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CADTH

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CADTH Reimbursement Recommendation

Estradiol (Imvexxy)

Indication: For the treatment of postmenopausal moderate-to-severe dyspareunia, a symptom of vulvar and vaginal atrophy

Sponsor: Knight Therapeutics Inc.

Final recommendation: Reimburse with conditions

CADTH

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Summary

CADTH

What Is the CADTH Reimbursement Recommendation for Imvexxy?

CADTH recommends that Imvexxy be reimbursed by public drug plans for the treatment of moderate-to-severe dyspareunia (painful sex) in women who are postmenopausal if certain conditions are met.

Which Patients Are Eligible for Coverage?

Imvexxy should only be covered in a similar manner as other vaginal estrogen products that include treatment of women who are postmenopausal and have moderate-to-severe painful sex.

What Are the Conditions for Reimbursement?

Imvexxy should only be reimbursed if it is cost saving for drug programs compared to the least costly local hormone therapy reimbursed for the treatment of moderate-to-severe painful sex, a symptom of vulvar and vaginal atrophy (VVA) in women who are postmenopausal.

Why Did CADTH Make This Recommendation?

Evidence from a clinical trial demonstrated that Imvexxy restores vaginal tissues, improves vaginal pH levels, and offers relief from moderate-to-severe painful sex better than placebo.

Based on public list prices, Imvexxy costs less than a tablet estradiol vaginal insert and costs more than the least costly treatment for moderate-to-severe painful sex in women who are postmenopausal, and there was no evidence to suggest it fulfills an unmet need in comparison with other available treatment options.

Based on public list prices, Imvexxy is expected to decrease costs to the public drug plans by $649,340 over 3 years.

Additional Information

What is Dyspareunia?

Dyspareunia is painful sex, a commonly reported symptom of VVA, which is common in women who are postmenopausal. The prevalence of VVA symptoms varies from 4% in early postmenopausal years to more than 80% in later years.

Unmet Needs in Dyspareunia

Patients may not respond to the currently available treatments for painful sex. Some patients find the application of other vaginal estrogen therapies difficult, uncomfortable, or messy.

How Much Does Imvexxy Cost?

Treatment with Imvexxy is expected to cost $414 per patient in the first year of use and $377 in the subsequent years.

Recommendation

The CADTH Canadian Drug Expert Committee (CDEC) recommends that the softgel estradiol vaginal insert (Imvexxy) be reimbursed for the treatment of postmenopausal moderate-to-severe dyspareunia, only if the conditions listed in Table 1 are met.

Rationale for the Recommendation

One phase III, randomized, double-blind, placebo-controlled study (REJOICE) comparing the efficacy and safety of softgel estradiol vaginal inserts with placebo in women who are postmenopausal and have moderate-to-severe dyspareunia was reviewed by CDEC. The REJOICE study demonstrated that, compared to placebo, treatment with softgel estradiol vaginal inserts (both 4 mcg and 10 mcg doses) led to statistically significant improvement on each of the 4 co-primary end points: 1) increase in the percentage of vaginal superficial cells; 2) decrease in the percentage of vaginal parabasal cells; 3) decrease in the percentage of vaginal pH; and 4) decrease in severity of the most bothersome symptoms (MBS) of dyspareunia associated with VVA (as measured by the VVA Symptoms Self-Assessment Questionnaire).

The clinical expert identified an unmet need for patients who do not respond to available treatments for dyspareunia or who find application of treatment options difficult, uncomfortable, or messy. However, no evidence was included to demonstrate that the softgel estradiol vaginal insert would meet this need. Given that no direct or indirect clinically relevant comparative evidence between the softgel estradiol vaginal insert and other vaginal estrogen therapies for women who are postmenopausal and have moderate-to-severe dyspareunia was available for this review, the potential benefit of the softgel estradiol vaginal insert compared with other treatments currently reimbursed in Canada remains unknown.

At the sponsor-submitted price for the softgel estradiol vaginal insert and publicly listed prices for comparators, the softgel estradiol vaginal insert was less costly than a tablet estradiol vaginal insert. However, compared with estrone and conjugated estrogen creams, the softgel estradiol vaginal insert ranged from cost savings to increased costs depending on the dose of the cream-based comparator.

Table 1: Reimbursement Conditions and Reasons

Reimbursement condition	Reason
Initiation	
1. Reimburse in a similar manner to currently funded vaginal estrogen products.	No robust evidence was reviewed to support a clinical benefit for the softgel estradiol vaginal insert compared with other vaginal estrogen therapies.

