CADTH

CADTH COMMON DRUG REVIEW

# CADTH Canadian Drug Expert Committee Recommendation

(Final)

**LANADELUMAB (TAKHZYRO — SHIRE PHARMA CANADA ULC)**
Indication: For the routine prevention of attacks of hereditary angioedema (HAE) in adolescents and adults.

**RECOMMENDATION**
The CADTH Canadian Drug Expert Committee (CDEC) recommends that lanadelumab be reimbursed for routine prevention of attacks of hereditary angioedema (HAE) only if the following conditions are met.

**Conditions for Reimbursement**

**Initiation criteria**
1. The patient is at least 12 years of age.
2. The diagnosis of HAE type I or II is made by a specialist physician who has experience in the diagnosis of HAE.
3. The patient has experienced at least three HAE attacks within any four-week period before initiating lanadelumab therapy that required the use of an acute injectable treatment.

**Renewal criteria**
1. An assessment of a response to treatment should be conducted three months after initiating treatment with lanadelumab.
2. A response to treatment is defined as a reduction in the number of HAE attacks for which acute injectable treatment was received within the initial three months of treatment with lanadelumab compared to the rate of attacks observed before initiating treatment with lanadelumab.
3. Following the initial three-month assessment, patients should be assessed for continued response to lanadelumab every six months.
4. Continued response is defined as no increase in the number of HAE attacks for which acute injectable treatment was received compared with the number of attacks observed prior to initiating treatment with lanadelumab.

**Discontinuation criteria**
1. Treatment with lanadelumab should be discontinued in patients who either respond inadequately or exhibit a loss of response, defined as follows:
   - 1.1 Inadequate response: No reduction in the number of HAE attacks for which acute injectable treatment was received during the first three months of treatment with lanadelumab.
   - 1.2 Loss of response: An increase in the observed number of HAE attacks for which acute injectable treatment was received before initiating treatment with lanadelumab.

**Prescribing conditions**
1. The patient must be under the care of a specialist experienced in the diagnosis and management of patients with angioedema.
2. Lanadelumab should not be used in combination with other medications used for long-term prophylactic treatment of angioedema (e.g., C1-INH).
3. The dose of lanadelumab should not be escalated to more than 300 mg every two weeks (q.2.w.) in cases of inadequate response or loss of response.

**Pricing conditions**
1. Reduced price.


| | |
|---|---|
| Service Line: | CADTH Drug Reimbursement Recommendation |
| Version: | 1.0 |
| Publication Date: | November 2019 |
| Report Length: | 10 Pages |

CADTH



**Funding:** CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

# LANADELUMAB (TAKHZYRO — SHIRE PHARMA CANADA ULC)

Indication: For the routine prevention of attacks of hereditary angioedema (HAE) in adolescents and adults

## Recommendation

The CADTH Canadian Drug Expert Committee (CDEC) recommends that lanadelumab be reimbursed for routine prevention of attacks of hereditary angioedema (HAE) only if the following conditions are met.

## Conditions for Reimbursement

**Initiation criteria**

1. The patient is at least 12 years of age.
2. The diagnosis of HAE type I or II is made by a specialist physician who has experience in the diagnosis of HAE.
3. The patient has experienced at least three HAE attacks within any four-week period before initiating lanadelumab therapy that required the use of an acute injectable treatment.

**Renewal criteria**

1. An assessment of a response to treatment should be conducted three months after initiating treatment with lanadelumab.
2. A response to treatment is defined as a reduction in the number of HAE attacks for which acute injectable treatment was received within the initial three months of treatment with lanadelumab compared with the rate of attacks observed before initiating treatment with lanadelumab.
3. Following the initial three-month assessment, patients should be assessed for continued response to lanadelumab every six months.
4. Continued response is defined as no increase in the number of HAE attacks for which acute injectable treatment was received compared with the number of attacks observed before initiating treatment with lanadelumab.

**Discontinuation criteria**

1. Treatment with lanadelumab should be discontinued in patients who either respond inadequately or exhibit a loss of response, defined as follows:
   - 1.1 Inadequate response: No reduction in the number of HAE attacks for which acute injectable treatment was received during the first three months of treatment with lanadelumab.
   - 1.2 Loss of response: An increase in the observed number of HAE attacks for which acute injectable treatment was received before initiating treatment with lanadelumab.

