

Member's Evidence Request response

Request Reference: ED22/082

Received: 01/04/22

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A: Question

My patient is taking Ryeqo for fibroids. She has been told that it is contraceptive and that she can't use hormonal contraception in addition. Is this correct?

B: Response

Ryeqo (R) a daily tablet, licensed for management of symptoms of uterine fibroids) contains a GnRH receptor antagonist (relugolix) together with addback HRT (oral estradiol 1mg po od and norethisterone 0.5mg po od).[1] GnRH antagonists avoid the initial flare-up effect associated with use of GnRH analogues; they offer immediate, dose-dependent suppression of ovarian function and the benefit of oral administration with resulting rapid reversibility on stopping treatment.[2,3]

GnRH agonists and antagonists suppress ovarian function and are thus theoretically contraceptive, but they are not licensed for contraception and the contraceptive effect relies on consistent, correct use. Services vary in their approach to contraception during use of a GnRH analogue or antagonist, but additional contraception is often advised.

The manufacturer of Ryeqo states that non-hormonal contraception should be used for the first month of Ryeqo use, but that after 1 month of correct use, ovarian suppression is adequate for contraception.[1] It would be expected also that a regular daily dose of 0.5mg oral norethisterone would confer a contraceptive cervical mucus effect. This does, however, depend heavily on correct use: the manufacturer advises additional contraceptive precautions for 7 days after 2 or more consecutive missed doses. The manufacturer also cautions that return to fertility is rapid after discontinuation of Ryeqo and that effective contraception should be discussed prior to discontinuation and initiated immediately upon stopping.

FSRH CEU recommends that if an individual has difficulty taking Ryeqo tablets consistently, they should be advised to use an additional effective contraceptive method. The manufacturer of Ryeqo advises that use of hormonal contraception should be avoided during use of Ryeqo.[1] Combined hormonal contraception should be avoided in this situation, but FSRH CEU has identified no studies investigating effect of use of progestogen-only contraceptives on ovarian suppression or on effectiveness of relugolix for fibroid-associated symptoms. An adverse effect would not be expected.

FSRH CEU suggests that if a copper IUD is not acceptable or not appropriate, bearing in mind the high typical use contraceptive failure rate of condoms, use of a progestogen-only implant or levonorgestrel-releasing IUS may be considered preferable to the risk of pregnancy that exists if Ryeqo is not consistently taken correctly.

C: References

1. emc. Gedeon Richter (UK) Ltd. Ryeqo 40mg/1mg/0.5mg film-coated tablets. Last updated on emc 11 Nov 2021. Available here: <https://www.medicines.org.uk/emc/product/12934/smpc#gref> (accessed 26/04/2022)
2. Donnez J, Dolmans MM. Endometriosis and medical therapy: from progestogens to progesterone resistance to GnRH antagonists: a review. *Journal of Clinical Medicine*. 2021 Jan;10(5):1085.
3. Donnez J, Dolmans MM. GnRH antagonists with or without add-back therapy: A new alternative in the management of endometriosis?. *International journal of molecular sciences*. 2021 Jan;22(21):11342.

Checked by SMRH

Enquiry response by EZC

The Clinical Effectiveness Unit (CEU) is funded by the FSRH and supported by NHS Lothian. The advice given in this Member's Enquiry Response has been prepared by the CEU and is based on a structured search and review of published evidence available at the date of preparation. The advice given here should be considered as guidance only. Adherence to it will not ensure a successful outcome in every case and it may not include all acceptable methods of care aimed at the same results. This response has been prepared as a service to FSRH members, but is not an official Faculty guidance product; Faculty guidance is produced by a different and lengthier process. It is not intended to be construed or to serve as a standard of medical care. Such standards are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances. Members are welcome to reproduce this response by photocopying or other means, in order to share the information with colleagues.