Reimbursement condition	Reason
Pricing	
2. The cost of the softgel estradiol vaginal insert should be negotiated to provide cost savings for drug programs relative to the least costly local hormone therapy reimbursed for the treatment of individuals with postmenopausal moderate-to-severe dyspareunia, a symptom of vulvar and vaginal atrophy.	At its submitted price, the softgel estradiol vaginal insert was cost saving in comparison with a tablet estradiol vaginal insert and more expensive than the least costly local hormone therapy reimbursed for postmenopausal moderate-to-severe dyspareunia. There is insufficient evidence to suggest the softgel estradiol vaginal insert fulfills an unmet need in comparison with the least expensive local hormone therapy reimbursed for postmenopausal moderate-to-severe dyspareunia.

Discussion Points

- CDEC discussed that moderate-to-severe dyspareunia is a symptom of VVA and that other vaginal estrogen products are reimbursed by most public drug plans for broader symptoms of VVA. The clinical expert indicated that the softgel estradiol vaginal insert would likely be used beyond the Health Canada indication in this broader patient population (i.e., women who are postmenopausal and have other VVA-related symptoms such as vaginal dryness) in clinical practice.
- CDEC noted that according to the clinical expert, not all patients respond to currently available treatments for dyspareunia, and that some treatment options are difficult, uncomfortable, or messy to administer. CDEC also discussed the pragmatic advantages of a softgel preparation compared to other formulations of vaginal estrogen therapies (e.g., tablet, ring, cream). However, no evidence on ease and acceptability of use was included to demonstrate that the softgel estradiol vaginal insert would meet this need. There was no input provided by clinician or patient groups.
- CDEC discussed the pricing of the softgel estradiol vaginal insert given the lack of clinically relevant direct and indirect comparative evidence between the estradiol vaginal insert and other vaginal estrogen therapies in women who are postmenopausal and have moderate-to-severe dyspareunia, as well the lack of long-term efficacy and safety data beyond 12 weeks. Given these gaps in evidence, CDEC was not able to conclude whether the softgel estradiol vaginal insert offered clinical benefit over currently available treatments.
- CDEC also discussed other doses of the softgel estradiol vaginal insert (8 mcg [2 × 4 mcg] and 14 mcg [4 mcg + 10 mcg]) based on input from drug plans, and noted that dose escalation from 4 mcg to 8 mcg or 14 mcg may occur in a small portion of patients, and acknowledged the uncertain benefit of dose escalation from 4 mcg to 8 mcg or 14 mcg and the potential impact on cost savings depending on the comparator of interest.
- CDEC noted that, according to the clinical expert, treatment response would be assessed at 3 to 6 months following initiation and again at 6 to 12 months, then yearly thereafter. CDEC discussed whether the softgel estradiol vaginal insert should be continued as long as needed for symptom management as symptoms may recur upon discontinuation and noted that currently available products in Canada of the same indication do not have limitations on treatment length.

- CDEC noted that the softgel estradiol vaginal insert should not be used in combination with other vaginal estrogen products.

Background

The estradiol vaginal insert has a Health Canada indication for the treatment of postmenopausal moderate-to-severe dyspareunia, 1 of the key symptoms of VVA. It is available as 4 mcg and 10 mcg 17beta-estradiol and is used intravaginally. According to the product monograph, treatment with an estradiol vaginal insert should start at the 4 mcg dosage strength, with dosage adjustment guided by the clinical response. The initial dose is 1 vaginal insert daily at approximately the same time for 2 weeks. The maintenance dose is 1 vaginal insert twice weekly, every 3 to 4 days.

The sponsor's reimbursement request was the same as the Health Canada–approved indication.

Sources of Information Used by the Committee

To make its recommendation, the Committee considered the following information:

- a review of 1 randomized controlled trial in women who are postmenopausal and have moderate-to-severe dyspareunia
- input from public drug plans that participate in the CADTH review process
- 1 clinical specialist with expertise diagnosing and treating patients with vaginal pain symptoms
- a review of the pharmacoeconomic model and report submitted by the sponsor.

Stakeholder Perspectives

The clinical expert indicated that not all patients respond to the available treatments for dyspareunia. Some treatment options are difficult, uncomfortable, or messy to administer. Some women are reluctant to initiate hormonal treatment due to the safety concerns regarding exogenous hormone therapy.

