NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

SINGLE TECHNOLOGY APPRAISAL

APPEAL HEARING

# Advice on Relugolix-estradiol-norethisterone acetate for treating moderate to severe symptoms of uterine fibroids [ID3842]: Decision of the panel

## Introduction

1. An appeal panel was convened on 7 September 2022 to consider an appeal against NICE’s final appraisal document, to the NHS, on relugolix-estradiol-norethisterone acetate for treating moderate to severe symptoms of uterine fibroids [ID3842].
2. The Appeal Panel consisted of:

* Dr Biba Stanton Chair
* Dr Justin Whatling Non-Executive Director of NICE
* Professor Peter Groves Health service representative
* Adrian Griffin Industry representative
* Rosemary Harris Lay representative

1. None of the members of the appeal panel had any competing interest to declare.
2. The panel considered an appeal submitted by Fibroid Embolisation: Information, Support, Advice (FEmISA), a patient organisation.
3. FEmISA was represented by:

* Ginette Camps-Walsh Coordinator

1. In addition, the following individuals involved in the appraisal were present and available to answer questions from the appeal panel:

* Professor Stephen O'Brien Chair, Technology Appraisal Committee C
* Helen Knight Acting Interim Director, Medicines Evaluation, NICE
* Ross Dent Associate Director, NICE

1. The appeal panel’s legal adviser, Amy Smith of DAC Beachcroft LLP, was also present.
2. The following member of the NICE appeal panel for highly specialised technologies and technology appraisals was present as a silent observer throughout the hearing and panel discussions.

* David Chandler Lay Representative

1. Under NICE’s appeal procedures, members of the public are admitted to observe appeal hearings and several members of the public and NICE staff observed the proceedings which were held via Zoom.
2. There are two grounds under which an appeal can be lodged:

Ground One: In making the assessment that preceded the recommendation, NICE has:

(a) Failed to act fairly; and/or

(b) Exceeded its powers.

Ground Two: The recommendation is unreasonable in light of the evidence submitted to NICE.

1. Dr Mark Chakravarty, NICE Lead non-executive director for appeals, in preliminary correspondence had confirmed that:

* FEmISA had potentially valid grounds of appeal under Ground 2.

1. The appraisal that is the subject of the current appeal provided advice to the NHS on relugolix-estradiol-norethisterone acetate for treating moderate to severe symptoms of uterine fibroids.
2. Relugolix is a gonadotrophin-releasing hormone (GnRH) antagonist which, in combination with estradiol and norethisterone, is indicated as an orally administered treatment for moderate to severe symptoms of uterine fibroids in adult women of reproductive age.
3. The numbering of appeal points in this letter reflects those that were used during the hearing. Reference is also made to their corresponding number in the original appeal letters. The text of this letter does not represent a verbatim account of the proceedings nor a documentation of the order of events that took place but rather, provides a brief summary of the appellant and committee submissions for the points that were discussed.
4. Before the appeal panel inquired into the detailed complaints, the following made a preliminary statement: Ginette Camps-Walsh, on behalf of FEmISA, and Professor Stephen O'Brien on behalf of the appraisal committee.

## Appeal by FEmISA

## Appeal Ground 2: The recommendation is unreasonable in the light of the evidence submitted to NICE.

### Appeal Ground 2.1(b) (To cover original appeal points 2.1(b) and 2.2(a)): The recommendation is unreasonable because the only clinical evidence submitted was for treatment duration of 1 year and the FAD states that Relugolix "can be used long term, which could mean improved and sustained symptom relief".

