not have a gynaecologist on the committee reviewing the evidence. If this is the case it is a serious flaw and is possibly why the information is incorrect. RCGP also does not appear to be a stakeholder.

* 1. *GnRH agonists are the most relevant comparators for relugolix–estradiol–norethisterone acetate” ……… “The ERG agreed that it was justifiable to exclude GnRH antagonists as comparators.”* It is not clear why the ERG agreed and how it can be justified.

In summary FEmISA would welcome a medicine that has proven safety and efficacy in controlling fibroid symptoms for longer, while awaiting effective hospital treatment. The side effects of GNRH agonists are unacceptable to many women and gynaecologists. There is insufficient evidence on efficacy and safety to recommend Relugolix as an effective long- term treatment for symptomatic fibroids. Its use needs to be monitored and longer-term data recorded, assessed and made available to MHRA and NICE before ‘long-term’ use is recommended. It could be useful in the short-term as waiting lists for gynaecology procedures are some of the longest of all clinical specialities as a recent RCOG report highlights - <https://rcog.shorthandstories.com/lefttoolong/index.html>

There is a significant danger that CCGs/ICSs will deny women access to proven hospital treatment for fibroids and demand that women are prescribed Relugolix instead, because it is considerably cheaper. This would deny women effective treatment for their fibroids.

Yours sincerely,

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