NCPE Assessment

Technical Summary

Fezolinetant (Veoza ®)

24005

April 2026

Applicant: Astellas Pharma Co. Ltd

Fezolinetant for the treatment of moderate to severe vasomotor symptoms (VMS) associated with menopause.

NCPE
National Centre for Pharmacoeconomics, Ireland

The National Centre for Pharmacoeconomics (NCPE) has issued a recommendation regarding the cost-effectiveness of fezolinetant (Veoza®). Following assessment of the Applicant's submission, the NCPE recommends that fezolinetant be considered for reimbursement if cost-effectiveness can be improved relative to existing treatments.

This recommendation should be considered while also having regard to the criteria specified in the Health (Pricing and Supply of Medical Goods) Act 2013.

The Health Service Executive (HSE) asked the NCPE to carry out an evaluation of the Applicant's (Astellas Pharma Co. Ltd) Health Technology Assessment of fezolinetant (Veoza®). The NCPE uses a decision framework to systematically assess whether a technology is cost-effective. This includes comparative clinical effectiveness and health related quality of life benefits, which the new treatment may provide and whether the cost requested by the pharmaceutical company is justified.

Following the recommendation from the NCPE, the HSE examines all the evidence which may be relevant for the decision; the final decision on reimbursement is made by the HSE. In the case of cancer drugs the NCPE recommendation is also considered by the National Cancer Control Programme (NCCP) Technology Review Group.

About the National Centre for Pharmacoeconomics

The NCPE are a team of clinicians, pharmacists, pharmacologists and statisticians who evaluate the benefit and costs of medical technologies and provide advice to the HSE. We also obtain valuable support from clinicians with expertise in the specific clinical area under consideration. Our aim is to provide impartial advice to help decision makers provide the most effective, safe and value for money treatments for patients. Our advice is for consideration by anyone who has a responsibility for commissioning or providing healthcare, public health or social care services.

Summary

In August 2025, Astellas Pharma Co. Ltd submitted a dossier which investigated the comparative clinical effectiveness, cost-effectiveness and budget impact of fezolinetant (Veoza®) for the treatment of moderate to severe vasomotor symptoms (VMS) associated with menopause. Astellas Pharma Co. Ltd. is seeking reimbursement of fezolinetant on the Community Drugs Scheme.

Menopause is the process where menstrual cycles stop and is recognised as having occurred after twelve consecutive months of amenorrhoea. During menopause ovarian insufficiency gives rise to changing hormone levels and oestrogen deficiency. Menopausal symptoms include vasomotor symptoms (VMS) (hot flushes, night sweats), sleeping difficulties, mood changes (depression, anxiety), low libido and sexual drive, urogenital symptoms (vaginal dryness, dyspareunia, increased urinary frequency), arthralgia, weight gain, fatigue, headache, and cognitive effects (forgetfulness, difficulty concentrating, brain fog). Menopause can also affect long-term health. Oestrogen deficiency after menopause has been shown to increase the risk of osteoporosis and heart disease.

Fezolinetant is a non-hormonal selective neurokinin 3 receptor antagonist. Thus, fezolinetant is not a hormone replacement therapy (HRT). By blocking neurokinin B binding on the kisspeptin/neurokinin B/dynorphin (KNDy) neuron, fezolinetant is postulated to improve VMS symptoms by restoring balance in KNDy neuronal activity in the thermoregulatory centre of the hypothalamus. Fezolinetant is only indicated for the treatment of moderate to severe VMS associated with menopause. The recommended dose is 45mg (one tablet) once daily. The product licence does not make any recommendation on treatment duration, but states that the benefit of long-term treatment should be periodically assessed since the duration of VMS can vary by individual. Fezolinetant is not recommended in individuals undergoing oncologic treatment for breast cancer or other oestrogen-dependent malignancies. A benefit-risk assessment is advised for individuals with previous breast cancer or other oestrogen-dependent malignancies who are no longer on any oncologic treatment.

The current standard of care for individuals experiencing moderate to severe VMS associated with menopause is HRT. HRT regimens are either oestrogen alone or, for individuals with an intact uterus, combination therapy of oestrogen and progestogen (henceforth referred to as 'combined HRT'). The purpose of the progestogen in combined HRT (in individuals with an intact uterus) is to reduce the risk of endometrial hyperplasia or endometrial carcinoma. HRT is available in oral and transdermal formulations.

