

CADTH COMMON DRUG REVIEW

CADTH Canadian Drug Expert Committee Recommendation

(Final)

VORTIOXETINE (TRINTELLIX — Lundbeck Canada Inc.)

Indication: For the treatment of major depressive disorder in adults.

RECOMMENDATION

The CADTH Canadian Drug Expert Committee recommends that vortioxetine be reimbursed for the treatment of major depressive disorder in adults if the following conditions are met.

Conditions for Reimbursement

1. Reimburse in a similar manner to other antidepressants for the treatment of patients with major depressive disorder.
2. The drug plan cost of treatment with vortioxetine should not exceed the drug plan cost of the least costly antidepressant currently reimbursed.

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VORTIOXETINE (TRINTELLIX — LUNDBECK CANADA INC.)

Indication: For the treatment of major depressive disorder in adults.

Recommendation

The CADTH Canadian Drug Expert Committee (CDEC) recommends that vortioxetine be reimbursed for the treatment of major depressive disorder (MDD) in adults if the following conditions are met.

Conditions for Reimbursement

1. Reimburse in a similar manner to other antidepressants for the treatment of patients with MDD.
2. The drug plan cost of treatment with vortioxetine should not exceed the drug plan cost of the least costly antidepressant currently reimbursed.

Reasons for the Recommendation

1. Vortioxetine (5 mg, 10 mg, and 20 mg) demonstrated statistically significant improvements in depressive symptoms, measured using the Montgomery-Åsberg Depression Rating Scale (MADRS) or the Hamilton Depression Rating Scale (HAM-D24), when compared with placebo in several double-blind, randomized-controlled trials (RCTs).
2. There is limited comparative data between vortioxetine and other antidepressants available in Canada. In one published indirect comparison, vortioxetine was found to be more effective than placebo in decreasing the severity of depressive symptoms. Based on this indirect comparison and the other data that are available, CDEC concluded that vortioxetine has similar efficacy to other antidepressants reimbursed for MDD, and that there is insufficient evidence that vortioxetine is more effective than the least costly antidepressant reimbursed for MDD.
3. Limitations in the evidence preclude any conclusions to be made regarding the comparative effects of vortioxetine on outcomes such as health-related quality of life (HRQoL), disability, cognitive function, and adverse effects.
4. At a submitted cost of \$2.95 to \$3.20 per day (for an annual drug cost of \$1,077 to \$1,169), the cost of vortioxetine is higher than the cost of other antidepressants reimbursed for MDD.

Implementation Considerations

- CDEC concluded that the evidence for vortioxetine does not support greater efficacy or safety than less costly alternative treatments for MDD. Therefore, vortioxetine should be reimbursed only if the pricing condition is met.

Discussion Points

- CDEC noted that MDD is a prevalent illness and a leading cause of disability in Canada and worldwide. CDEC considered patient input provided to CADTH and heard input from clinician experts regarding an expectation that, for patients, new treatments for MDD will improve quality of life, increase ability to participate in daily activities, improve mood, improve comorbid conditions such as anxiety, and be well tolerated. Of these, CDEC concluded that the evidence for vortioxetine only sufficiently addressed improvement in mood, for which the magnitude of benefit versus placebo was moderate based on reported minimal clinically important differences (MCIDs) for the depression symptom scales used in the RCTs.
- CDEC noted that based on the STAR-D trial, approximately 30% of patients achieve remission of a major depressive episode with the first selected antidepressant medication. As a result, patients with MDD may need to try several antidepressants before achieving improved symptoms, quality of life, and functioning. CDEC heard clinician expert input that despite the availability of several antidepressants, there is a need for more treatment options with different mechanisms of action.
- CDEC discussed the potential place in therapy for vortioxetine. The cost-effectiveness of vortioxetine beyond first-line treatment of patients with MDD could not be determined based on the available studies. Patients with mild depression, treatment-resistant depression, comorbid psychiatric illnesses, substance abuse, or those at risk of suicide were excluded from the vortioxetine trials. Given the prevalence of comorbid conditions among those with MDD, the exclusion of these patients limits the

generalizability of the findings of the vortioxetine studies. Based on the available evidence, CDEC could not identify a subgroup of patients that would most likely benefit from treatment with vortioxetine over other available treatment options.

