

## Reimbursement Recommendation

# Ubrogepant (Ubrelevy)

**Indication:** For the acute treatment of migraine, with or without aura, in adults

**Sponsor:** AbbVie Corporation

**Final recommendation:** Reimburse with conditions

# Summary

## What Is the Reimbursement Recommendation for Ubrelvy?

Canada's Drug Agency (CDA-AMC) recommends that Ubrelvy be reimbursed by public drug plans for the acute treatment of migraine, with or without aura, in adults if certain conditions are met.

## Why Did CDA-AMC Recommend Reimbursement?

The Canadian Drug Expert Committee (CDEC) determined that Ubrelvy demonstrates acceptable clinical value compared with appropriate comparators (triptans) in adult patients with migraine. This determination was enough for CDEC to recommend that Ubrelvy be reimbursed. Evidence from 2 clinical trials showed that patients who had a migraine attack and took Ubrelvy were more likely to be pain free or have less severe pain, and they were less likely to have symptoms associated with migraine, when compared with patients taking a placebo pill. Evidence from an indirect treatment comparison was associated with limitations and did not consistently demonstrate meaningful differences between Ubrelvy and publicly funded oral triptans that are commonly used to treat migraine attacks. While acknowledging the uncertainty of the indirect treatment comparison, CDEC found it reasonable to consider Ubrelvy and publicly funded oral triptans comparable.

## Which Patients Are Eligible for Coverage?

Ubrelvy should only be covered for adults with migraine, with or without aura.

## What Are the Conditions for Reimbursement?

Ubrelvy should only be reimbursed if initiated in adults with a history of migraine attacks associated with moderate to severe headache pain. Alternatively, public drug plans may choose to align the reimbursement criteria for Ubrelvy with existing formulary criteria for triptans, where such criteria exist. In either case, the cost of Ubrelvy should not exceed the least costly oral triptan used for the same indication.

Important budget impact considerations must be addressed for health systems to be able to adopt Ubrelvy.

## Review Background

- Migraine is a common neurologic disorder characterized by recurrent, often unilateral, throbbing headaches of moderate or severe intensity that worsens with physical activity and can be accompanied by photophobia, phonophobia, nausea, and/or vomiting. It may be preceded by bothersome prodromal and/or aura symptoms.
- An estimated 8.3% of people in Canada reported having been diagnosed with migraine between 2010 and 2011.
- Ubrogepant (Ubrovelvy) has been approved by Health Canada for the acute treatment of migraine, with or without aura, in adults. The sponsor is seeking reimbursement for this patient population.
- Ubrogepant is a small molecule, high-affinity calcitonin gene–related peptide (CGRP) receptor antagonist (gepant) that blocks the binding of CGRP to its receptor and antagonizes CGRP receptor function. It is available as an oral tablet, and the dosage recommended in the product monograph is 50 mg or 100 mg. If needed, an optional second dose may be taken at least 2 hours after the initial dose. The maximum daily dose is 200 mg.
- **Treatment costs:** At the submitted price of \$16.32 per 50 mg or 100 mg tablet, the cost of ubrogepant is expected to be \$16 to \$33 per migraine attack based on the Health Canada–recommended dosage.

## Highlights of Input From Interested Parties

The patient groups (the Canadian Migraine Society; Migraine Canada and Migraine Québec provided a joint submission) noted the following regarding impacts of the disease, unmet needs, and important outcomes:

- Patients highlighted that migraine negatively affects multiple areas of daily living, including family and social life, mental health, professional life, ability to attend school, and physical activity.
- Patients indicated that current treatment options, such as nonsteroidal anti-inflammatory drugs (NSAIDs) and triptans, may be ineffective, associated with intolerable side effects, or contraindicated for some patients.
- Important treatment goals for patients include the prevention of developing medication overuse headaches (MOHs), suitability for treating patients with other medical comorbidities, effective relief, reduced frequency of migraine attacks, and reduced intensity of migraine attacks while maintaining functioning in activities of daily living.