In addition to VMS, HRT is also widely used to treat many of the other oestrogen deficiency symptoms associated with menopause (sleeping difficulties, mood changes, sexual function, urogenital symptoms, arthralgia, fatigue, headache, cognitive effects). HRT also has additional long-term health benefits. It has been shown to have a significant protective effect against osteoporosis as well as atherosclerosis progression, coronary heart disease and death from cardiovascular causes. Oral oestrogen is associated with a small increased risk of stroke. This risk increases with age and dose of oestrogen. Oral HRT is also associated with an increased risk of venous thromboembolism (VTE), which increases with age. There is also a small increased risk of breast cancer associated with HRT. However, in general the benefits of HRT are considered to outweigh the risks for most individuals with menopausal symptoms aged less than 60 years or within 10 years of menopause.

National guidelines recommend that individuals with history of breast cancer, cardiovascular disease or other circumstances requiring specialist advice, are referred to a menopause specialist. Several complex menopause clinics are established across Ireland. Patients with hormone receptor positive breast cancer or specific types of hormone sensitive ovarian cancer experiencing moderate to severe VMS are generally advised to consider non-hormonal treatments. Most other patients can be offered HRT first-line, although some clinicians may adopt a more cautious approach to using HRT in individuals with underlying conditions. Non-hormonal treatments for moderate to severe VMS include selective serotonin re-uptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs). Gabapentin and oxybutynin are also used, though less frequently than SSRIs and SNRIs.

The Applicant suggests that fezolinetant will be used to treat moderate to severe VMS in individuals considered unsuitable for HRT (henceforth referred to as the 'HRT-unsuitable subpopulation'). This place in therapy is much narrower than the full licensed indication. The Applicant considers no active treatment to be the relevant comparator in the HRT-unsuitable subpopulation. The Review Group consider that non-hormonal treatments (particularly SSRIs and SNRIs) are relevant comparators in the HRT-unsuitable subpopulation. In the HRT-suitable subpopulation the relevant comparator is HRT.

1. Comparative effectiveness of fezolinetant

The clinical trial programme for fezolinetant includes three randomised double-blind, placebo-controlled trials: two 12-week trials followed by 40-week extension periods (SKYLIGHT 1 and 2), and a 24-week trial (DAYLIGHT). The trials included individuals born female who were confirmed as postmenopausal and seeking treatment for relief for VMS. Only individuals experiencing seven or more moderate to severe VMS per day were eligible. Most participants in SKYLIGHT 1 and 2, and all participants in DAYLIGHT, were considered 'HRT unsuitable'[1].

Participants were randomised in a 1:1:1 ratio to receive either fezolinetant 45mg, fezolinetant 30mg, or placebo once daily (SKYLIGHT 1 and 2), or in a 1:1 ratio to receive either fezolinetant 45mg or placebo once daily (DAYLIGHT). The fezolinetant 30mg dosage regimen is not licensed and is not discussed further here. SKYLIGHT 1 and 2 had four co-primary, patient-reported endpoints: the mean change from baseline in the daily frequency and severity of moderate to severe VMS at week 4 and at week 12. The primary (and key secondary) endpoints in DAYLIGHT were mean change from baseline in daily frequency (and severity) of moderate to severe VMS at week 24.

In SKYLIGHT 1 and 2, fezolinetant significantly reduced the daily frequency of VMS compared with placebo at week 12 (SKYLIGHT 1: least squares (LS) mean difference; -2.6; 95%

[1] Defined as: HRT-contraindicated: undiagnosed vaginal bleeding, history of breast cancer or oestrogen dependent tumours, arterial thromboembolic disease, hypersensitivity to oestrogen and progesterone therapy, porphyria; HRT-caution: history of diabetes mellitus, hyperlipidemia, smoking (current), migraine, obesity, systemic lupus erythematosus, epilepsy, family history of breast cancer in a first-degree relative or mutation of breast cancer gene; HRT-stoppers: discontinued HRT due to lack of efficacy, HRT-related side effects, advised by healthcare provider to stop due to length of time on HRT, or due to participant's age ≥ 60 years; HRT-averse: made an informed choice to not take HRT after a consultation about the benefit risks.

confidence interval [CI] -3.4 to -1.7; p < 0.001; SKYLIGHT 2: LS mean difference -2.5; 95% CI -3.6 to -1.5, p < 0.001). In both trials, fezolinetant also significantly reduced the daily severity of VMS compared with placebo at week 12 (SKYLIGHT 1: LS mean difference -0.2; 95% CI -0.4 to -0.1, p = 0.007; SKYLIGHT 2: LS mean difference -0.3; 95% CI -0.5 to -0.1, p < 0.001). The week 4 co-primary endpoints were also met. In DAYLIGHT, fezolinetant significantly reduced the daily frequency (LS mean difference -1.9; 95% CI -2.6 to -1.2; p < 0.001) and daily severity (LS mean difference -0.4; 95% CI -0.6 to -0.2, p < 0.001) of VMS compared with placebo at week 24. The reductions in daily VMS frequency that were observed in the pivotal trials (reductions of 2 or more daily VMS events relative to placebo) were considered to be clinically meaningful by the Committee for Medicinal Products for Human Use.