- Adverse events occurred more frequently with vortioxetine than with placebo, especially gastrointestinal upset predominated by nausea. CDEC heard clinician expert input that the effects are generally mild to moderate in severity and of short duration (typically subsiding after the first few weeks). CDEC also heard from clinician experts that such adverse effects could impact treatment adherence; however, other antidepressants also have adverse effects that may contribute to nonadherence.
- Sexual dysfunction was noted as an important adverse effect associated with several existing antidepressants. CDEC reviewed one RCT specifically addressing sexual dysfunction, which found statistically significant mean improvements with vortioxetine versus escitalopram for the change from baseline in the Changes in Sexual Functioning Questionnaire Short-Form (CSFQ-14). The clinical relevance of the differences was unclear because the MCID is unknown. As well, pooled analyses from Health Canada found that vortioxetine 10 mg and 20 mg had higher incidences of treatment-emergent sexual dysfunction compared with placebo and vortioxetine 5 mg. However, it is unclear if vortioxetine would have less sexual dysfunction than other available classes of antidepressants.
- CDEC noted that there was variance in the results of the indirect comparison of vortioxetine versus other antidepressants. The indirect evidence did not clearly demonstrate that vortioxetine offers superior efficacy or safety compared with other currently available antidepressants. Therefore, CDEC felt that there is insufficient evidence to justify a price premium over the least expensive antidepressant reimbursed for the treatment MDD.

Background

Vortioxetine has a Health Canada indication for the treatment of MDD in adults. Vortioxetine is an antidepressant that is thought to act through the modulation of serotonin neurotransmission in the central nervous system. It is available as 5 mg, 10 mg, 15 mg, and 20 mg tablets. The Health Canada–approved starting and recommended dosage is 10 mg vortioxetine once daily for adults younger than 65 years of age. Depending on individual patient response, the dosage may be increased to a maximum of 20 mg vortioxetine once daily, as tolerated. A dosage decrease to a minimum of 5 mg vortioxetine once daily may be considered for patients who do not tolerate higher doses. The recommended starting dosage for patients older than 65 years of age is 5 mg vortioxetine once daily.

Submission History

Vortioxetine was previously reviewed in 2015 for the treatment of MDD in adults but was voluntarily withdrawn by the manufacturer before a final CDEC recommendation was developed.

Summary of Evidence Considered by CDEC

The committee considered the following information prepared by the CADTH Common Drug Review: a systematic review of RCTs of vortioxetine and a critique of the manufacturer’s pharmacoeconomic evaluation. The committee also considered input from a clinical expert with experience in treating patients with MDD, and patient group–submitted information about outcomes and issues important to patients.

Summary of Patient Input

Five patient groups — the Mood Disorders Society of Canada, the Canadian Mental Health Association (National), the Alberta branch of Canadian Mental Health Association, the Stigma-Free Society, and the Hope and Me – Mood Disorders Association of Ontario — provided patient input for this submission. Patient perspectives were obtained through focus groups, meetings, interviews, and online surveys. The following is a summary of the key input from the perspective of the patient groups.

- MDD is a chronic, complex, and disabling disease that may negatively impact a person’s life in different ways. Specifically, survey respondents indicated that MDD affected sleep, appetite, mood, relationships, exercise, work, and the ability to do the activities they used to enjoy. The financial burden due to lost employment and out-of-pocket costs can be profound, and many patients are subjected to stigma related to the condition.
- Many patients reported having tried multiple medications to treat their depression, and most of them reported severe side effects, including memory loss, worsening of symptoms, or complications of other conditions that they had. Consequently, medication-

related side effects had an impact on patients' overall quality of life and willingness and ability to seek new treatments. For some individuals, the medications had no impact.

- Access to a broader range of medications that were also affordable would help patients find the antidepressant that works better for them to address the emotional, cognitive, and physical effects of MDD.

Clinical Trials

The systematic review included 22 RCTs that evaluated the efficacy and safety of vortioxetine (5 mg to 20 mg daily) in adults with MDD over six to 12 weeks of therapy (21 short-term trials) or up to 64 weeks (one relapse prevention study). The trials were designed to test the difference between vortioxetine and placebo (17 RCTs), venlafaxine (one noninferiority study), or escitalopram (three RCTs). One other trial was designed to compare vortioxetine as add-on therapy to selective serotonin reuptake inhibitors (SSRIs) or vortioxetine as monotherapy, with SSRI monotherapy. Seven placebo-controlled trials also included an active reference group (duloxetine, venlafaxine, or paroxetine). The number of patients enrolled in each study ranged from 40 to 766 with a median of 458 patients per study.