**Prescribing conditions**

1. The patient must be under the care of a specialist experienced in the diagnosis and management of patients with angioedema.
2. Lanadelumab should not be used in combination with other medications used for long-term prophylactic treatment of angioedema (e.g., C1-INH).
3. The dose of lanadelumab should not be escalated to more than 300 mg every two weeks (q.2.w.) in cases of inadequate response or loss of response.

**Pricing conditions**

1. Reduced price.

## Reasons for the Recommendation

1. The available evidence suggests that lanadelumab offers a clinically meaningful benefit in patients with type I or type II HAE. In the HELP-03 study, lanadelumab 300 mg administered q.2.w. was associated with a statistically significant and clinically important reduction in the rate of HAE attacks from day 0 to 182. Compared with placebo, the percentage reduction in the least squares (LS) mean attack rate with 300 mg lanadelumab q.2.w. was 86.9% (95% CI, –92.828 to –76.150; *P* < 0.001). Treatment with 300 mg lanadelumab was also associated with a reduction in the following end points compared with placebo: rate of moderate and severe HAE; rate of high-morbidity HAE attacks (i.e., attacks that were severe, resulted in hospitalization, hemodynamically significant, or laryngeal); and the rate of HAE attacks that required acute treatment. Further, treatment with lanadelumab 300 mg q.2.w. resulted in a statistically significant and clinically meaningful improvement in health-related quality of life, as measured by the Angioedema Quality of Life questionnaire (AE-QoL) which was an exploratory outcome. The minimal clinically important difference in the AE-QoL total score of six points was achieved by 37% of patients in the placebo group, and by 81% of patients in the lanadelumab 300 mg q.2.w. group (odds ratio versus placebo: 7.20, *P* = 0.01).
2. Enrolment in the clinical trials included in the CADTH review (HELP-03 and HELP-04) was limited to patients with type I or II HAE; therefore, there is no clinical evidence to support the reimbursement of lanadelumab for patients with other forms of angioedema.
3. Lanadelumab has not been studied in combination with other long-term prophylactic treatments.
4. Lanadelumab offers a potential advantage over currently available drugs used for long-term prophylaxis as it is not derived from human plasma and is administered using a less frequent dosing regimen (q.2.w. compared with every three to four days).
5. The annual drug cost of lanadelumab ($533,988 with q.2.w. dosing) is substantially higher than the cost of other C1-INHs. Based on the CADTH reanalysis of the sponsor's economic model, the incremental cost-utility ratio (ICUR) for lanadelumab compared with Cinryze was more than $6 million per quality-adjusted life-year (QALY). A price reduction of at least 59% is required to achieve an ICUR below $50,000 per QALY compared with Cinryze. Given the lack of comparative efficacy data between lanadelumab and C1-INHs and the limitations associated with the sponsor's indirect treatment comparison (ITC), there is considerable uncertainty in the relative clinical efficacy of lanadelumab compared with C1-INHs; consequently, the cost-effectiveness of lanadelumab is highly uncertain.

## Implementation Considerations

- A definitive diagnosis of HAE type I and II requires testing C1 esterase level and activity, as well as C1q levels (to rule out acquired angioedema for which lanadelumab is not indicated). CDEC suggested that given the uncertainty regarding the availability of these tests and the potential for such tests to place an additional financial burden on the public health care system, the sponsor should be required to ensure that these tests are available and financed to support the implementation of the reimbursement of lanadelumab.
- To determine which patients would be eligible for reimbursement of lanadelumab, the current attack rate may be used for patients who are not receiving long-term prophylactic treatment and a historical attack rate may be used for those who are already receiving long-term prophylactic treatment and intend to transition to lanadelumab.
- Although defining a specific threshold for the reduction in the number of HAE attacks is difficult, clinical experts consulted by CADTH suggested that a minimum reduction of 50% in the number of HAE attacks for which acute treatment was received could be considered clinically meaningful.
- Patients on long-term prophylactic treatment will continue to require access to on-demand treatments that are used in the management of acute attacks.

## Discussion Points

- There is a lack of comparative evidence assessing the benefit of lanadelumab with relevant comparators (i.e., C1-INHs) for long-term prophylaxis. The ITC conducted by the sponsor was limited by clinical and methodological heterogeneity across the [redacted] studies, including different study designs ([redacted]), treatment durations ([redacted]), eligibility criteria ([redacted]), and protocols for rescue therapy and concomitant long-term prophylactic treatment. These differences resulted in considerable uncertainty regarding comparative efficacy of lanadelumab versus C1-INH. [redacted] were not assessed in the sponsor's ITC.