Most women who are menopausal and have VVA-related symptoms are likely to benefit from vaginal estrogen therapy. In the clinical expert's opinion, the estradiol vaginal insert is another form of existing medication for treatment of VVA, including dyspareunia. It would be used as a first-line treatment or after failure on other treatments for women who are suitable to receive estrogen replacement for VVA.

The clinical expert also indicated that in clinical practice, treatment response is assessed based on a patient's self report of improvement in symptoms. This is a clinically meaningful outcome measure. The expert suggested treatment response be assessed at 3 to 6 months

following initiation of treatment, and again at 6 to 12 months, then yearly thereafter if continued treatment is required.

Estradiol vaginal inserts are likely prescribed in an outpatient ambulatory clinic setting by a family physician or gynecologist. The drug can be self-administered by the patient in their own home.

Drug Program Input

Input was obtained from the drug programs that participate in the CADTH reimbursement review process. The following were identified as key factors that could potentially impact the implementation of a CADTH recommendation for the softgel estradiol vaginal insert:

- considerations for initiation of therapy
- considerations for prescribing of therapy
- generalizability of trial populations to the broader populations in the jurisdictions
- system and economic issues.

The clinical experts consulted by CADTH provided advice on the potential implementation issues raised by the drug programs.

Table 2: Responses to Questions From the Drug Programs

Implementation issues	Response
Relevant comparators	
No evidence comparing efficacy and safety versus currently funded vaginal estrogen products. Comparisons to placebo (phase III, REJOICE) and tablet estradiol vaginal insert 10 mcg (in a pharmacokinetic study) only.	CDEC noted that there is only one trial (REJOICE) that compared the softgel estradiol vaginal insert to placebo demonstrating superiority in reducing severity of dyspareunia and one pharmacokinetic study comparing to tablet estradiol vaginal insert 10 mcg demonstrating lower systemic exposure for the softgel estradiol vaginal insert. CDEC acknowledged that therapy selection may be based on application acceptability and patient preference; however, CDEC felt that overall there is inadequate information to guide the selection of the softgel estradiol vaginal insert over a tablet estradiol vaginal insert or the other vaginal estrogen product given the lack of comparative evidence.
Other vaginal estrogen products (e.g., tablet estradiol vaginal insert 10 mcg, conjugated estrogens vaginal creams) are listed as an open benefit under most public plans, except in British Columbia where tablet estradiol vaginal insert is not reimbursed.	CDEC acknowledged open benefit listings for other vaginal estrogen products under most public plans (except in British Columbia where tablet estradiol vaginal insert is not reimbursed).
Considerations for initiation of therapy	
Other vaginal estrogen products (e.g., tablet estradiol vaginal insert 10 mcg, conjugated estrogens vaginal creams) were not reviewed by CADTH but are listed as an open benefit under most public plans; therefore, consider criteria that indicates to "reimburse in a similar manner to currently funded vaginal estrogen products."	CDEC acknowledged and agreed to recommend the reimbursement of the softgel estradiol vaginal insert in a similar manner to currently funded vaginal estrogen products.