Key limitations of the reviewed studies included the short duration of most trials (up to eight weeks); possible unblinding from gastrointestinal adverse events due to vortioxetine, which may bias subjective outcomes; and the magnitude of withdrawals (i.e., more than 19% in seven studies) or differential losses to follow-up (four studies). Data comparing vortioxetine with other antidepressants were limited, and considering the inclusion and exclusion criteria of the trials, the findings are generalizable only to a select MDD patient population.

Outcomes

Outcomes were defined a priori in the CADTH Common Drug Review systematic review protocol. Of these, the committee discussed depression symptom severity, measured using the MADRS or the HAM-D (17- or 24-item versions); disability, measured using the Sheehan Disability Scale (SDS); cognitive function, measured using the Digit Symbol Substitution Test (DSST) or the Rey Auditory Verbal Learning Test (RAVLT); HRQoL; and time to relapse.

The primary outcome in 14 short-term efficacy trials was the change from baseline to week six or eight for either the MADRS or the HAM-D24. Four short-term trials examined cognitive function as the primary outcome based on the change from baseline in the DSST or a composite of the DSST and the RAVLT. The other studies evaluated sexual function (Study 318) and Clinical Global Impression – Improvement scale scores (Liebowitz et al.), and one study did not specify the primary outcome (Levada et al.). One trial used a withdrawal design (Study 11985A) where patients who had achieved remission of their MDD with 12 weeks of vortioxetine therapy were randomized to placebo or continuation of vortioxetine: time to relapse over 24 weeks was the primary outcome.

- The Short Form 36 Health Survey is a generic HRQoL measure that includes eight domains: physical functioning, bodily pain, vitality, social functioning, mental health, general health, and role limitations due to physical or emotional problems. Each domain is scored from 0 to 100, with higher scores indicating better a health status.
- The EuroQol 5-Dimensions 3-Levels (EQ-5D-3L) questionnaire consists of five domains (mobility, self-care, usual activities, pain or discomfort, and depression or anxiety) each rated on a three-point index from 1 (no problems) to 3 (extreme problems). The EQ-5D also includes a 20 cm Visual Analogue Scale that has end points labelled 0 and 100, with respective anchors of "worst imaginable health state" and "best imaginable health state." Estimates of MCID for the EQ-5D-3L index score in the general population have ranged from 0.033 to 0.074.
- The Quality of Life Enjoyment and Satisfaction Questionnaire – Short Form was reported in two RCTs (13267A and 13926A). This questionnaire is designed to assess the degree of enjoyment and satisfaction experienced by patients in various areas of daily life. The questionnaire consists of 14 items with a total score that ranges from 14 to 70 (higher scores indicate better quality of life). No MCID was identified.
- The SDS measures the extent to which the patient's global functioning is impaired by depressive symptoms. With this self-reported, three-item scale, patients rate the extent to which their work, social life or leisure activities, and home life or family responsibilities are impaired by symptoms (0 indicates no disability; 10 indicates extreme disability). Total scores range from 0 to 30, with higher scores indicating more severe disability. The MCID is not known.

- Both the MADRS and the HAM-D are physician-rated measures of the severity of depression symptoms. The MADRS includes 10 items with a maximum total score of 60, whereas the HAM-D24 includes 24 items with a maximum of 76 points and the HAM-D17 has 17 items with a maximum of 53 points. For these instruments, higher scores indicate more severe symptoms. There is evidence to support the validity of the MADRS, with an MCID of two. The validity of the HAM-D24 is not known, although the HAM-D17, which is the core of the HAM-D24, has evidence of validity and an MCID of two or three.
- In the trials, response was defined as a 50% or greater decrease from baseline in MADRS score or HAM-D24 score at the end of the treatment period (week six or eight). Remission was defined as a MADRS total score of 10 or less or a HAM-D17 total score of seven or less. In the longer-term relapse prevention study (Study 11985A), relapse was defined as a MADRS score of 22 or greater, or as lack of efficacy (as judged by investigator opinion).
- The DSST is a measure of cognitive functioning focused on psychomotor speed. It is a timed task requiring patients to match geometric symbols to corresponding numbers as designated by an answer key. The number of correct symbol–number pairs given within the prescribed time limit determines the raw DSST score, ranging from 0 to 133. The RAVLT is a brief cognitive function test that assesses immediate memory span, capacity for new learning and recognition, and susceptibility to interference. Patients are asked to recall two or more lists of 15 nouns that have been read out loud to them after various lengths of time and in various formats, with one point awarded for every correctly recalled word. In Study 14122A, the primary outcome was the composite z score of the DSST and RAVLT. No evidence to support the validity or MCID for the DSST, RAVLT, or the composite z score of DSST and RAVLT in MDD was identified in the literature search conducted by CADTH.