1. Ginette Camps-Walsh, for FEmISA, explained that in the context of the evidence of efficacy and safety of relugolix-estradiol-norethisterone acetate, treatment for up to 1 year would be supported by FEmISA. She later added that FEmISA consider Relugolix is certainly a good option as a “holding treatment” prior to in-hospital treatment, given that it can be prescribed within its marketing authorisation for more than 6 months (unlike GnRH agonists, although many agonists are in fact prescribed for longer). She submitted, however, that longer term treatment could not be supported by the current evidence available. She expressed particular concern for women of Afro-Caribbean heritage in whom fibroids may develop in their 20s. She stated that the average age for women presenting with symptoms of fibroids in the NHS is 42 years, and said that presentation in these women may be at a much younger age than average. She stated that the average age of the menopause is 52 years and submitted that in some Afro-Caribbean women, treatment may therefore be needed for more than 30 years. She concluded that since the only evidence available on the safety and efficacy of relugolix-estradiol-norethisterone acetate is up to 1 year, the possibility of treatment of this duration may be very unsafe and that sustained efficacy cannot be assumed.
2. Stephen O'Brien, for NICE, explained that it was important to look at the evidence available and who is responsible for safety monitoring. He explained the committee is required to make its judgments on the basis of the evidence available to it. He emphasised that it is the role of the MHRA and not NICE to determine the safety of treatments. He stated that (1) the pharmacovigilance data available for relugolix-estradiol-norethisterone acetate does not indicate any safety concerns, albeit with limited follow up and (2) while there may be a possibility of a negative impact of this treatment on bone density, no evidence was put to the committee to substantiate this. He explained that the committee had considered it reasonable, on the basis of the evidence, not to restrict the duration of treatment with relugolix-estradiol-norethisterone acetate to 1 year in its recommendation, as the committee saw no compelling reason to do so. He noted that there is a mechanism through the MHRA to limit treatment duration.
3. Ginette Camps-Walsh responded that she considers there to be a “world of difference” between not restricting a treatment and recommending it for long term use. Furthermore, she indicated that the Summary of Product Characteristics (SPC) for relugolix-estradiol-norethisterone acetate recommends that a DEXA scan be undertaken after 1 year of treatment to determine bone density. She concludes that this indicates a concern about the possible development of osteoporosis and asked why the committee felt able to recommend long term use. She went on to express the opinion that current arrangements for treatment safety surveillance are inadequate (a view, she considered, was shared by the conclusions of Baroness Cumberlege’s report 'First do no harm') and that – while those arrangements were not NICE’s responsibility - this was something that NICE must consider.
4. Stephen O'Brien expressed sympathy for the concerns that had been raised by Ginette Camps-Walsh regarding the effectiveness of current arrangements for pharmacovigilance in the NHS and observed that safety issues sometimes emerge with treatments many years after they have been assessed by MHRA or NICE. Nonetheless, he explained that the committee can only be guided by the evidence available for relugolix-estradiol-norethisterone acetate and had noted from the trials, that when discontinuation of treatment had been encountered, it had usually been because of logistical challenges associated with trial participation rather than because of adverse events. He stated that if the committee had heard concerns it would have acted. He re-iterated that the committee had considered whether it was appropriate to limit the duration of treatment but concluded that there was no logical or reasonable reason to constrain the duration of treatment with relugolix-estradiol-norethisterone acetate. He further indicated that in every appraisal the trial and follow up evidence considered by the committee will be of limited duration. This does not mean that the committee will only recommend treatment for the same period.
5. Following questioning from the appeal panel, Stephen O'Brien explained that the conclusion of the committee that relugolix-estradiol-norethisterone acetate "can be used long term", as stated in the Final Appraisal Document (“FAD”), was based on the absence of any licensing restriction on the duration of treatment or evidence to suggest treatment restriction was necessary. He stated that the committee were intending to explain that the medicine *“could”* be used long term, i.e. this was an option or a choice for clinicians and patients, but was not recommending that patients “must” use it long term.
6. With regard to the evidence of efficacy and safety considered by the committee, he paid reference to the LIBERTY and PEARL trials with follow up over a period of several years. He also drew attention to the consideration that was given by the committee to treatment discontinuation rates. These were modelled, he reported, for the assessment of cost effectiveness, and were presented in graphical form on slide 26 of the presentation that was provided to the committee at its meeting on 6 April 2022.