- The number of patients included in the HELP-03 study who were younger than 18 years of age was small; this was acknowledged by regulatory authorities and was considered to be reasonable given the rarity of HAE. Although there is considerable uncertainty in the subgroup analyses for patients younger than 18 years of age, the point estimates favoured lanadelumab compared with placebo despite the small sample size; the results of the subgroup analysis by age were consistent with overall study results.
- There is no commonly accepted threshold for the frequency of HAE attacks that would warrant initiating long-term prophylactic therapy. The mean baseline attack rate of patients in HELP-03 was between three and four within a four-week period, which, according to the clinical experts consulted by CADTH, is consistent with the attack rate of patients likely to initiate long-term prophylactic therapy in clinical practice.
- CDEC discussed that the number of HAE attacks should be reported for treatment initiation and at each subsequent reassessment in order to evaluate initial and continued response to treatment.
- In the HELP-03 trial, lanadelumab 300 mg q.4.w. was associated with a statistically significant reduction in the rate of HAE attacks from day 0 to 182 compared with placebo, with the percentage of reductions in the LS mean rate of 73.3% (95% CI, –82.379 to –59.456; $P < 0.001$). However, no evidence was available to evaluate the efficacy or safety of lanadelumab 300 mg q.4.w. in patients who were previously controlled on the 300 mg q.2.w. dosage regimen. Physicians may consider lengthening the dosing interval of lanadelumab in some patients. As per the dosage recommendations in the Health Canada approved product monograph, a dosing interval of 300 mg q.4.w. may be considered if the patient is well-controlled (e.g., attack free) for more than six months.

## Background

Lanadelumab is indicated for the routine prevention of attacks of HAE in adolescents and adults. The recommended dose of lanadelumab is 300 mg q.2.w.; however, a dosing interval of 300 mg q.4.w. may be considered if the patient is well-controlled (e.g., attack free) for more than six months. It is available as a single-use vial containing 300 mg lanadelumab in 2 mL of solution for subcutaneous (SC) injection.

## Summary of Evidence Considered by CDEC

CDEC considered the following information prepared by CADTH: a systematic review of pivotal and protocol-selected studies, a long-term extension phase study, an indirect comparison, and a critique of the manufacturer's pharmacoeconomic evaluation. CDEC also considered input from a panel of clinical experts with experience in treating patients with HAE, and patient group–submitted information about outcomes and issues that are important to individuals living with HAE.

### Summary of Patient Input

One patient group responded to CADTH's call for patient input for the lanadelumab submission (HAE Canada). Patient perspectives were obtained from an online survey of patients and caregivers. The following is a summary of key input from the perspective of the patient group:

- Given the burden of illness on patients with HAE and the ever-present risk of experiencing a life-threatening laryngeal attack, patients feel that improved preventive treatments are urgently needed.
- Greater control of attacks would ameliorate the ever-present anxiety and fear many patients experience due to unpredictable attacks and reduce the negative impact on a patient's ability to work, pursue education, travel, exercise, do household chores, and socialize with family and friends.
- The ability to select a drug based on the route of administration would be valued by patients and SC administration would be preferred in comparison with intravenous (IV) administration. Treatments that require IV administration require patients to expend much time travelling to and undergoing treatment, particularly for those patients who have difficulty administering the infusion in their home. Administering IV treatments at home can be difficult and uncomfortable with some patients reporting damage to their veins, or concern about damage to their veins after years of treatment.
- Patients expressed a desire for effective treatments not derived from human plasma.