Efficacy

Although HRQoL and disability were identified as key efficacy outcomes of interest to patients, none of the included studies were designed or powered to test for these outcomes. Eight trials included HRQoL as a secondary or exploratory outcome, and the findings were inconsistent between trials. Both the placebo and active treatment groups generally showed improvement in HRQoL scores; however, statistically significant differences were observed for vortioxetine versus placebo in some studies only, with other trials showing no differences between groups.

The change from baseline in the SDS was reported as a secondary outcome in 13 short-term trials and in the relapse prevention study. Most studies found no statistically significant difference between the vortioxetine and control groups. Meta-analysis of disability data from 11 short-term trials showed statistically significant differences between vortioxetine 10 mg and 20 mg versus placebo with a mean difference (MD) of -1.4 (95% confidence interval [CI], -2.0 to -0.8) for the 10 mg dose, and -1.8 points (95% CI, -2.8 to -0.9) for the 20 mg dose. Vortioxetine 5 mg and 15 mg doses did not show statistically significant differences compared with placebo in the pooled analysis. The clinical importance of these findings, however, is unclear given the uncertain validity of the SDS and the lack of MCID.

With regards to depression symptom severity, six of the 13 short-term placebo-controlled trials did not demonstrate statistically significant differences between vortioxetine and placebo in the primary outcome of depression symptom severity (change from baseline to end of treatment in MADRS or HAM-D24 scores), four studies showed statistically significant differences between vortioxetine and placebo, and in three trials statistically significant differences were observed for the highest dose of vortioxetine tested (20 mg or 10 mg per day), but not the lower vortioxetine doses included in those studies. Meta-analysis of the change from baseline in MADRS or HAM-D total score showed that vortioxetine (5 mg, 10 mg, and 20 mg) was statistically significantly different than placebo. The differences favouring vortioxetine were generally small (pooled primary outcome standardized mean difference, -0.24 to -0.40) but exceeded the MCID of two for MADRS score (MD, -2.4 to -3.7), with substantial between-study heterogeneity ($I^2 > 50\%$). Although the CADTH meta-analysis of all short-term efficacy trials showed statistically significant differences for most vortioxetine doses compared with placebo, the generally small differences observed, and the variable treatment effects across studies, makes the clinical significance of the differences unclear. As well, the variability in treatment effects and heterogeneity across studies reduces confidence in the findings. The meta-analysis of the secondary outcomes, response and remission, showed similar results to the primary outcome, with some vortioxetine doses showing statistically significant differences versus placebo, but with substantial between-study heterogeneity.

Study 13926A found vortioxetine to be noninferior to venlafaxine as the upper bounds of the 95% CIs did not exceed the noninferiority margin of $+2.5$ points on the MADRS scale (MD, -1.2 ; 95% CI, -3.03 to 0.63 , for the full analysis set; and MD, 0.19 ; 95% CI, -1.61 to 1.99 , for the per-protocol population). This noninferiority margin may be overly large, considering that the MCID of the MADRS is estimated at two points, and pooled data from a number of antidepressant trials showed an MD of two points between

active treatments and placebo. This trial was also limited by the extent of withdrawals, which were also imbalanced between groups (vortioxetine, 18%, and venlafaxine, 27%), and the use of the last observation carried forward approach to impute missing outcome data. The available head-to-head data are suggestive of a smaller treatment effect for vortioxetine relative to venlafaxine and duloxetine; however, definitive conclusions cannot be made. The CADTH pooled analysis suggests that vortioxetine may be less effective than duloxetine in reducing depression symptom severity; however, the differences observed were small and of unclear clinical significance.