7. He clarified that the statement in the FAD that relugolix-estradiol-norethisterone acetate "can be used long term", was not meant to represent a recommendation for long term use, nor a suggestion that relugolix-estradiol-norethisterone acetate should be used outside of its marketing authorisation. Rather, the recommendations in the FAD were based on the conclusion of the committee that the available published evidence and expert opinions received indicated that relugolix-estradiol-norethisterone acetate is a clinically and cost-effective treatment option for women with symptomatic fibroids for which there is no regulatory restriction on treatment duration. He concluded, however, that these distinctions could have been made clearer in the wording of the FAD.
8. Stephen O'Brien further explained that in appraisals of relatively expensive drugs (e.g. cancer drugs), the company may limit treatment duration for costs reasons. For this appraisal, because relugolix-estradiol-norethisterone acetate is relatively inexpensive, there was no reason to impose a restriction on treatment duration.
9. Asked how important the possibility of long term use was for the committee’s recommendation, Stephen O'Brien stated that the committee always considers benefits not captured in the model as these may give flexibility around the threshold at which the committee is prepared to recommend a treatment as cost effective within the NHS. He confirmed that this was why the committee was thinking about the potential for long term use. However, he said that this did not greatly sway the committee’s thinking in this appraisal.
10. Ross Dent, for NICE, added that it was important to be clear the committee has not recommended relugolix-estradiol-norethisterone acetate “for long term use”. Rather, the committee has recommended it for use within its marketed authorisation (which permits use for an unlimited duration). NICE would expect clinicians to use it within its marketing authorisation. He explained that, after making that recommendation, the rest of the FAD explains *how* the committee decided to recommend relugolix-estradiol-norethisterone acetate for use within its marketed authorisation, and paragraph 3.12 of the FAD explains how the committee considered benefits not captured in the model. He noted that a clinical expert had explained that the relevant comparator (a GnRH agonist) can only be used for 6 months under its marketing authorisation (owing to concerns around bone mineral density loss) although in practice there was sometimes longer unlicensed use. He also noted that there is a suggestion to carry out a DEXA scan with relugolix-estradiol-norethisterone acetate at 1 year to check bone density. However, the clinical experts had said that relugolix-estradiol-norethisterone could be used for longer than 1 year to the benefit of patients, and this could be an advantage in particular to younger patients and black African Caribbean patients who are often diagnosed younger and do not want surgical options to preserve fertility.
11. Helen Knight, for NICE, explained that the statement in the FAD that relugolix-estradiol-norethisterone acetate “can be used long term" was in the context of the time limitations that are associated with other treatments used in the same clinical context. She reported that in the SPC for relugolix-estradiol-norethisterone acetate, reference is made to safety data in women treated for up to 104 weeks, which is considerably longer than is recommended for other non-surgical treatments used in women with symptomatic fibroids. She reiterated that the wording of the FAD does not require all patients to use relugolix-estradiol-norethisterone acetate or to use it for a specified time period, but rather to identify it as a treatment option. NICE would expect treatment to be given in line with the marketing authorisation and SPC and there to be consideration of the clinical risk:benefit assessment and careful clinical monitoring over time.
12. Asked by the panel how clinicians would interpret the phrase “long term”, Stephen O’Brien acknowledged that this is ambiguous but in his mind this would mean five to ten years, though he could not be sure how the clinicians involved in the appraisal did in fact interpret this. He added that he would expect responsible clinicians to flag any potential issue, even of minor concern, at the earliest possible stage and that they had not done so.
13. Following questioning from the appeal panel, Ross Dent explained the economic modelling that was undertaken during this appraisal, particularly in the context of the considerations around the possible long-term use of relugolix-estradiol-norethisterone acetate. He confirmed that both the company and external review group's (ERG) calculated “base case” incremental cost-effectiveness ratios (ICERs) for relugolix-estradiol-norethisterone acetate treatment suggested that relugolix-estradiol-norethisterone acetate was cost effective (as usually measured by NICE). He explained, however, that this was based on an indirect clinical comparison of the two treatments in the absence of any direct comparative evidence. Given the consequent uncertainties in the clinical evidence, he explained that the committee also considered a modelled scenario in which the effectiveness of relugolix-estradiol-norethisterone acetate was no better than the comparator GnRH agonists. This led to an increase in the ICER values for relugolix-estradiol-norethisterone acetate, but even then the committee considered that there were sufficient “likely additional benefits” not captured in the economic model (as described in section 3.12 of the FAD) to 'tip the balance' towards cost effectiveness in this scenario.
