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Newcastle University

Health Technology Briefing
August 2023

Elinzanetant for the treatment of moderate to severe vasomotor symptoms (hot flashes) associated with the menopause

Company/Developer	Bayer AG

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 33813	NICE TSID: Not available	UKPS ID: 670561

Licensing and Market Availability Plans

Currently in phase III development.

Summary

Elinzanetant is in clinical development for the treatment of vasomotor symptoms (hot flashes) in women undergoing the menopause. The menopause occurs between 45 and 55 years of age and is caused by declining hormone levels. The declining hormone levels mean that neurons (nerve cells) in the hypothalamus (small part in the brain) become hyperactive and disrupt body heat control mechanisms, resulting in hot flashes. The symptoms of these are a sudden feeling of warmth, a rapid heartbeat and perspiration. Over one-third of women report severe symptoms, which can last 10 years or more after the last menstrual period. Vasomotor symptoms may have a negative impact on sleep, mood and quality of life. Current treatments include hormone replacement therapy, but this is not suitable for all women because of medical contraindications, personal preference or an increased risk of disease including some cancers. Therefore, there is a need for effective nonhormonal therapy for menopause-related vasomotor symptoms.

Elinzanetant is a type of neuron receptor antagonist. It targets neuron receptors in the hypothalamus that are implicated in causing hot flashes. Elinzanetant is taken orally once a day. If licensed, elinzanetant would offer a new treatment option for women with menopause-associated vasomotor symptoms.

Proposed Indication

Moderate to severe vasomotor Symptoms (hot flashes) associated with the menopause.[1-3]

Technology

Description

Elinzanetant (BAY3427080)[2] is a novel, selective neurokinin 1,3 receptor (NK-1,3R) antagonist . It targets both NK-1 and NK-3 receptors, which are implicated in the aetiology of vasomotor symptoms.[4] Blocking these receptors could therefore reduce vasomotor symptoms.[5]

Elinzanetant is currently in clinical development for the treatment of post-menopausal vasomotor symptoms. In the phase III clinical trials OASIS 1, OASIS-2 and OASIS-3 patients are given 120 mg elinzanetant orally once daily for either 26 weeks (NCT05042362 and NCT05099159) or 52 weeks (NCT05030584).[1-3]

Key Innovation

Hormone replacement therapy (HRT) is currently the most effective treatment approved for the management of vasomotor symptoms. However, many women are not candidates for HRT because of medical contraindications, personal preferences or because of an increased risk of cardiovascular disease, thromboembolic disease or certain cancer types.[4,6] An alternative approach is the use of antagonists for the NK-1 and NK-3 receptors in the hypothalamus. The advantage of these is that they are a nonhormonal option and could therefore be used where HRT is not suitable.[4]

If licenced, elinzanetant will provide a new treatment option for women with post-menopausal vasomotor symptoms.

Regulatory & Development Status

Elinzanetant does not currently have marketing authorisation in the EU/UK for any indication.

Elinzanetant is not currently in phase II or III development for any other indication.

Patient Group

Disease Area and Clinical Need

The menopause is a natural part of ageing that usually occurs between 45 and 55 years of age and is caused by declining hormone levels. Symptoms include irregular periods, anxiety and mood swings as well as vasomotor symptoms such as hot flashes (HF).[7] The symptoms of a HF include a sudden feeling of warmth spreading through the chest, neck and face; a flushed appearance with red, blotchy skin; a rapid heartbeat and perspiration, mostly on the upper body. The duration of a HF varies but can be as long as five minutes, and can be so intense that they interrupt daily activities.[8] HF are most commonly caused by changing hormone levels before, during and after menopause. Current research suggests that HF occur when decreased oestrogen levels cause the hypothalamus to become more sensitive to slight changes in body temperature.[8]

Around 80% of women in the UK going through the menopause (approximately 1.5 million) experience HFs and night sweats, and approximately 25% report problematic symptoms affect their quality of life.[9,10]

Recommended Treatment Options

NICE currently recommends HRT to menopausal women experiencing vasomotor symptoms after discussing the short-term and longer-term benefits and risks. Oestrogen and progestogen are recommended for women with a uterus, and oestrogen alone for women without a uterus.[11]

Clinical Trial Information	
Trial	**OASIS-1, NCT05042362;** A Double-blind, Randomized, Placebo-controlled Multicenter Study to Investigate Efficacy and Safety of Elinzanetant for the Treatment of Vasomotor Symptoms Over 26 Weeks in Postmenopausal Women **Phase III:** active, not recruiting **Location:** Six EU countries, USA and Israel **Primary completion date:** July 2023
Trial Design	Randomised, parallel assignment, quadruple-blinded
Population	N = 396 (actual); postmenopausal women aged 40-65 years; with moderate to severe HF associated with the menopause and seeking treatment for this condition; completed Hot Flash Daily Diary for at least 11 days during the two weeks preceding baseline visit; and has recorded at least 50 moderate or severe HF (including night-time HF) over the last 7 days that the diary was completed.
Intervention(s)	120 mg elinzanetant orally once daily
Comparator(s)	Matched placebo
Outcome(s)	**Primary outcome measures:** • Mean change in frequency of moderate to severe HF [Time frame: baseline to Week 4] • Mean change in frequency of moderate to severe HF [Time frame: baseline to Week 12] • Mean change in severity of moderate to severe HF [Time frame: baseline to Week 4] • Mean change in severity of moderate to severe HF [Time frame: baseline to Week 12] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Clinical Trial Information	
Trial	**OASIS-2, NCT05099159;** A Double-blind, Randomized, Placebo-controlled Multicenter Study to Investigate Efficacy and Safety of Elinzanetant for the Treatment of Vasomotor Symptoms Over 26 Weeks in Postmenopausal Women **Phase III:** active, not recruiting **Location:** Six EU countries, USA, Canada, Norway and Switzerland **Primary completion date:** June 2023