With regards to quality of life measures, in the SKYLIGHT 1 and 2 trials, the difference relative to placebo in PROMIS SD SF 8b scores (a measure of sleep disturbance) was statistically significant at week 12 in SKYLIGHT 2 only. Participants in the fezolinetant arms had statistically significant improvements in menopause-specific quality of life (MENQOL) scores relative to participants in the placebo arms across both trials at week 12. In DAYLIGHT, the differences relative to placebo in PROMIS SD SF 8b scores and MENQOL scores were statistically significant at week 24.

The generalisability of the trial outcomes to the population likely to receive fezolinetant in clinical practice is unclear. Only individuals with a high baseline VMS frequency were included and individuals experiencing perimenopause were excluded. Individuals undergoing oncologic treatment for breast cancer or other oestrogen-dependent malignancies were excluded. The SmPC states that fezolinetant is not recommended for use in this population as the safety and efficacy are unknown. Further, individuals with previous breast cancer or other oestrogen-dependent malignancies and no longer on any oncologic treatment were also excluded. The SmPC states that a decision to treat these individuals with fezolinetant should be based on a benefit-risk consideration for the individual.

The Review Group also consider that there is a high risk of bias in the primary outcomes across all trials due to the extent and handling of missing data.

No direct comparative evidence was available to inform the comparison with HRT in the HRT-suitable subpopulation and the comparison with non-hormonal treatments (defined by the Applicant as SSRIs) in the HRT-unsuitable subpopulation. Therefore, the Applicant conducted network meta-analyses (NMAs) to obtain comparative effectiveness estimates, in these subpopulations, for the reduction of moderate to severe VMS frequency. VMS severity, an important patient-relevant outcome was not included in the NMAs. No other menopausal symptoms or long-term consequences of menopause were considered in the NMAs as fezolinetant is only licensed for the treatment of moderate to severe VMS.

The inclusion criteria for the NMA to inform the relative efficacy of fezolinetant and HRT (henceforth referred to as the HRT-NMA), were overly restrictive. HRT was classed according to presentations: oral oestrogen alone, transdermal oestrogen alone and oral combined HRT. Although a number of randomised controlled trials (RCTs) of transdermal combined HRT were identified these were not included in the HRT-NMA as the specific products were not reimbursed in Ireland. The Applicant's rationale for classifying HRT by whether it is oestrogen alone or combined is unclear. This approach results in unnecessary separate connections in the network leading to less robust estimates of relative efficacy.

The HRT-NMA included SKYLIGHT 1 and 2, and seven RCTs of HRT. In terms of the outcome, change from baseline in daily frequency of moderate to severe VMS at week 12, the results from the HRT-NMA suggest that fezolinetant is associated with a non-significant reduction in VMS frequency versus oral combined HRT. However, fezolinetant was associated with a non-significant increase in VMS frequency versus both oral oestrogen alone and transdermal oestrogen alone. The difference in results between oral combined HRT and oral oestrogen alone HRT lack face validity as inclusion of progestogen is not expected to impact efficacy. Furthermore, all results had large credible intervals, reflecting considerable uncertainty. As such, no firm conclusions can be made on the relative efficacy of fezolinetant versus HRT in reducing VMS frequency or severity. We further note that HRT, unlike fezolinetant, also treats many other symptoms of menopause besides VMS.

Five RCTs were included in the NMA used to inform a comparison between fezolinetant and SSRIs in the HRT-unsuitable subpopulation (henceforth referred to as the SSRI-NMA). The included RCTs were: SKYLIGHT 1 and 2 (HRT-unsuitable participants), DAYLIGHT and two

RCTs evaluating the efficacy of paroxetine for the treatment of VMS (N30-003 and N30-004). The results from this NMA suggest that fezolinetant is more effective than paroxetine in terms of the outcome change from baseline in daily frequency of moderate to severe VMS at week 12 (mean difference -1.04; 95% Credible Interval -1.86 to -0.23). Heterogeneity across the RCTs used to inform the SSRI-NMA may bias the results. Clinical opinion suggests the efficacy of paroxetine for the treatment of VMS is representative of the efficacy of the SSRI treatment class in general. Apart from this comparison with paroxetine, no evidence was presented on the comparative evidence of fezolinetant versus other non-hormonal treatments in treating moderate to severe VMS.