14. Stephen O'Brien confirmed that the committee had noted that the base case ICERs were broadly favourable in both the company and ERG calculations. He provided additional perspective by indicating that this is rare and, in this appraisal, allowed the committee to reach a decision and agree its guidance recommendations at a single meeting. In light of the favourable ICERs, he explained that the “likely additional benefits” listed at paragraph 3.12 were not particularly influential in the committee's decision-making.
15. Ginette Camps-Walsh submitted that in the absence of clinical data, long term safety cannot be assumed. She cited the example of the drug esmya (ulipristal acetate) in which unanticipated evidence of liver dysfunction emerged as a complication of long-term use. She raised the concern that similar adverse events could emerge with the long-term use of relugolix-estradiol-norethisterone acetate. She expressed concern that the committee had been driven by the relatively low cost of the drug.
16. Stephen O'Brien expressed the view that the long-term safety of relugolix-estradiol-norethisterone acetate can only be established through its use. He considered it would not be reasonable for NICE to limit treatment duration to one year owing to the absence of longer term data. He re-iterated the fact that the FAD does not recommend relugolix-estradiol-norethisterone acetate for long term use but rather recommends it for use within its marketing authorisation. He also confirmed that the health economic analysis facilitated a positive recommendation but that there was no intention to promote the use of relugolix-estradiol-norethisterone acetate as a cost-effective alternative to already established treatments.
17. Stephen O'Brien further explained that the role of the committee is to produce timely evidence-based guidance recommendations to support patients, clinicians, the pharmaceutical industry and commissioners in their decision-making. In this regard, there is a tension between the need for timeliness in undertaking appraisals to support clinical services and the availability of a mature evidence base to inform these. He re-iterated that recommendations are made by the committee based on the evidence available to it and that this will inevitably be associated with some residual uncertainties in regard to long term efficacy and safety.
18. Helen Knight confirmed that it is not the role of NICE to judge the safety of treatments and the committee does not conclude in its appraisals whether a product is safe or not. She stated that this is the responsibility of regulators. She explained that adverse events and safety signals are relevant to NICE appraisals but only in so far as they may influence the assessment of cost effectiveness. She stated that relugolix-estradiol-norethisterone acetate has received a full and non-conditional licence from the European Medicines Agency and that if, in the future, this was changed or revoked, then NICE would respond to that if necessary. She also confirmed that it is not unusual for NICE to make recommendations for treatments that may be used in clinical practice for a longer duration than that of the clinical data.
19. Stephen O'Brien expressed the desire of the committee to be constructive and observed that they would have liked to engage with FEmISA at the committee meeting in April 2022, which FEmISA chose not to attend. He went on to ask Ginette Camps-Walsh what she would have preferred that the committee had included in the FAD.
20. In response, Ginette Camps-Walsh expressed the view that the guidance should not have suggested that relugolix-estradiol-norethisterone acetate “can be used long term” since the licence does not stipulate a recommended treatment period. Furthermore, she considered that there should be a recommendation in the FAD that patients be monitored carefully and that clinicians be reminded of their responsibilities in this regard, as outlined in the Cumberlege Report "First do no harm". She added that FEmISA have the same concerns about efficacy, though safety is their prime consideration.
21. Ginette Camps-Walsh also noted that she disagreed with an earlier comment that relugolix-estradiol-norethisterone acetate is advantageous for younger patients, given there was no long-term evidence. Ross Kemp clarified that this was a comment made by the clinical experts to the committee.
22. Helen Knight commented that NICE want to ensure its guidance documents are as clear as possible and acknowledge FEmISA’s concerns. She added that NICE thought it was sufficiently clear that the FAD does not recommend that relugolix-estradiol-norethisterone acetate should be used long term but rather that it should be used with its marketing authorisation, which allows the clinician and patient to discuss appropriate treatment duration case by case.