Trial Design	Randomised, parallel assignment, quadruple-blinded
Population	N = 400 (actual); postmenopausal women aged 40-65 years; with moderate to severe HF associated with the menopause and seeking treatment for this condition; completed Hot Flash Daily Diary for at least 11 days during the two weeks preceding baseline visit; and has recorded at least 50 moderate or severe HF (including night-time HF) over the last 7 days that the diary was completed.
Intervention(s)	120 mg elinzanetant orally once daily
Comparator(s)	Matched placebo
Outcome(s)	**Primary outcome measures:** • Mean change in frequency of moderate to severe HF [Time frame: baseline to Week 4] • Mean change in frequency of moderate to severe HF [Time frame: baseline to Week 12] • Mean change in severity of moderate to severe HF [Time frame: baseline to Week 4] • Mean change in severity of moderate to severe HF [Time frame: baseline to Week 12] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Clinical Trial Information	
Trial	**OASIS-3,** NCT05030584**;** A Double-blind, Randomized, Placebo-controlled Multicenter Study to Investigate Efficacy and Safety of Elinzanetant for the Treatment of Vasomotor Symptoms Over 52 Weeks in Postmenopausal Women **Phase III:** active, not recruiting **Location:** Six EU countries, UK, USA and Canada **Primary completion date:** March 2023
Trial Design	Randomised, parallel assignment, double-blinded
Population	N = 628 (actual); postmenopausal women aged 40-65 years; with moderate to severe HF associated with the menopause and seeking treatment for this condition; completed a Hot Flash Daily Diary for at least 11 days during the two weeks preceding baseline visit; and is showing eligibility with respect to previous inclusion criterion during this time period.
Intervention(s)	120 mg elinzanetant orally once daily
Comparator(s)	Matched placebo
Outcome(s)	**Primary outcome measure:** Mean change in frequency of moderate to severe HF [Time frame: baseline to Week 12].

	See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of elinzanetant was confidential at the time of producing this briefing.

Relevant Guidance

NICE Guidance

- NICE guideline in development. Estetrol for treating vasomotor symptoms associated with the menopause in people aged 40 to 65 (GID-TA11059). Expected date of publication to be confirmed.
- NICE guideline in development. Fezolinetant for treating vasomotor symptoms associated with the menopause (GID-TA11058). Expected date of publication to be confirmed.
- NICE guideline in development. Menopause: diagnosis and management (GID-NG10241). Expected date of publication: March 2024.
- NICE guideline. Menopause: diagnosis and management (NG23). November 2015, updated December 2019.
- NICE quality standard. Menopause (QS143). February 2017.
- NICE interventional procedure guidance. Transvaginal laser therapy for urogenital atrophy (IPG697). May 2021.

NHS England (Policy/Commissioning) Guidance

No relevant guidance identified.

Other Guidance

- Primary Care Women's Health Forum. Menopause - Guidance on management and prescribing HRT for GPs. 2020.[12]
- Royal College of Nursing. Menopause: RCN guidance for nurses, midwives and health visitors. 2020.[13]

Additional Information

References

1 Clinicaltrials.gov. *A Study to Learn More About How Well Elinzanetant Works and How Safe it is for the Treatment of Vasomotor Symptoms (Hot Flashes) That Are Caused by Hormonal Changes Over 26 Weeks in Women Who Have Been Through the Menopause (OASIS-1)*. 2023. Available from: https://clinicaltrials.gov/ct2/show/NCT05042362 [Accessed 12 June 2023].

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9 Hickey M, Szabo RA, Hunter MS. Non-hormonal treatments for menopausal symptoms. *BMJ*. 2017;359(j5101). Available from: https://doi.org/10.1136/bmj.j5101.

10 UK Parliament. *Research briefing: Support for people experiencing menopausal symptoms*. 2021. Available from: https://commonslibrary.parliament.uk/research-briefings/cdp-2021-0078/ [Accessed 15 June 2023].

11 National Institute for Health and Care Excellence (NICE). *Menopause: diagnosis and management*. 2019. Available from: https://www.nice.org.uk/guidance/ng23/chapter/Recommendations [Accessed 20 June 2023].

12 Primary Care Women's Health Forum. *Guidance on management and prescribing HRT for GPs*. 2020. Available from: https://pcwhf.co.uk/resources/guidance-on-management-and-prescribing-hrt-for-gps/ [Accessed 15 June 2023].

13 Royal College of Nursing. *Menopause: RCN Guidance for Nurses, Midwives and Health Visitors*. 2020. Available from: https://www.rcn.org.uk/Professional-Development/publications/rcn-menopause-guidance-for-nurses-midwives-and-health-visitors-uk-pub-009326 [Accessed 15 June 2023].

NB: This briefing presents independent research funded by the National Institute for Health and Care Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.