## Clinical Trials

The CADTH systematic review included one double-blind, placebo-controlled, randomized controlled trial (HELP-03) that investigated the use of lanadelumab in patients with type I and type II HAE. The study was conducted in four phases:

- A long-term prophylactic (LTP) therapy washout phase where adult patients who were using LTP were required to undergo a washout period of at least two weeks before the start of the run-in period. LTP washout was not permitted in adolescent patients (i.e., between 12 and 18 years of age).
- A four to eight-week run-in phase to determine the patient's baseline rate of HAE attacks and to select the patients who would be eligible for randomization (i.e., only those with a baseline HAE attack of at least one investigator-confirmed HAE attack per four weeks).
- A 26-week double-blind treatment phase where eligible patients were randomized (3:2:2:2) to receive SC injections of placebo (n = 41), lanadelumab 150 mg q.4.w. (n = 27), lanadelumab 300 mg q.4.w. (n = 28), or lanadelumab 300 mg q.2.w. (n = 27). Randomization was stratified by the baseline HAE attack rate that was reported during the run-in period (i.e., one to less than two attacks per four weeks, two to less than three attacks per four weeks, and greater than or equal to three attacks per four weeks). CADTH has focused only on the Health Canada–approved dosage regimens of lanadelumab (i.e., 300 mg q.2.w. and 300 mg q.4.w.).
- A follow-up phase where patients who completed the double-blind treatment phase were given the option to enroll in the open-label extension phase study (HELP-04); those who did not participate in HELP-04 were to undergo an eight-week follow-up period for safety and additional evaluations.

## Outcomes

Outcomes were defined a priori in the CADTH systematic review protocol. Of these, CDEC discussed the following:

- Investigator-confirmed HAE attacks — events with symptoms or signs consistent with an HAE attack in at least one of the following locations: peripheral angioedema (cutaneous swelling involving an extremity, the face, neck, torso, and/or genitourinary region); abdominal angioedema (abdominal pain, with or without abdominal distention, nausea, vomiting, or diarrhea); laryngeal angioedema (stridor, dyspnea, difficulty speaking, difficulty swallowing, throat tightening, or swelling of the tongue, palate, uvula, or larynx).
- Number of moderate or severe investigator-confirmed HAE attacks — the severity of an HAE attack was assessed by the study investigator using the following criteria as reported by the patient: mild (transient or mild discomfort); moderate (mild to moderate limitation in activity, some assistance needed); and severe (marked limitation in activity, assistance required).
- Number of high-morbidity HAE attacks — defined as any attacks that had at least one of the following characteristics: severe, resulted in hospitalization (except hospitalization for observation for a period of less than 24 hours), hemodynamically significant (systolic blood pressure < 90, required IV hydration, or was associated with syncope or near-syncope) or laryngeal.
- Time to the first investigator-confirmed HAE attack after first attack after day 0 (i.e., after a single dose of lanadelumab), day 14 (i.e., approximately 50% steady state), day 28 (i.e., after two or three lanadelumab doses for q.4.w. and q.2.w., respectively), and day 70 (i.e., steady state).
- Percentage of HAE attack-free days and the proportion of patients who did not experience an HAE attack for intervals of one month, three months, or until the end of the study (i.e., day 182).
- AE-QoL — an angioedema-specific, patient-reported, health-related quality of life measure that consists of 17 questions in four domains: functioning, fatigue/mood, fears/shame, and food.

The primary end point of HELP-03 was the number of investigator-confirmed HAE attacks from day 0 to 182.[5] Pre-specified secondary end points which accounted for multiplicity of testing included: the number of investigator-confirmed HAE attacks requiring acute treatment, number of moderate or severe investigator-confirmed HAE attacks, and the number of investigator-confirmed HAE attacks occurring from day 14 to day 182.

## Efficacy

For the primary end point, the 300 mg q.4.w. and q.2.w. doses of lanadelumab were associated with statistically significant and clinically important reductions in the rate of HAE attacks from day 0 to 182. Compared with placebo, the percentage reductions in the LS mean rate with 300 mg lanadelumab were 73.3% (95% confidence interval [CI], –82.379 to –59.456; *P* < 0.001) and 86.9% (95% CI, –92.828 to –76.150; *P* < 0.001) in the q.4.w. and q.2.w. groups, respectively. Treatment with lanadelumab was also associated with reductions in HAE attack rates when the data were analyzed using alternative timeframes (i.e., day 7 to 182, day 14 to 182, and day 70 to 182). Compared with placebo, treatment with 300 mg lanadelumab was associated with a reduction in the following end points: rate of moderate and severe HAE, rate of high-morbidity HAE attacks (i.e., attacks that were severe, resulted in hospitalization, hemodynamically significant, or laryngeal), and the rate of HAE attacks that required acute treatment. The sponsor conducted responder analyses based on reductions in HAE attacks of at least 50%, 60%, 70%, 80%, and 90% with 300 mg lanadelumab being favoured over placebo for all analyses. There were few laryngeal attacks or HAE attacks that resulted in an emergency room (ER) visit or admission to hospital.

