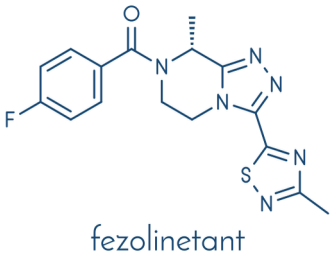
Fezoninitant - non-hormonal treatment for vasomotor symptoms

New non-hormonal options for controlling vasomotor symptoms are now available and more are on the way. So, what are they, why are they needed and who are they appropriate for?



fezolinetant

While hormone replacement or menopause hormone therapy (HRT/MHT) primarily involving oestrogen is the gold standard for treating vasomotor symptoms, it is not suitable for everyor and some people prefer not to take it which is why alternative options are important.

How many people are affected by vasomotor symptoms?

Every individual's menopause journey is unique. The type of menopause (natural/surgical medical), age at menopause (premature, early, or above 45) and the nature, frequency, and severity of symptoms (mild to severe) vary widely between individuals. Menopause symptoms affect about 80% of women and in a third, they can be severe. They can have an adverse impact on quality of life/work and can also have a negative impact on long-term health.

How menopause symptoms are managed depends on nature of symptoms, individual's medical history and personal choice of treatments. Lifestyle interventions, non-hormonal therapies or medications and hormone replacement therapy/menopause hormone therapy (HRT/MHT) are all options that can be considered with their pros and cons.

What are the current non-hormonal options?

Currently there remains a need for licensed non-hormonal medications for effective treatment of vasomotor symptoms such as hot flushes and night sweats of menopause (which then indirectly impact sleep, energy levels, mood, and brain function). For women who do not wish to take HRT/MHT as personal choice or have medical contraindications such as a history of hormone sensitive cancers or have persistent side effects from HRT/MHT - there are limited licensed medical treatment options which in the UK include:

- Antidepressants (SSRI/SNRIs)
- Gabapentin
- Clonidine
- Pregabalin.

These are used off-label and side effects include nausea, dry mouth, insomnia, dizziness, constipation, low libido, and weight gain which limit tolerance.

What is fezolinetant and how does it work?

After decades of research and development - the NK3 receptor antagonists are one such novel pharmacological option. Fezolinetant is the first drug in this class of medications which was licensed for use in the UK in 2024. There are other similar molecules which are in trials/development currently including elinzanetant which is NK1 and NK3 receptor blocker.

Vasomotor symptoms of menpoause such as hot flushes and night sweats are attributed to a narrowing of the brain's hypothalamic thermoneutral zone triggered by altered control mechanisms in the setting of declining oestrogen levels. This results in activation of symptoms by smaller elevations in core body temperature than before menopause. A central nervous system network of kisspeptin, neurokinin B, and dynorphin (KNDy) neurons located within the hypothalamic preoptic nucleus, activates the NK3R receptor and causes vasomotor symptoms when oestrogen levels drop. Blocking the NK3R can therefore reduce symptoms.

Is fezolinitant effective?

Since it was licensed for use in the UK last year, Fezolinetant (45 mg oral daily dose) has proven to be a useful and effective non-hormonal treatment option for many women who cannot or do not wish to take HRT/MHT as a treatment for moderate to severe hot flushes and for those who suffer from persistent side effects of hormone treatment, especially bleeding and progestogen sensitivity.

It is early days to compare the various different preparations that are emerging in this group of drugs but certainly both fezolinetant and elinzanetant appear effective in reducing the frequency and severity of vasomotor symptoms. Based on the clinical trials which looked at the effects of Fezolinetant for up to 52 weeks, it appears to start working within the first week of initiation and the efficacy continued throughout the trial duration. It reduces both the frequency of vasomotor symptoms and their severity (about 50-60% drop in vasomotor symptoms from baseline).

Are there side effects?

Side effects of fezolinetant include headaches, insomnia, diarrhoea, and elevation of blood liver enzyme levels. About 1-2.5% of the study population in the trials were noted to have raised liver enzyme levels after starting the drug and these generally subsided after stopping the medication.

Since fezolinetant was licensed for use there have been cases of liver injury reported with its use as part of post-marketing surveillance and guidelines have been put in place by the regulatory bodies for healthcare professionals to perform liver enzyme assessments before and after starting fezolinetnat for up to at least 3 months. Endometrial safety (womb lining) of fezolinetant has also been evaluated in trials and no adverse impact on endometrium noted.

Specific trials assessing the use of fezolinetant in women post-breast cancer, have not been completed yet. However, the medication has been utilised off-label in breast cancer survivors once the active cancer treatment has been completed and based on individualised assessment and discussions between the healthcare provider and the patient.

The medication is not advised for use in individuals with pre-existing liver or kidney problems and those taking certain medications including HRT/MHT.

Currently, fezolinetant is not available for prescription on the NHS, but this may change in the future. As more research becomes available and with more real-world prescribing experience, we will gain more knowledge about the utility of NK-3R antagonist medications in future.