Implementation issues	Response
Considerations for prescribing of therapy	
In the product monograph of the softgel estradiol vaginal insert, it indicates that "generally, women should be started at the 4 mcg dosage strength. Dosage adjustment should be guided by clinical response." 1. What proportion of patients may not respond to the 4 mcg dose and need to escalate to the 10 mcg dose? 2. How long would the 4 mcg dose be tried before escalating the dose? While the 4 mcg and 10 mcg estradiol inserts are priced the same, the total drug cost of the softgel estradiol vaginal insert versus a tablet estradiol vaginal insert could be higher when accounting for patients who were unresponsive to the 4 mcg dose and needed to titrate up to 10 mcg. Would dose escalation to 8 mcg (i.e., 2 × 4 mcg inserts) or 14 mcg (i.e., 4 mcg + 10 mcg) occur in practice? If so, what portion of patients would need these doses? The total drug cost would be double at these doses.	CDEC noted that the clinical expert estimated that half of the patients need to escalate to the 10 mcg dose. According to the clinical expert, the 4 mcg dose would be used for 3 to 4 months before escalating to the 10 mcg dose if symptoms have not improved at that time. CDEC discussed that dosing of 2 vaginal inserts at a time (8 mcg or 14 mcg) is outside what is recommended in the product monograph. According to the clinical expert, dose escalation (from 4 mcg to 8 mcg or 14 mcg) would only be used in women unresponsive to the usual dosage, and following a discussion of risks and benefits. The expert estimated that only a small proportion of these patients would use a higher dose (8 mcg or 14 mcg), as this is not the standard treatment regimen with uncertain benefit.
Generalizability	
Is there any reason to believe that the softgel estradiol vaginal insert could not be used more broadly, for example, in patients with other causes of estrogen deficiency and/or for symptoms of vaginal atrophy, other than dyspareunia? • The softgel estradiol vaginal insert is indicated for the treatment of postmenopausal moderate-to-severe dyspareunia, a symptom of vulvar and vaginal atrophy. Tablet estradiol vaginal insert is indicated for the treatment of the symptoms of vaginal atrophy due to estrogen deficiency. Given the differences in the Health Canada–approved indications of the softgel estradiol vaginal insert and the tablet estradiol vaginal insert, and other vaginal estrogen products listed as an open benefit under most public plans, consider criteria that indicates to "reimburse in a similar manner to currently funded vaginal estrogen products."	CDEC noted that dyspareunia is one of the VVA-related symptoms in women who are postmenopausal. CDEC discussed that although the Health Canada–approved indication for the softgel estradiol vaginal insert is "for the treatment of postmenopausal moderate-to-severe dyspareunia is one of the VVA-related symptoms in postmenopausal women," the clinical expert indicated that the softgel estradiol vaginal insert would be considered for use in a broader population — women who are postmenopausal and have other VVA-related symptoms, such as vaginal dryness, are likely to benefit from vaginal estrogen therapy (e.g., estradiol insert) in clinical practice. As a result, CDEC agreed to reimburse the softgel estradiol vaginal insert in a similar manner to currently funded vaginal estrogen products.
System and economic issues	
The sponsor expects that the softgel estradiol vaginal insert will displace market share primarily from the tablet estradiol vaginal insert, as it's the most similar comparator used to treat dyspareunia in terms of formulation and administration. Compared to available treatments, the cumulative 3-year budget impact was a savings of $649,340. Tablet estradiol vaginal insert is not funded in British Columbia.	The clinical expert indicated that it is reasonable to assume that of the market the softgel estradiol vaginal insert captures, 99% is from the tablet estradiol vaginal insert, given the similarity in formulation and administration.

Implementation issues	Response
Confidential negotiated prices may exist for the tablet estradiol vaginal insert, conjugated estrogens vaginal creams, and the estradiol vaginal ring. If there is a lack of evidence to demonstrate superiority of the softgel estradiol vaginal insert versus comparators, consider a pricing condition in which the drug plan cost for the softgel estradiol vaginal insert does not exceed the drug plan cost of the least costly vaginal estrogen product.	CDEC highlighted that there is a lack of evidence against comparators and uncertainty with respect to the confidential negotiated prices of the comparator products. As a result, CDEC has recommended the price of the softgel estradiol vaginal insert be negotiated to provide cost savings in comparison with the least costly vaginal estrogen product.

CDEC = Canadian Drug Expert Committee.

Clinical Evidence

Pivotal Studies

Description of Studies

One phase III study (REJOICE, N = 574) was submitted to support the clinical benefit of estradiol vaginal inserts. The trial enrolled women who were postmenopausal and have moderate-to-severe symptoms of vaginal pain associated with sexual activity.

The REJOICE study was a double-blind, placebo-controlled randomized controlled trial that assessed the efficacy and safety of the estradiol vaginal insert for the treatment of postmenopausal moderate-to-severe dyspareunia. Eligible patients were randomized to receive estradiol vaginal insert 4 mcg, 10 mcg, or 25 mcg, or placebo for 12 weeks. The results for the estradiol vaginal insert 25 mcg group are not reported in this report because this dose is not approved for use. The co-primary efficacy end points were 1) change from baseline to week 12 in percent change in superficial cells compared to placebo; 2) change from baseline to week 12 in percent change in parabasal cells compared to placebo; 3) change from baseline to week 12 in percent change in pH compared to placebo; and 4) change from baseline to week 12 on the severity of the MBS of dyspareunia (vaginal pain associated with sexual activity) associated with VVA (using the VVA Symptoms Self-Assessment Questionnaire) compared to placebo. The average age of the women participating in the REJOICE study was 59 to 60 years old. The majority of the women were White (86% to 88%). Gynecological history was similar across treatment groups, except that more patients in the estradiol 4 mcg or 10 mcg groups had prior hysterectomy (46% to 47% with estradiol versus 39% with placebo), bilateral oophorectomy (26% to 27% versus 21%) and surgical menopause (39% to 40% versus 34%). The mean time since menopause was 13.9 to 14.2 years and prior hormone replacement therapy was used in 17.6% to 19.3% of women. Baseline assessments of parabasal cells, superficial cells, vaginal pH, and severity of MBS of dyspareunia were similar across treatment groups. For study participation, patients needed to identify that their MBS was moderate-to-severe dyspareunia. The mean baseline severity score for dyspareunia across treatment groups was 2.6 to 2.7.