The median time to first HAE attack was [redacted] in the placebo group, [redacted] in the lanadelumab 300 mg q.4.w. group, and [redacted] in the lanadelumab 300 mg q.2.w. group.

The differences in AE-QoL total score between the lanadelumab and placebo groups were [redacted] and [redacted] for 300 mg q.4.w. and q.2.w. groups, respectively. The minimal clinically important difference in the AE-QoL total score of six points was achieved by 37% of patients in the placebo group, 63% of patients in the lanadelumab 300 mg q.4.w. group (odds ratio versus placebo: 2.91, *P* = 0.04) and by 81% of patients in the lanadelumab 300 mg q.2.w. group (odds ratio versus placebo: 7.20, *P* = 0.01). However, AE-QoL was an exploratory outcome and not adjusted for multiplicity. There were no differences observed between the 300 mg lanadelumab groups and the placebo group for changes from baseline in the EQ-5D-5L.

## Harms (Safety)

The proportion of patients who reported at least one adverse event in HELP-03 was greater in the lanadelumab 300 mg groups (96.3% and 86.2% in the q.2.w. and q.4.w. groups, respectively) compared with the placebo group (75.6%). Injection-site pain was the most commonly reported adverse event in all treatment groups. The proportion of patients who reported injection-site pain was similar in the placebo and lanadelumab 300 mg q.4.w. groups (29.3% and 31.0%, respectively), but was greater in the lanadelumab 300 mg q.2.w. group (51.9%). Injection-site erythema and bruising were also more commonly reported in the lanadelumab 300 mg groups than in the placebo groups. Viral upper respiratory tract infection and headache were more commonly reported in the lanadelumab 300 mg q.2.w. group (37.0% and 33.3%, respectively) compared with the lanadelumab 300 mg q.4.w. group (24.1% and 17.2%, respectively) and the placebo group (26.8% and 19.5%, respectively).

There were no deaths reported in the HELP-03 study. Serious adverse events (SAEs) were reported for three patients in the lanadelumab 300 mg q.4.w. group (3 events) and one patient in the lanadelumab 300 mg q.2.w. group (1 event). No SAEs were reported in the placebo group. Events reported in the lanadelumab 300 mg q.4.w. group included pyelonephritis (kidney infection), meniscus injury, and bipolar disorder. A single serious event of a catheter site infection was reported in the lanadelumab 300 mg q.2.w. group. Withdrawals due to adverse events were rare with only a single event in both the placebo and lanadelumab 300 mg q.4.w. groups and no events in the lanadelumab 300 mg q.2.w. group.

## Indirect Treatment Comparison

Given the absence of head-to-head studies, CADTH reviewed a sponsor-submitted ITC to investigate the comparative efficacy and safety of lanadelumab against other LTP used for management of HAE. The ITC consisted of a Bayesian network meta-analysis comparing three doses of lanadelumab (i.e., 150 mg q.4.w., 300 mg q.4.w., and 300 mg q.2.w.) against [redacted]. The evidence network was sparse and limited to [redacted]. [redacted] which included [redacted] were excluded from the ITC evidence network. The results demonstrated [redacted]

[redacted]. Although the sponsor reported that lanadelumab q.2.w. was superior to [redacted] for HAE attack rate (rate ratio: [redacted]), important limitations with the ITC prevent drawing any conclusions regarding comparative efficacy of lanadelumab and [redacted]. Most notably, there is considerable clinical and methodological heterogeneity across the [redacted] studies, including different study designs ([redacted]), treatment durations ([redacted]), eligibility criteria ([redacted]), protocols for rescue therapy, and concomitant LTP usage.

## Cost and Cost-Effectiveness

At a submitted price of $20,538 per vial, the average annual cost for lanadelumab is $533,988 per patient at a dosing interval of every two weeks.