Although the effect of vortioxetine on cognitive function tests was measured in six studies, the findings were heterogeneous. Hence, the impact of vortioxetine on cognition is unclear. Study 14122A reported statistically significant improvement in the composite z score of the DSST and RAVLT for patients receiving vortioxetine compared with patients receiving placebo; however, three other studies (studies 15905A, 15906A, and 15907A) found no statistically significant differences between vortioxetine and the control groups (SSRI, escitalopram, or placebo) in the change from baseline in DSST (the primary outcome in these studies).

Among patients who responded to treatment with vortioxetine during a 12-week open-label period in the relapse prevention study (Study 11985A), those who were randomized to vortioxetine were statistically significantly less likely to experience relapse compared with those who received placebo over the course of a 24-week double-blind period.

Harms (Safety)

The overall frequency of adverse events was higher among those receiving vortioxetine than placebo; nausea was the most common adverse event in the vortioxetine groups. Withdrawals due to adverse events were also reported more frequently among those on the higher doses of vortioxetine (15 mg and 20 mg) compared with placebo. The incidence of serious adverse events, including suicidal behaviour and serotonin syndrome, was low and similar between groups, although the studies were not powered to detect differences in rare adverse events. Moreover, the duration of most studies was limited to six to eight weeks.

With regards to sexual function, vortioxetine was found to statistically significantly improve treatment-related sexual dysfunction based on the change from baseline to week eight in CSFQ-14 scores, compared with escitalopram, among patients with SSRI-related sexual dysfunction at baseline. Both groups showed improvement in their CSFQ-14 scores and, although the between-group differences favoured vortioxetine, the clinical significance of the change score is unknown. Treatment-emergent sexual dysfunction was reported more frequently among those receiving vortioxetine 10 mg to 20 mg per day than those receiving placebo or vortioxetine 5 mg, based on pooled Health Canada data from the Arizona Sexual Experience Scale instrument. Self-reported sexual dysfunction was low and likely under-reported. Given the lack of comparative evidence to other classes of antidepressants, it is unclear if vortioxetine would cause less sexual dysfunction compared with other available classes of antidepressants.

No substantial increases in body weight were observed in the short-term studies, and in the longer-term relapse prevention trial, the proportion of patients with clinically important weight gain was similar between vortioxetine and placebo. Abrupt cessation of vortioxetine was associated with an increased incidence of adverse events, including headache, sudden outbursts of anger, mood swings, increased dreaming or nightmares, muscle tension or stiffness, dizziness, confusion or trouble concentrating, insomnia, and runny nose.

Indirect Treatment Comparisons

One published indirect comparison (network meta-analysis [NMA]) and one manufacturer-submitted analysis provided evidence used to inform the pharmacoeconomic analysis. Cipriani et al. based their analysis on an evidence base of 522 double-blind, short-term RCTs that evaluated the treatment response and acceptability of 21 antidepressant drugs. In this analysis, all approved dosages of antidepressants were pooled, whereas in the manufacturer-submitted analysis, dosage data from Cipriani et al. were divided and analyzed separately as high- and low-dosage groups, based on the World Health Organization's defined daily dose. Vortioxetine was found to be more efficacious than placebo in achieving response, defined as a 50% or greater reduction in the total score on a standardized observer-rating scale for depression (odds ratio, 1.66; 95% credible interval, 1.45 to 1.92) and as acceptable as placebo (odds ratio, 1.01; 95% credible interval, 0.86 to 1.19), based on the proportion of patients who withdrew from the study for any reason. Based on the primary analysis that included placebo and active controlled trials, the response rate and acceptability of vortioxetine were similar to other antidepressants. Data from the manufacturer-submitted analysis by dose showed similar results.

These NMAs support a general finding that most drugs used for the acute treatment of MDD have similar efficacy and all are more efficacious than placebo.

Cost and Cost-Effectiveness

Vortioxetine is available in multiple strengths: 5 mg, 10 mg, and 20 mg. The recommended starting dosage is 10 mg per day for adults and the dose may be increased to a daily maximum of 20 mg or reduced to 5 mg daily for individuals unable to tolerate higher doses. The recommended starting dosage for adults 65 years of age and older is 5 mg daily, and caution is advised in treating elderly patients with doses greater than 10 mg. The manufacturer submitted prices of \$2.81 per 5 mg tablet, \$2.95 per 10 mg tablet, and \$3.20 per 20 mg tablet.