Efficacy Results

After 3 months of treatment, the REJOICE study met its objective by demonstrating improvement in favour of both doses of the estradiol vaginal insert versus placebo on the

4 co-primary end points: change from baseline to week 12 in the percentage of parabasal cells, superficial cells, vaginal pH, and severity of dyspareunia. One of the outcomes was the change from baseline in patient-reported severity of dyspareunia, which was consistent with clinical practice, according to the clinical expert.

At week 12, vaginal dryness was improved with both doses of the estradiol vaginal insert compared with placebo, while only the estradiol 10 mcg group had improved vulvar and/or vaginal itching or irritation versus placebo. The expert indicated that the results of these secondary efficacy outcomes were consistent with the primary outcomes, which favoured estradiol over placebo; however, the differences between estradiol and placebo may not be considered clinically important.

According to the clinical expert, patient-reported symptom relief is a clinically relevant outcome in the study population. In the REJOICE trial, a VVA Symptoms Self-Assessment Questionnaire was used to self-assess patient's symptoms of VVA, including vaginal pain associated with sexual activity, vaginal dryness, and vulvar and/or vaginal itching or irritation. However, no information was provided in the submission describing the validity and reliability of this questionnaire, nor was a minimal clinically important difference reported in the indicated population. Although estradiol vaginal inserts appeared to be efficacious versus placebo, it is difficult to determine whether the magnitude of benefit observed is clinically significant.

Severity of VVA (no atrophy, mild, moderate, and severe atrophy) was evaluated using a vaginal mucosa assessment scale, which examines vaginal secretions, epithelial integrity, epithelial surface thickness, and colour during pelvic examination. Normal vaginal secretions, epithelial integrity, epithelial surface thickness, and colour at week 12 were more likely to be observed in patients treated with estradiol (4 mcg and 10 mcg) compared to placebo.

Treatment with an estradiol vaginal insert was associated with improved sexual function in women who were postmenopausal, measured by the Female Sexual Function Index. The 10 mcg dose of estradiol showed statistically significant improvements in Total Score, Lubrication and Pain. There were no statistically significant differences between estradiol 4 mcg and placebo.

Harms Results

During the 3-month study period, the frequency of treatment-emergent adverse events was similar between the 2 doses of estradiol vaginal insert and placebo: estradiol 4 mcg = 50.8%, estradiol 10 mcg = 49.2%, and placebo = 57.8%. Commonly reported adverse events were nasopharyngitis, upper respiratory tract infection, back pain, headache, vaginal discharge, and vulvovaginal pruritus. Patients in the placebo group were more likely to report vaginal discharge and vulvovaginal pruritus compared to those in the estradiol groups. Three patients in the estradiol 10 mcg group reported serious adverse events, while no serious adverse events were reported in the estradiol 4 mcg and placebo groups. The frequency of withdrawal due to adverse events was 1.0%, 1.6%, and 2.6% in the estradiol 4 mcg group, estradiol 10 mcg group, and placebo group, respectively. In terms of adverse events of particular interest for the review, the frequency of vaginal hemorrhage, cervical dysplasia, and breast mass was numerically higher in the placebo group compared with the estradiol groups.

Critical Appraisal

In the REJOICE study, differences were noted in the patients' baseline characteristics between the 4 mcg and 10 mcg estradiol insert groups and the placebo group. The data suggest that more patients in the estradiol inserts groups had a hysterectomy and bilateral oophorectomy; therefore, compared to those in the placebo group, a higher proportion of these patients were surgically menopausal. It is unknown whether patients with surgical menopause will respond differently to treatments than those with natural menopause, and whether these imbalances would affect interpretation of the results.

Both subjective (e.g., self-reported symptom relief or change in sexual function) and objective efficacy outcomes (e.g., change in percentage of superficial cells and vaginal pH) were evaluated in the REJOICE study. Although self-reported outcomes are considered clinically relevant in practice to measure treatment response, according to the clinical expert, there are no published minimal clinically important differences identified for such outcome measures in women who are postmenopausal. Therefore, it is unclear whether the scales used and the reported between-group differences are clinically meaningful.