The sponsor submitted a cost-utility analysis over a lifetime horizon from a Canadian publicly funded health care payer perspective, comparing lanadelumab and plasma-derived C1-INHs, including both Cinryze IV and Berinert IV as a single blended comparator. The sponsor also included no prophylaxis as part of a scenario analysis upon the request of CADTH. The sponsor used a cohort Markov model with two health states (alive with HAE and death). Average attack rates and attack duration for lanadelumab and C1-INHs were obtained from the HELP-03 trial and an ITC filed by the sponsor. The sponsor assumed Berinert IV to have the same efficacy as Cinryze IV because of the lack of studies assessing the effect of Berinert IV in preventing long-term HAE attacks. Health utility values were based on two sources: a utility value for patients experiencing an HAE attack based on a cohort study of Swedish patients with HAE; and, a health utility increment due to a more preferential route of administration and less frequent drug administration. The sponsor reported that lanadelumab dominated C1-INHs as it was associated with lower health care costs ($9,091,303 versus $10,866,545 for C1-INHs) and improved QALYs (24.347 versus 22.955 for C1-INHs). The probability that lanadelumab is cost-effective was 100% at a willingness-to-pay threshold (WTP) of $50,000 per QALY.

CADTH identified the following key limitations with the sponsor's economic analysis:

- There is substantial uncertainty in the comparative efficacy and safety of lanadelumab and [redacted] obtained from a [redacted] ITC given the substantial differences in trial design, key eligibility criteria, treatment duration, protocols for rescue therapy, and outcome measures.
- The sponsor assumed that the efficacy of Berinert IV was equal to that of Cinryze IV. It is questionable whether the efficacy data of Cinryze IV can represent the efficacy of all C1-INHs.
- C1-INHs were inappropriately included in the analysis as a single blended comparator — the cost-effectiveness of lanadelumab compared with each C1-INH was not reported.
- The sponsor excluded no prophylaxis from their reference-case analysis. No prophylaxis is a relevant comparator in patients with a very low frequency of HAE attacks, according to the clinical experts consulted by CADTH.
- The sponsor assumed that after six months, 80% of patients receiving lanadelumab switched from q.2.w. to q.4.w. dosing. There is no evidence to support this assumption.
- The Swedish study used to derive utility values in attack-free HAE patients showed that attack frequency and older age were associated with reduced health utility scores and that the number of days since the last attack had a positive correlation with health utility scores. The manufacturer did not describe why their health utility algorithm did not account for the number of days since the last attack.
- The health utility increment due to a more preferential mode of drug administration was obtained from an adult UK general population, which may not reflect the health utility of patients in Canada and it is uncertain if this is applicable in the treatment of HAE.
- The percentage of patients with HAE attacks requiring hospitalization (10%) or ER visits (100%) was overestimated in the sponsor's submission. According to clinical experts only patients with severe attacks would require an ER visit or hospitalization because most attacks can be self-treated by patients.
- Additionally, the unit cost of an ER visit was underestimated, as it only included ER physician fees but did not include other costs associated with an ER visit such as the cost of other health care professionals, and other costs not directly related to patient care such as general administration, information technology and capital expenses.
- The sponsor did not account for HAE-specific mortality.

The CADTH base case considered no prophylaxis as a comparator; considered Cinryze IV and Berinert IV as individual comparators; and, added direct and indirect hospital costs to ER physician costs as reported by the Ontario Case Costing Initiative. Cinryze IV was also removed as a rescue therapy, as it is not approved for the treatment for HAE acute attacks in Canada. Furthermore, the proportion of patients who switch to a less frequent dosing regimen, that is q.4.w., from month six onward was reduced from 80% to 0%. CADTH found lanadelumab would be cost-effective compared with no prophylaxis if the WTP threshold is less than $6,872,940 per QALY; Cinryze IV and Berinert IV were extendedly dominated and dominated respectively. A price reduction of at least 84.7% is required for lanadelumab to be cost-effective at a WTP threshold of $50,000 per QALY. CADTH also included a scenario analysis that excluded no prophylaxis, where the ICUR for lanadelumab was $6,981,558 per QALY compared with Cinryze IV; Berinert IV was dominated. A price reduction of at least 58.6% is required for lanadelumab to be cost-effective at a WTP threshold of $50,000 per QALY.

The cost-effectiveness of lanadelumab compared with C1-INHs should be interpreted with caution given the limitations of the sponsor's ITC such as the substantial differences in trial design, key eligibility criteria, treatment duration, protocols for rescue therapy and outcome measures.

## 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.

## October 16, 2019 Meeting

## Regrets

Two CDEC members did not attend.

## Conflicts of Interest

None