2. Safety of fezolinetant

SKYLIGHT 4 was a randomised, 52-week double-blind trial comparing the safety of fezolinetant to placebo in women who were postmenopausal and considered unsuitable for HRT. Incidences of adverse events were generally similar across treatment arms. The following adverse drug reactions were reported: diarrhoea (4% in the fezolinetant arm versus 3% in the placebo arm), insomnia (4% versus 2%) and abdominal pain (2% versus 1%). No significant adverse effects on endometrial and bone safety were identified with the use of fezolinetant during the regulatory assessment. Monitoring of liver function is recommended during treatment in patients with known or suspected hepatic disorder. Fezolinetant is not recommended for use in patients undergoing oncologic treatment for breast cancer or other oestrogen-dependent malignancies as the safety in this population is unknown.

3. Cost effectiveness of **fezolinetant**

The Applicant considered two subpopulations (i) HRT-suitable (comparison with HRT) and (ii) HRT-unsuitable (comparison with no active treatment and SSRI). The HRT-suitable subpopulation was informed by the pooled SKYLIGHT 1 and 2 trials. The HRT-unsuitable subpopulation was informed by the DAYLIGHT trial. As noted in section 1, the clinical trial populations are not fully representative of patients who may receive fezolinetant in clinical practice.

Non-hormonal treatments (e.g. SSRIs, SNRIs, gabapentin or oxybutynin) are used in clinical

practice to treat VMS in individuals who have contraindications to HRT. However, the Applicant has only presented a comparison for one of these treatment classes (SSRI).

Methods

The Applicant submitted a Markov state transition cost-effectiveness model (CEM) comprising six health states. Four health states were defined based on average daily moderate to severe VMS frequency (0 ≤ VMS Frequency < 2, 2 ≤ VMS Frequency < 7, 7 ≤ VMS Frequency < 9, and VMS Frequency ≥ 9). The remaining two health states captured natural VMS cessation and death. Individuals in the VMS frequency health states could be "on-treatment" or "off-treatment" and they could also transition to the VMS cessation and death health states. The Review Group had concerns with the model structure including the arbitrary definition of VMS frequency health states and omission of VMS severity, which is an important patient-relevant outcome. Treatment arms were modelled independently so the impact of changing the relative treatment effect could not be explored. There are also other symptoms of menopause (other than VMS) and long-term consequences of menopause that are not captured by the CEM.

A four-week cycle length was used and a half-cycle correction was applied. The Applicant used a ten-year time horizon. In each cycle, individuals accrued quality adjusted life years (QALYs) and incurred costs specific to the treatment arm and health state occupied.

The treatment effects captured by the CEM were the change from baseline in daily frequency of moderate to severe VMS. This was implemented through transition probability matrices. Data from the pivotal trials were used to estimate on-treatment transition probabilities in the fezolinetant arm. In the HRT-suitable subpopulation, the results from the HRT-NMA were used to estimate on-treatment transition probabilities for the various HRT presentations. In the HRT-unsuitable subpopulation, data from the placebo arm of the DAYLIGHT trial and the pooled SKYLIGHT 1 and 2 trials (HRT-unsuitable participants) were used to estimate the on-treatment transition probabilities in the no active treatment arm. The SSRI-NMA results were used to estimate on-treatment transition probabilities in the SSRI arm. A structured expert elicitation exercise was conducted to elicit the transition probabilities for a 'natural history cohort'. This cohort was used to inform off-treatment transition probabilities across all arms. However, this natural history cohort was not aligned

with the model population (which had much higher baseline VMS frequencies). Transitions to the VMS cessation health state were based on the literature. Mortality rates across all treatment arms were based on the general female population in Ireland. Treatment-independent health related quality of life values (utilities), collected in the pivotal RCTs, were applied to the health states in the CEM. Health-related quality of life improved with decreasing VMS frequency. The benefits of HRT in addressing other menopause-related symptoms were not accounted for in the CEM.