Multiplicity was controlled for in the REJOICE study based on a closed fixed sequence serial testing procedure, with the 4 co-primary end points being included. Outcomes outside of the testing hierarchy, such as health-related quality of life (measured with the Female Sexual Function Index), should be viewed as supportive evidence for the overall effects of estradiol vaginal inserts and need to be interpreted with caution, due to the possible inflated type I error.

This was a 3-month study; therefore, long-term safety (on endometrium and breast, or in general) and efficacy data are unavailable for the 2 doses of the estradiol vaginal insert. There is a lack of direct or indirect evidence from the included evidence to demonstrate comparative efficacy and safety of the estradiol vaginal insert versus other local hormonal therapies in the study population.

Indirect Comparisons

No indirect treatment comparisons were identified for this review.

Other Relevant Evidence

No other relevant studies were identified for this review.

Other Considerations

A bioavailability study compared the 10 mcg dose of the softgel estradiol vaginal insert with another vaginal estrogen therapy (a 10 mcg dose of the tablet estradiol vaginal insert) in healthy women who were postmenopausal. The results suggested that the extent of systemic exposure of estradiol 10 mcg was statistically significantly lower than that of the 10 mcg tablet estradiol vaginal insert. The lack of comparative safety data between these makes it unknown at present whether there are differences in the safety profiles in the indicated population.

Economic Evidence

Cost and Cost-Effectiveness

At the submitted price of $3.63 per tablet insert, the softgel estradiol vaginal insert costs $414 per patient annually in the first year of use and $377 in subsequent years of use. CADTH conducted a reanalysis of the sponsor-submitted cost comparison, considering all relevant local hormone therapies; costs in the first and subsequent years of use; and the lowest available list price for conjugated estrogen creams and the estradiol ring. The annual cost or cost savings with the softgel estradiol vaginal insert depend on the choice of comparator. Compared with the existing tablet estradiol vaginal insert, annual cost savings with the softgel estradiol vaginal insert were $78 per person in the first year and $71 per person in subsequent years of use. Compared with cream-based comparators, annual per person incremental costs ranged from cost savings of $450 to increased costs of $338, depending on the dose of the cream-based comparator. The incremental cost compared with the estradiol ring was $115 in the first year and $79 in subsequent years of use. The incremental costs were calculated based on publicly available list prices of comparators and may not reflect actual prices paid by Canadian public drug plans. Additionally, the price of conjugated estrogens vaginal creams and the estradiol vaginal ring comparator varies across jurisdictions, and as such, incremental costs will vary across jurisdictions.

The cost comparison assumes clinical similarity between the softgel estradiol vaginal insert and the other local hormone therapies included in the analysis. Based on a sponsor-submitted bioequivalence study, the 10 mcg dose of the softgel estradiol vaginal insert is likely clinically similar to a tablet estradiol vaginal insert at the same dose in healthy women who are postmenopausal. The clinical review conducted by CADTH noted that there was a lack of direct or indirect clinical evidence comparing the softgel estradiol vaginal insert to local hormone therapies in the indicated population (women who are menopausal and have dyspareunia). As a result, the cost comparison with the tablet estradiol vaginal insert is likely appropriate, while the appropriateness of the cost comparison with the cream and ring-based local hormone therapies is associated with uncertainty.

Budget Impact

CADTH identified the following key limitations with the sponsor's analysis: uncertainty in the estimated market size of the target population and in the anticipated market uptake of the softgel estradiol vaginal insert, as well as a reliance on publicly available listed prices for included comparators. CADTH did not conduct base-case reanalyses, and instead accepted the sponsor's estimated budgetary savings of $649,340 over 3 years for the reimbursement of the softgel estradiol vaginal insert, including drug costs, markups, and dispensing fees. However, the presence of confidential prices paid by the jurisdictions is likely to reduce or eliminate these savings, depending on the discounts in place.

CADTH

Canadian Drug Expert Committee (CDEC) Information

Members of the Committee

Dr. James Silvius (Chair), Dr. Sally Bean, Mr. Dan Dunsky, Dr. Alun Edwards, Mr. Bob Gagne, Dr. Ran Goldman, Dr. Allan Grill, Dr. Christine Leong, Dr. Kerry Mansell, Dr. Alicia McCallum, Dr. Srinivas Murthy, Ms. Heather Neville, Dr. Danyaal Raza, Dr. Emily Reynen, and Dr. Peter Zed.

Meeting date: November 24, 2021.

Regrets: Three CDEC members did not attend.

Conflicts of interest: None.