The clinician groups (the Canadian Headache Society Advocacy Committee and the National General Neurology Group) and the clinical experts consulted by CDA-AMC noted the following regarding unmet needs arising from the disease and the place in therapy for the drug under review:

- The clinical experts consulted for this review and clinician groups agreed there is a need for better tolerated, effective, and accessible treatments that reduce disability and medication overuse.

- The clinical experts consulted for this review and clinician groups agreed that ubrogepant would fill a treatment gap by offering an alternative:
  - as a first-line acute migraine treatment for patients for whom NSAIDs and triptans are contraindicated or those at risk for MOHs
  - as a second-line and beyond acute migraine treatment for patients for whom NSAIDs and triptans are ineffective or not tolerable or for those at risk for MOHs.

The participating public drug programs raised potential implementation issues related to considerations for initiation, renewal, discontinuation, and prescribing of therapy.

## Recommendation

With a vote of 14 in favour to 0 against, CDEC recommends that ubrogepant be reimbursed for the acute treatment of migraine, with or without aura, in adults only if the conditions listed in [Table 1](#) are met.

**Table 1: Reimbursement Conditions and Reasons**

| Reimbursement condition                                                                                                                                                                                 | Reason                                                                                                                                                                                                                                                                    | Implementation guidance                                                                                      |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------|
| <b>Initiation</b>                                                                                                                                                                                       |                                                                                                                                                                                                                                                                           |                                                                                                              |
| 1. Treatment with ubrogepant should be initiated in adults with a history of migraine attacks with moderate to severe headache pain.                                                                    | In the pivotal ACHIEVE I and ACHIEVE II trials, ubrogepant improved clinical outcomes in adults with a history of 2 to 8 migraine attacks of moderate to severe intensity per month. CDEC agreed that results could be generalized to patients with any attack frequency. | Migraine diagnosis can be made according to the International Classification of Headache Disorders criteria. |
| 2. Alternatively, public drug plans may consider aligning initiation criteria for ubrogepant with the criteria established for triptans within their respective formularies, where such criteria exist. | Based on the committee's assessment of the evidence, ubrogepant appears to have similar clinical value relative to triptans. Therefore, initiation criteria can align with those of triptans in each public drug plan formulary.                                          | —                                                                                                            |
| <b>Pricing</b>                                                                                                                                                                                          |                                                                                                                                                                                                                                                                           |                                                                                                              |
| 3. The drug program cost of ubrogepant should be negotiated so that it does not exceed the drug program cost of treatment with the least costly oral triptan used for the same indication.              | Based on the committee's assessment of the evidence, ubrogepant appears to have similar clinical value relative to triptans. Therefore, the drug program cost of ubrogepant should be no more than that of the least costly oral triptans.                                | —                                                                                                            |
| <b>Feasibility of adoption</b>                                                                                                                                                                          |                                                                                                                                                                                                                                                                           |                                                                                                              |
| 4. The economic feasibility of the adoption of ubrogepant must be addressed.                                                                                                                            | At the submitted price, the incremental budget impact of ubrogepant is expected to be greater than \$40 million in years 1, 2, and 3.                                                                                                                                     | —                                                                                                            |

CDEC = Canadian Drug Expert Committee.

## Rationale for the Recommendation

### Clinical Value

Based on the totality of the clinical evidence, CDEC concluded that ubrogepant demonstrates acceptable clinical value compared with appropriate comparators (triptans) in adult patients with migraine. Given that ubrogepant is expected to be an alternative to triptans, NSAIDs, or acetaminophen, *acceptable clinical value* refers to at least comparable value versus triptans, NSAIDs, or acetaminophen.

