**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Health Technology Evaluation**

# Fezolinetant for treating vasomotor symptoms associated with the menopause

**Draft scope**

## Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of fezolinetant within its marketing authorisation for treating vasomotor symptoms associated with the menopause.

## Background

The menopause occurs when menstruation stops and the end of natural reproductive life is reached. Usually, it is defined as having occurred when there has been no naturally occurring period for 12 consecutive months. It is a natural part of ageing. Changes associated with menopause occur when the ovaries stop maturing eggs and secreting oestrogen and progesterone. The experience of symptoms varies (length and severity) but most people will have some vasomotor symptoms associated with the decrease in oestrogen. Vasomotor symptoms include hot flushes and night sweats caused by constriction and dilatation of blood vessels in the skin that can lead to a sudden increase in blood flow to allow heat loss. Vasomotor symptoms have been linked to problems with sleep, quality of life and depression.

Menopause usually occurs between 45 and 55 with an average age of 51 years. The prevalence of problematic vasomotor symptoms that need treatment is estimated to be 25%[1], and the prevalence decreases with age to 15% at age 55 to 59, 6% at age 60-69 and only 3% at over 70[2]. However, medical intervention is often not sought out so the true prevalence of vasomotor symptoms may be much higher, with studies showing that up to 80% may experience vasomotor symptoms as part of the menopause[3].

Hormone replacement therapy (HRT) is the main treatment option for menopausal symptoms. Other treatments that have been used include lifestyle advice, herbal remedies, other complementary (alternative) therapies and antidepressants (NG23). NICE recommends the following treatment options for vasomotor symptoms associated with menopause:

- oestrogen and progestogen for those with a uterus; or oestrogen alone for those without a uterus (NG23).
- selective serotonin reuptake inhibitor (SSRI) antidepressants for those with breast cancer, but not for those taking tamoxifen (NG101).

NG101 also notes that HRT should be stopped if breast cancer is diagnosed and should not be offered when there is a history of breast cancer unless in exceptional circumstances. An update to NG23 is currently considering cognitive behavioural therapy (CBT) for menopausal symptoms including vasomotor symptoms. Short term and long-term risk and benefits of each treatment should be discussed with the treating clinician.

**The technology**

Fezolinetant (brand name unknown, Astellas Pharma Ltd).

Fezolinetant does not currently have a marketing authorisation in the UK for treating vasomotor symptoms associated with the menopause. It has been studied in several phase 3 clinical trials compared with placebo in women with vasomotor symptoms (hot flushes). Two trials were focused on moderate to severe flushes, and in another one only those for whom HRT is not suitable were included.

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| **Intervention(s)** | Fezolinetant |
| **Population(s)** | People with moderate to severe vasomotor symptoms associated with the menopause |
| **Subgroups** | If the evidence allows the following subgroups will be considered:<br>• People for whom HRT is not suitable or contraindicated<br>• People at risk of or with breast cancer<br>• By presence or not of a uterus |
| **Comparators** | Established clinical management without fezolinetant, including:<br>• Hormonal pharmaceutical treatments (such as oestrogen and progestogen combination, or oestrogen alone)<br>• Non-hormonal pharmaceutical treatments (such as SSRIs)<br>• Psychological therapies / cognitive behavioural therapy (subject to NICE guideline review)<br>• Non-pharmacological / other complementary therapies (including isoflavones, black cohosh, St John's Wort) |
| **Outcomes** | The outcome measures to be considered include:<br>• Change in frequency of vasomotor symptoms<br>• Change in severity of vasomotor symptoms<br>• Sleep disturbance<br>• Psychological symptoms (anxiety, low mood)<br>• Adverse effects of treatment<br>• Health-related quality of life. |

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| **Economic analysis** | The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.<br><br>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.<br><br>Costs will be considered from an NHS and Personal Social Services perspective. |
| **Other considerations** | Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator. |
| **Related NICE recommendations** | **Related NICE guidelines:**<br><br>Menopause: diagnosis and management (2019). NICE guideline 23. Current undergoing partial update.<br><br>Early and locally advanced breast cancer: diagnosis and management (2018). NICE guideline 101.<br><br>**Related NICE guidelines in development:**<br><br>Menopause: diagnosis and management. Publication expected August 2023.<br><br>**Related interventional procedures:**<br><br>Removal, preservation and subsequent reimplantation of ovarian tissue to prevent symptoms from the menopause (2022). NICE interventional procedures guidance 738.<br><br>**Related quality standards:**<br><br>Menopause (2017). NICE quality standard 143. |
| **Related National Policy** | The NHS Long Term Plan, 2019. NHS Long Term Plan<br><br>Department for Health and Social Care, 2022. Women's Health Strategy, priority area 13<br><br>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019), chapter 9<br><br>NHS Digital (2022). NHS Outcomes Framework England, March 2022 Annual Publication, indicator 2.1 (proportion of people feeling supported to manage their condition), 4a.1 (patient experience of GP services) |

**Questions for consultation**

Is the population appropriate?

Where do you consider fezolinetant will fit into the existing treatment pathway for menopause?

Would fezolinetant be used as an add-on treatment to other treatment options for treating vasomotor symptoms associated with menopause?

Have all relevant comparators been included? What are the relevant comparators for people who cannot or chose not to have hormone replacement therapy? Is tibolone considered a hormone replacement therapy or should it be listed separately as a comparator?

How are SSRIs used in the NHS for treating vasomotor symptoms associated with menopause?

- Are SSRIs being used only in women with breast cancer? Or
- Are they being used to manage vasomotor symptoms for other women without breast cancer as well, i.e. as a second-line after HRT?
- If they are being used to manage vasomotor symptoms, which SSRIs are being used?

Are the proposed subgroups relevant and appropriate? Are there other relevant subgroups to be considered? What are the relevant comparators for each subgroup?

How long would treatment be expected to last?

Would fezolinetant be a candidate for managed access?

Do you consider that the use of fezolinetant can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

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 proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which fezolinetant will be licensed;

- 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

**References**

1. Hickey, M., Szabo, R.A. and Hunter, M.S. (2017) Non-hormonal treatments for menopausal symptoms. British Medical Journal 359. [Abstract]

2. BMJ Best Practice. Menopause. Accessed 2 May 2023.

3. Woods, N.F. and Mitchell, E.S. (2005) Symptoms during the menopause: prevalence, severity, trajectory, and significance in women's lives. American Journal of Medicine 118(S12B), 14-24. [Abstract]