23. In response to a question from the panel later in the hearing, Stephen O’Brien confirmed that, even taken together, the potential for long term use of relugolix-estradiol-norethisterone acetate and the fact that it preserves the uterus were not critical to the positive recommendation. Furthermore, he said that factors in paragraph 3.12 overall did not carry much weight in the decision-making, as both the company and ERG ICER’s were considerably below £20,000 (but he accepted that this could have been clearer in the FAD and particularly section 1).
24. Ginette Camps-Walsh expressed concern about the long term efficacy of relugolix-estradiol-norethisterone acetate, particularly in comparison with hospital treatments.
25. Stephen O’Brien said that the committee did not suggest that relugolix-estradiol-norethisterone acetate should replace other treatments but rather recommended it as an option that would give patients more choice. He accepted that there is uncertainty about the long term efficacy of relugolix-estradiol-norethisterone acetate but emphasised that the committee’s remit is to make a reasonable decision based on the evidence available to it. He pointed out that this is not an unusual situation, because NICE balances the need for longer term evidence with the need to allow access to new medicines in a timely way.
26. The Appeal Panel concluded as follows. The panel agreed that the FAD does not recommend long term use of relugolix-estradiol-norethisterone acetate, but recommends the use of relugolix-estradiol-norethisterone acetate within its market authorisation. The panel noted that it is not uncommon for NICE to make recommendations for treatments that may be used in clinical practice for a longer duration than that of the clinical data.
27. The panel noted that judging the safety of a product, and monitoring its long term safety, is a responsibility of the regulator rather than of NICE. The panel also noted that the committee had not been presented with any evidence to suggest long term safety concerns with relugolix-estradiol-norethisterone acetate that might be relevant to its decision making.
28. The panel judged that the mention of “long term” use of relugolix-estradiol-norethisterone acetate in the FAD formed part of explaining the rationale for the committee’s decision (in the context of considering any additional benefits of the drug that may not have been captured in the model). More specifically, the committee’s reference to the possible additional benefit that relugolix-estradiol-norethisterone acetate “can be used long term” was made in the context of the distinction between relugolix-estradiol-norethisterone acetate (where the marketing authorisation does not limit the duration of treatment) and the comparator GnRH agonist (where the marketing authorisation restricts use to six months). The panel noted that the committee had seen evidence both from the trials and from clinical experts that relugolix-estradiol-norethisterone acetate is used for more than six months. The panel accepted that it was reasonable to have considered this factor as one potential benefit of treatment that was not captured in the model.
29. The panel considered how this factor had influenced the committee’s decision to recommend relugolix-estradiol-norethisterone acetate. The panel accepted the committee’s explanation at the hearing that this factor (and indeed all the potential uncaptured benefits in paragraph 3.12 taken together) had little weight in reaching a positive recommendation. This was because both the company and ERG base case gave cost-effective ICERs. The panel also judged that it was reasonable that the committee noted the uncertainty in the model and therefore went on to consider the potential uncaptured benefits.
30. The appeal panel concluded, therefore, that the committee had not acted unreasonably in concluding that an additional likely benefit not captured in the economic model was that relugolix-estradiol-norethisterone acetate can be used long term or in making a positive recommendation for the use of relugolix-estradiol-norethisterone acetate in women with symptomatic fibroids.
31. The appeal panel agreed with the comments made by NICE representatives that the wording of the FAD could have been clearer in explaining what was meant by “long term use” of relugolix-estradiol-norethisterone acetate, and the purpose, context and importance of referring to this. However, the panel did not accept that any statements in the FAD were inaccurate or that any lack of clarity amounted to unreasonableness.
32. The appeal panel therefore dismissed the appeal on this point.
33. However, the appeal panel requests that the sections in the FAD that state that relugolix-estradiol-norethisterone acetate can be used long term are amended to clarify that the likely uncaptured benefit considered by the committee was the fact that there is no restriction on the duration of treatment in the marketing authorisation for relugolix-estradiol-norethisterone acetate (in contrast with the comparator).
34. The appeal panel also noted that Section 1 of the FAD (which is intended to provide an explanation, in lay terms, about how the committee reached its decision) does not seem to reflect the weight of evidence that was considered important by the committee in its decision making. The appeal panel recommends that NICE considers re-wording this section to better reflect the committee’s reasoning, as described during the hearing and set out above, in relation to whether the ICERs were within the normal range considered by NICE to be cost effective and the importance of the “likely additional benefits” identified in paragraph 3.12.