Evidence from 2 double-blind, placebo-controlled, parallel-group, single-attack trials (the ACHIEVE I and ACHIEVE II trials) showed that ubrogepant results in added clinical benefit compared with placebo in adult patients with migraine, with or without aura. The ACHIEVE I and II trials demonstrated that, compared to placebo (n = 559 in ACHIEVE I and n = 563 in ACHIEVE II), ubrogepant 50 mg (n = 556 in ACHIEVE I and n = 562 ACHIEVE II) and ubrogepant 100 mg (n = 557 in ACHIEVE I) result in clinically meaningful and generally statistically significant improvements in headache pain freedom, pain relief, and being free of the most bothersome migraine-associated symptom 2 hours after the initial dose, as well as sustained pain freedom and sustained pain relief at 2 and 24 hours after the initial dose. CDEC noted that while a numerically higher percentage of patients treated with ubrogepant 50 mg or 100 mg were satisfied with their study medication 2 hours after the initial dose compared to placebo, this outcome was not included in the hierarchical multiple testing procedure, and the absolute between-group differences did not reach the threshold considered clinically meaningful. The multicentre, randomized, open-label UBR-MD-04 trial informed on the durability of benefits across multiple attacks over a 52-week treatment period. Results showed that across all treated attacks over 52 weeks, treatment with ubrogepant 50 mg or ubrogepant 100 mg resulted in similar rates of satisfaction with the study medication, headache pain freedom, and pain relief 2 hours after the initial dose. However, CDEC noted that without a comparison to placebo or other active treatments, it remains unclear whether results observed for long-term efficacy of ubrogepant can be attributed to the drug itself. The committee noted that the harms associated with ubrogepant appeared to be consistent with its known safety profile and did not raise concern.

The indirect treatment comparison of ubrogepant versus publicly funded oral triptans (i.e., almotriptan, eletriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan) was associated with limitations and did not consistently demonstrate significant differences in efficacy or safety outcomes between the various treatments. While acknowledging the uncertainty, CDEC found it reasonable to consider ubrogepant and publicly funded oral triptans broadly comparable.

Further information on the committee's discussion around clinical value is provided in the Summary of Deliberation section.

### Developing the Recommendation

The determination of acceptable clinical value was sufficient for CDEC to recommend reimbursement of ubrogepant. As part of the deliberation on whether to recommend reimbursement, the committee also considered unmet clinical need, unmet nonclinical need, and health inequity. Information on this discussion is

provided in the Unmet Clinical Need and Distinct Social and Ethical Considerations domains in the Summary of Deliberation section.

Because CDEC recommended that ubrogepant be reimbursed, the committee also deliberated on whether reimbursement conditions should be added to address important economic considerations, health system impacts, or social and ethical considerations, or to ensure clinical value is realized. The resulting reimbursement conditions, with accompanying reasons and implementation guidance, are stated in [Table 1](#).

## Summary of Deliberation

CDEC considered all domains of value of the deliberative framework before developing its recommendation: clinical value, unmet clinical need, distinct social and ethical considerations, economic considerations, and impacts on health systems. For further information on the domains of value, refer to [Expert Committee Deliberation at Canada's Drug Agency](#).

The committee considered the following key discussion points, organized by the 5 domains of value.