In addition to the significant limitations described previously, the Review Group are also concerned that no meaningful conclusions can be made from the results of the HRT-NMA, on the relative efficacy of fezolinetant versus HRT in terms of treating moderate to severe VMS. The additional benefits of HRT in terms of treating other menopausal symptoms (sleeping difficulties, mood changes, sexual function, urogenital symptoms, arthralgia, fatigue, headache, cognitive effects) are also not accounted for. The Review Group were unable to address these limitations. However, to address several assumptions informing treatment effectiveness in the CEM, that the Review Group considered inappropriate, an NCPE exploratory base case was conducted. The Review Group made a number of changes to the Applicant base case. These included:

- Increasing the model time horizon to lifetime
- Health-related quality of life values from the pivotal RCTs informed by EQ-5D data collected directly in the pivotal trials rather than a disease specific measure.
- Maintaining relative treatment effect observed in DAYLIGHT by basing all transitions in the no active treatment arm on the DAYLIGHT placebo arm rather than the natural history cohort
- Aligning the approach used to extrapolate transition probabilities across the fezolinetant, HRT and SSRI treatment arms.

Results

Deterministic incremental cost-effectiveness ratios (ICERs) generated under the Applicant and NCPE exploratory base case assumptions are shown in Table 1 and Table 2, respectively. In light of the aforementioned limitations with the CEM and, in the case of the HRT comparison, failure to account for the additional health benefits of HRT, the results of the

Applicant and NCPE exploratory base cases should be interpreted with caution.

In light of the small QALY gain for fezolinetant seen in the HRT comparison, the Review Group consider that, in an alternative CEM (in which the other benefits of HRT are also considered), then the incremental QALY gain would favour HRT. Given that fezolinetant is more costly than HRT, it is therefore expected that fezolinetant would be dominated by HRT in an alternative CEM (in which the benefits of HRT were also considered).

Table 1: Applicant base case incremental cost-effectiveness results

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
HRT-suitable subpopulation (note benefits of HRT in treating menopausal symptoms other than VMS have not been accounted for in the CEM)					
Weighted HRT[a]	1,875	7.03	-	-	-
Fezolinetant	3,415	7.07	1,541	0.04	38,429[b]
HRT-unsuitable subpopulation (comparison with no active treatment)					
No active treatment	1,640	7.07	-	-	-
Fezolinetant	3,424	7.14	1,784	0.07	26,816[c]
HRT-unsuitable subpopulation (comparison with SSRI)					
SSRI	1,861	7.08	-	-	-
Fezolinetant	3,424	7.14	1,563	0.06	27,832[d]

QALY: Quality adjusted life year; ICER: incremental cost effectiveness ratio; SSRI: selective serotonin reuptake inhibitor; HRT: hormone replacement therapy

[a] Weighted ICER based on market share assumptions. ICER vs Oral oestrogen alone products €36,135/QALY (10% market share); ICER vs transdermal oestrogen alone products €39,996/QALY (83% market share); ICER vs oral combined HRT product €27,906/QALY (7% market share)

[b] Corresponding probabilistic ICER using 300 iterations: €33,755/QALY

[c] Corresponding probabilistic ICER using 300 iterations: €26,449/QALY

[d] Corresponding probabilistic ICER using 300 iterations: €27,989/QALY

Note: Figures in the table are rounded, and so calculations may not be directly replicable. Costs and QALYs are discounted at an annual rate of 4%

Table 2: NCPE exploratory base case incremental cost-effectiveness results

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
HRT-suitable subpopulation (note benefits of HRT in treating menopausal symptoms other than VMS have not been accounted for in the CEM)					
Weighted HRT[a]	2,329	13.61	-	-	-
Fezolinetant	3,926	13.64	1,598	0.02	69,264[b]
HRT-unsuitable subpopulation (comparison with no active treatment)					
No active treatment	2,163	14.18	-	-	-
Fezolinetant	4,102	14.21	1,939	0.03	60,420[c]
HRT-unsuitable subpopulation (comparison with SSRI)					
SSRI	2,410	14.17	-	-	-
Fezolinetant	4,005	14.23	1,595	0.06	25,624

QALY: Quality adjusted life year; ICER: incremental cost effectiveness ratio; SSRI: selective serotonin reuptake inhibitor; HRT: hormone replacement therapy

[a] Weighted ICER based on market share assumptions. ICER vs HRT mono oral €62,392/QALY (10% market share); ICER vs HRT mono TDS €73,014/QALY (83% market share); ICER vs HRT combi oral €47,473/QALY (7% market share)
[b] Corresponding probabilistic ICER using 300 iterations: €64,747/QALY
[c] Corresponding probabilistic ICER using 300 iterations: €53,305/QALY
[d] Corresponding probabilistic ICER using 300 iterations: €20,360/QALY
Note: Figures in the table are rounded, and so calculations may not be directly replicable. Costs and QALYs are discounted at an annual rate of 4%

A Price-ICER analysis was conducted to estimate the reductions in the price to wholesaler of fezolinetant, which would be required for fezolinetant to meet the €45,000/QALY and €20,000/QALY thresholds. Results are presented in Table 3.