The manufacturer submitted a cost-utility analysis considering vortioxetine versus other antidepressants for the treatment of MDD episodes as first-line treatment, from the perspective of a Canadian publicly funded health care payer, over a one-year time horizon. Comparators included serotonin-noradrenaline reuptake inhibitors (duloxetine and venlafaxine), SSRIs (citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline), and two treatments with different mechanisms of action (bupropion and mirtazapine). The model consisted of a combined decision tree and Markov model using a hypothetical cohort of patients with MDD who are treatment naive. Patients transition to subsequent treatment due to relapses, short- and long-term adverse events, or lack of treatment efficacy. The manufacturer submitted an NMA to inform the comparative efficacy and withdrawal due to adverse events between vortioxetine and comparators. The manufacturer stratified treatments according to dose for remission rates and discontinuation due to adverse events. Based on the sequential analysis, the manufacturer reported that bupropion is the preferred option if a decision-maker is willing to pay \$49,000 per quality-adjusted life-year (QALY); duloxetine is the preferred option if a decision-maker is willing to pay between \$50,000 and \$89,000 per QALY; and vortioxetine the preferred option if the decision-maker is willing to pay more than \$89,000 per QALY.

CADTH identified the following key limitations of the manufacturer's submitted economic analysis:

- The stratification of trials according to dose in the manufacturer's NMA was considered inappropriate by CADTH clinical reviewers.
- The manufacturer included unadjusted rates for adverse events to emphasize the safety profile of vortioxetine.
- The manufacturer assumed patients experiencing a relapse would have the same utility as failing to achieve remission.
- Multiple adverse events were assumed to result in an equal utility decrement; however, these adverse events are not expected to have a substantial impact on patient quality of life.
- Treatment acquisition costs were incorrectly applied in the model.
- Subsequent treatments (i.e., second- and third-line treatment) were included as part of the manufacturer's base-case analysis; however, to isolate the treatment effect of vortioxetine in the first-line setting, CADTH considered a common treatment sequencing approach for second- and third-line treatments.
- The clinical expert consulted by CADTH and the Canadian Network for Mood and Anxiety Treatments guidelines highlighted quetiapine as a relevant augmentation treatment, which was not included in the manufacturer's submission.

CADTH addressed some of the previously described limitations by adding quetiapine as an augmentation treatment option, applying unstratified dosing, altering the relapse utility, modifying long-term adverse event probabilities, re-calculating treatment costs, and applying a common treatment sequencing. Based on CADTH's reanalyses, vortioxetine was dominated by duloxetine and escitalopram (i.e., associated with greater costs and fewer QALYs). The difference in QALYs between vortioxetine and all comparators was minimal, suggesting a similar overall treatment benefit for patients with MDD.

At the current daily price of \$2.95 to \$3.20, price reductions would be required for vortioxetine to be equal in cost to generic duloxetine (a 67% to 70% price reduction), generic bupropion (an 80% to 82% reduction), or generic escitalopram (an 89% to 90% reduction). The cost-effectiveness of vortioxetine beyond first-line treatment of patients with MDD has not been evaluated by the manufacturer.

September 18, 2019 Meeting (Initial)

CDEC Members

Dr. James Silvius (Chair), Dr. Ahmed Bayoumi, Dr. Bruce Carleton, Dr. Alun Edwards, Mr. Bob Gagne, Dr. Ran Goldman, Dr. Allan Grill, Dr. Peter Jamieson, Mr. Allen Lefebvre, Ms. Heather Neville, Dr. Rakesh Patel, Dr. Emily Reynen, Dr. Yvonne Shevchuk, and Dr. Adil Virani.

Regrets

One CDEC member did not attend.

Conflicts of Interest

None

January 15, 2020 Meeting (Reconsideration)

CDEC Members

Dr. James Silvius (Chair), Dr. Ahmed Bayoumi, Dr. Bruce Carleton, Dr. Alun Edwards, Mr. Bob Gagne, Dr. Ran Goldman, Dr. Allan Grill, Mr. Allen Lefebvre, Ms. Heather Neville, Dr. Rakesh Patel, Dr. Danyaal Raza, Dr. Emily Reynen, Dr. Yvonne Shevchuk, and Dr. Adil Virani.

Regrets

Two CDEC members did not attend.

Conflicts of Interest

None