### Clinical Value

- **Appropriate comparators:** CDEC noted that triptans, NSAIDs, and acetaminophen are all appropriate comparators for ubrogepant in the target population. CDEC agreed that most patients try over-the-counter NSAIDs and acetaminophen before seeking care. Therefore, while all 3 treatments are important comparators, triptans — being antimigraine-specific medications and typically the first-line treatment prescribed in the primary care setting for acute migraine — are the most relevant comparators.
- **Efficacy versus placebo:** Two randomized controlled trials (the ACHIEVE I and ACHIEVE II trials; N = 2,247 in the modified intention-to-treat population) demonstrated that compared to placebo, treatment with ubrogepant 50 mg or 100 mg resulted in higher percentages of patients who were satisfied with the study medication 2 hours after the initial dose (with between-group differences ranging from 11.7 percentage points to 13.0 percentage points), achieved pain freedom 2 hours after the initial dose (with between-group differences ranging from 7.4 percentage points to 9.4 percentage points), and had sustained pain freedom at 2 and 24 hours after the initial dose (with between-group differences ranging from 4.1 percentage points to 6.8 percentage points). Additionally, more patients treated with ubrogepant achieved pain relief 2 hours after the initial dose (with between-group differences ranging from 11.5 percentage points to 15.5 percentage points), had sustained pain relief at 2 and 24 hours after the initial dose (with between-group differences ranging from 15.5 percentage points to 17.2 percentage points), and were free of their most bothersome migraine-associated symptoms 2 hours after the initial dose (with between-group differences ranging from 10.0 percentage points to 11.5 percentage points). Because the ACHIEVE I and ACHIEVE II trials were limited to participants having up to 1 treated migraine attack, a long-term extension study

(the UBR-MD-04 trial; N = 1,254) informed on the effects of ubrogepant 50 mg or 100 mg for treating acute migraine attacks over 52 weeks. This trial showed that both doses of ubrogepant (i.e., 50 mg and 100 mg) resulted in similar rates of satisfaction with the study medication, pain freedom, and pain relief 2 hours after the initial dose of treatment. However, CDEC noted that without a comparison to placebo or usual care, it remains unknown if the observed effects can be attributed to the drug itself. Importantly, positive outcomes were observed in only a minority of attacks across the 52-week period, which suggests that therapeutic goals are not fully met by ubrogepant in many patients.

- Clinical importance of treatment effects:** CDEC noted that important outcomes for patients include preventing MOHs, reducing the pain and intensity of migraine attacks, and maintaining functioning in activities of daily living. CDEC discussed that while the clinical experts consulted for this review did not anticipate ubrogepant would cause MOHs, the certainty of this effect is unknown given the lack of submitted evidence. Based on expert input that a 5 percentage point between-group difference would be clinically meaningful for the following outcomes, CDEC noted that differences between treatment groups versus those receiving placebo in the proportions of patients achieving pain relief and sustained pain relief were clinically relevant. Also based on a 5 percentage point between-group difference being clinically meaningful, the differences between treatment groups versus those receiving placebo were likely clinically relevant for the outcomes of achieving pain freedom, sustaining pain freedom, and being free of their most bothersome migraine-associated symptom. While proportionally more patients who received ubrogepant were satisfied with their medication 2 hours after the initial dose than those who received placebo, CDEC noted that the between-group differences versus placebo were lower than the clinically meaningful threshold of 15 percentage points for this outcome suggested by experts.
- Harms findings versus placebo:** Reducing harms was an important outcome for patients, and the clinical experts consulted for this review noted that treatment-emergent adverse events (TEAEs) that occurred within 48 hours of the initial dose or optional second dose were the most clinically relevant harms outcome. Based on a 10 percentage points between-group difference threshold suggested by experts, CDEC noted that treatment with ubrogepant did not result in a clinically meaningful difference in TEAEs within 48 hours of the initial dose or optional second dose compared to placebo in the ACHIEVE I and ACHIEVE II trials (between-group differences ranged from –3.3 percentage points to 5.4 percentage points). CDEC also noted no serious adverse events occurred within 48 hours of the initial dose and no patients stopped treatment or died due to an adverse event throughout the course of the ACHIEVE I and ACHIEVE II trials. No new safety concerns were identified among patients who continued to treat migraine attacks with ubrogepant over the 52-week long-term extension study, and rates of adverse events were generally similar to those reported by the group receiving usual care.
- Certainty of the evidence:** Using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, the certainty of evidence was rated as high for pain relief and sustained pain relief. The certainty of evidence for pain freedom and sustained pain freedom (which used a definition similar to *pain relief*, albeit with more stringent pain requirements), satisfaction

with the study medication 2 hours after the initial dose, and occurrence of a TEAE within 48 hours of the initial or optional second dose was rated as moderate due to serious imprecision in the between-group differences. CDEC noted that while there was some variability in the point estimates for sustained pain freedom between the trials, the 95% confidence intervals overlapped sufficiently. Certainty of evidence for the absence of the most bothersome migraine-associated symptom 2 hours after the initial dose was rated as high in the ACHIEVE II trial and as moderate in the ACHIEVE I trial due to serious imprecision in the between-group differences.