### Appeal Ground 2.2(b): The recommendation is unreasonable because the FAD states that Relugolix "preserves the uterus and fertility".

1. Ginette Camps-Walsh, for FEmISA, submitted that the marketing authorisation for relugolix-estradiol-norethisterone acetate states, as a caution about unwanted pregnancy, that when treatment is stopped, ovulation returns. While she accepts that the use of relugolix-estradiol-norethisterone acetate preserves the uterus and that this is a benefit, she stated that it cannot be assumed that the return of ovulation, after stopping treatment, equates to a return of fertility. She further stated that no evidence of fertility, teratogenicity, or pregnancy rates had been collected in the LIBERTY trials and this is in contrast to invasive treatments such as myomectomy or uterine artery embolisation, for which evidence of pregnancy rates, and therefore fertility, are available. She expressed the specific concern that following withdrawal of treatment with relugolix-estradiol-norethisterone acetate, fibroids may revert to pre-treatment status and therefore may continue to impair fertility. She said that we don’t know the effect of relugolix-estradiol-norethisterone acetate on fertility, so the FAD should not state that it preserves fertility.
2. Stephen O'Brien, for NICE, said that the committee had heard from clinical experts that relugolix-estradiol-norethisterone acetate can avoid the need for surgery and therefore preserve the uterus.
3. He accepted that there is no definitive evidence of the impact of relugolix-estradiol-norethisterone acetate on fertility. However, he argued that there was no reason that this lack of evidence should have prevented a positive recommendation. He said that many drugs might have potential long term effects on fertility but this does not prevent NICE from making a recommendation for their use. He said that there had been no intention to imply that there was evidence that relugolix-estradiol-norethisterone acetate preserves fertility *per se*. The statement in the FAD that this treatment “preserves the uterus and fertility” was intended to mean that by preserving the uterus, the treatment preserves the potential for fertility (in contrast to some surgical options).
4. Stephen O’Brien acknowledged that the wording of the FAD regarding the effect of relugolix-estradiol-norethisterone acetate on fertility could have been clearer.
5. Stephen O'Brien went on to explain that the committee’s identification of “likely additional benefits” that this treatment “preserves the uterus and fertility” was not a key driver in the committee's conclusions about the clinical and cost effectiveness of relugolix-estradiol-norethisterone acetate. Rather, this was considered as one of a number of “likely additional benefits” that were not captured in the economic model but which could impact beneficially on QALY gains. He confirmed that these were minor considerations in the committee’s decision-making in arriving at a positive recommendation in the FAD, because the ICER in both the company and ERG base case had been in the cost-effective range.
6. Ginette Camps-Walsh stated that she supported the conclusion that treatment with relugolix-estradiol-norethisterone acetate “preserves the uterus”. However she suggested the FAD should state that its impact on fertility is unknown, given the importance of this particularly for younger women. She explained the need for careful monitoring, particularly when this treatment is used in younger patients.
7. Following questioning from the appeal panel, Ross Dent, for NICE, explained that the role of the FAD is to describe how the committee arrived at its decisions and recommendations and that it is not intended to be a clinical guideline or SPC. He indicated that NICE can only clarify what influenced the committee’s decision making in the FAD.
8. Helen Knight, for NICE, explained that the statement in the FAD that relugolix-estradiol-norethisterone acetate "preserves the uterus and fertility" was made in the context of a comparison with other treatments for women with symptomatic fibroids that permanently remove the uterus and possibility of pregnancy. She confirmed that there was no intention, with this statement, to make a judgment about the impact of relugolix-estradiol-norethisterone acetate on long term fertility.