Table 3: Results of Price-ICER analysis[a]

	HRT-suitable[b] (vs HRT)	HRT-unsuitable (vs no active treatment)	HRT-unsuitable (vs SSRI)
ICER	**% reduction[c] in fezolinetant PtW**		
€45,000/QALY	41	38	N/A
€20,000/QALY	74	84	29

PtW: price to wholesaler; QALY: quality adjusted life year; ICER: incremental cost effectiveness ratio; SSRI: selective serotonin reuptake inhibitor; HRT: hormone replacement therapy
[a] Analyses were conducted using the NCPE exploratory base case assumptions
[b] The benefits of HRT in treating menopausal symptoms other than VMS have not been accounted for in the CEM
[c] Expressed as a total rebate (inclusive of the Framework Agreement Rebate)

Sensitivity analysis

The probability of cost-effectiveness for fezolinetant versus its comparators are presented in Table 4. Due to the previously discussed limitations, these probabilities do not reflect the full uncertainty associated with the results of the cost-effectiveness analysis. Results should be interpreted with caution.

Table 4: Probability of cost effectiveness for fezolinetant vs comparators (NCPE exploratory base case)

	HRT-suitable (vs HRT)[b,c]		HRT-unsuitable (vs no active treatment)		HRT-unsuitable (vs SSRI)	
Threshold (€/QALY)	Applicant base case	NCPE exploratory base case	Applicant base case	NCPE exploratory base case	Applicant base case	NCPE exploratory base case
20,000	1%	0%	12%	41%	3%	36%
45,000	90%	16%	97%	48%	99%	90%

[a] Results based on probabilistic analysis using 300 iterations
[b] Probability of the cost-effectiveness of fezolinetant versus weighted HRT comparator
[c] The benefits of HRT in treating menopausal symptoms other than VMS have not been accounted for in the CEM

4. Budget impact of fezolinetant

The price to wholesaler of one pack of fezolinetant 45mg tablets (pack size: 30) is €55. The total cost per patient per year is €722. This cost is higher than the annual cost of HRT

(ranging from €80 to €280) or the annual cost of paroxetine (€163).

The Applicant assumes that fezolinetant will only be prescribed to individuals who are HRT-unsuitable. The proportion of individuals who are HRT unsuitable is based on clinical opinion. Fezolinetant is assumed to have a 6% market share in Year 1, increasing to 22% in Year 5. Consequently 1,587 individuals are assumed to be treated with fezolinetant in Year 1 increasing to 6,210 in Year 5. Based on this the Applicant estimates the five-year cumulative gross budget impact in the HRT-unsuitable subpopulation to be €14 million.

Market share predictions in the HRT-unsuitable population appear very low. Furthermore, the definition of HRT unsuitability is likely to vary considerably across clinical practice.

5. Patient Organisation Submission

A patient-group submission was received during the course of this assessment. This submission will form part of the information that the HSE considers when making their drug-funding decision.

6. Conclusion

The NCPE recommends that fezolinetant be considered for reimbursement if cost-effectiveness can be improved relative to existing treatments.

The Applicant's cost-effectiveness evaluation considers the relative efficacy of fezolinetant in treating moderate to severe VMS. In the comparison versus HRT, the additional benefits of HRT, in terms of treating other menopausal symptoms (sleeping difficulties, mood changes, sexual function, urogenital symptoms, arthralgia, fatigue, headache, cognitive effects), are not considered. As such, HRT is expected to provide more benefits, than fezolinetant, in those who can take HRT. Therefore, the HSE may wish to implement prescribing guidelines should a decision be made to reimburse fezolinetant.

Next steps

The NCPE Assessment Report, recommendation and Patient Organisation Submission, will be

considered by the HSE when making their decision on reimbursement, while also having regard to the criteria specified in the Health (Pricing and Supply of Medical Goods) Act 2013.

Further information on this process may be found **here.**