9. The Appeal Panel concluded as follows. The appellant and committee agreed that it was accurate to state that treatment with relugolix-estradiol-norethisterone acetate preserves the uterus. The panel accepted the committee’s statement at the hearing that in saying that relugolix-estradiol-norethisterone acetate “preserves the uterus and fertility” they intended to highlight the advantage of preserving the uterus and therefore the potential for fertility, unlike some surgical options. They accepted that the committee did not intend to imply that there is definitive evidence on the impact of this treatment on fertility.
10. The panel judged that the statement in the FAD that relugolix-estradiol-norethisterone acetate “preserves the uterus and fertility” formed part of explaining the rationale for the committee’s decision. The panel agreed that preserving the potential for future pregnancy is a likely additional benefit of treatment, in the context of other treatments, such as hysterectomy. The panel accepted that it was reasonable to have considered this factor as one likely benefit of treatment that was not captured in the model.
11. The panel considered how this factor had influenced the committee’s final decision to recommend relugolix-estradiol-norethisterone acetate. The panel accepted the committee’s explanation at the hearing that this factor (and indeed all the likely uncaptured benefits in paragraph 3.12 taken together) were a minor factor in reaching a positive recommendation. This was because both the company and ERG base case gave cost-effective ICERs. The panel also judged that it was reasonable that the committee noted the uncertainty in the model and therefore went on to consider the potential uncaptured benefits.
12. The appeal panel agreed with the comments made by NICE representatives that the wording of the FAD could have been clearer by focusing on preservation of the uterus and avoiding any potential implication that the committee had considered definitive evidence of the impact of this treatment on fertility. However, the panel did not accept that any statements in the FAD were inaccurate when read in context, and therefore the way in which this part of the FAD is expressed is not unreasonable.
13. The appeal panel concluded that the committee had not acted unreasonably in considering that a “likely additional benefit” of relugolix-estradiol-norethisterone is that it preserves the uterus and therefore the potential for future fertility or in making a positive recommendation for the use of relugolix-estradiol-norethisterone acetate in women with symptomatic fibroids."
14. The appeal panel therefore dismissed the appeal on this point.
15. While the appeal panel found no unreasonableness in the committee’s decision-making, it supports the proposal made by NICE to re-word the relevant sections of the FAD to provide additional clarification on this point. It would be useful to make clear that the relevant “likely additional benefit” that the committee had in mind was that treatment with relugolix-estradiol-norethisterone acetate preserves the uterus, in contrast with some surgical interventions (and to avoid making reference to the effect of relugolix-estradiol-norethisterone acetate on fertility).

## Conclusion and effect of the appeal panel’s decision

1. The appeal panel therefore dismissed the appeal on all grounds.
2. The appeal panel draws to the attention of NICE paragraphs 48, 49 and 64 of this letter in which specific areas are discussed where re-wording of the FAD might be considered.
3. There is no possibility of further appeal against this decision of the appeal panel. However, this decision and NICE’s decision to issue the final guidance may be challenged by applying to the High Court for permission to apply for a judicial review. Any such application must be made within 3 months of NICE publishing the final guidance.