- **Efficacy versus triptans:** One network meta-analysis (NMA) was provided to indirectly inform the comparative effects of ubrogepant 50 mg and 100 mg to those of publicly funded triptans based on 86 trials. CDEC discussed that results were generally uncertain, with wide credible intervals that crossed the null, and included the potential that either ubrogepant or oral triptans could be favoured, depending on the comparison. CDEC observed that certain triptans, such as eletriptan 40 mg and rizatriptan 10 mg, appear to be more efficacious than ubrogepant for some outcomes. CDEC also noted there was substantial between-trial heterogeneity that reduced certainty in the NMA results.
- **Clinical value:** Based on the preceding considerations, CDEC determined that ubrogepant demonstrated acceptable clinical value versus triptans, though there remains some uncertainty. While there was no information available to inform on the effects of ubrogepant versus NSAIDs and acetaminophen, CDEC agreed that many patients would have tried these medications before seeking care.



## Unmet Clinical Need

- **Input on unmet clinical need:** Based on patient and clinician input, CDEC noted a need for alternative treatment options that provide effective relief, are suitable for treating patients with medical comorbidities, and do not cause MOHs. CDEC also noted that clinicians further identified a need for medications that reduce the need for repeat rescue medications or emergency care visits and reduce the transformation of episodic migraine to chronic migraine.
- **Severity of the disease:** Based on patient and clinician input, CDEC discussed that migraine is a seriously debilitating disease that negatively affects multiple areas of daily living, including family life, social life, mental health, professional life, ability to attend school, and physical activity.
- **Availability of treatment options:** Patient groups noted that while existing treatments for migraine, such as NSAIDs and triptans, are effective for some patients, others have intolerable side effects or contraindications, leaving patients with few options. Additionally, current treatments for migraine can only be taken for up to 10 days per month due to the risk for MOHs, leaving patients with chronic migraine unable to treat many of their migraine attacks. As noted previously, CDEC discussed that while the clinical experts consulted for this review did not anticipate ubrogepant to cause MOHs, the certainty of this effect is unknown given the lack of evidence.



## Distinct Social and Ethical Considerations

- **Unmet nonclinical need:** Based on patient group input, CDEC discussed that patients with migraine experience productivity loss and negative financial effects due to difficulties in career progression. This negative effect of migraine was particularly impactful among young women, because migraine is more common in this demographic group.
- **Equity considerations:** Clinical expert input highlighted that patients with lower socioeconomic status, those living in Indigenous and racialized communities, and those living in rural or remote settings are more likely to experience migraine. CDEC acknowledged that patient and clinician input noted how current restrictive drug coverage policies further exacerbate these inequities, underscoring the importance of having accessible, migraine-specific acute treatment options to reduce disparities in care and outcomes.



## Economic Considerations

- **Health impacts of ubrogepant versus relevant comparators:** Relative to the triptans, ubrogepant is predicted to result in slightly more quality-adjusted life years gained per patient than most triptans, but slightly fewer than eletriptan 40 mg, rizatriptan 10 mg, sumatriptan 100 mg, and zolmitriptan 2.5 mg, over a 2-year time horizon.
- **Cost of ubrogepant versus relevant comparators:** Ubrogepant is predicted to be associated with additional health care costs compared to the triptans (incremental costs range from \$440 to \$1,099 per patient) over a 2-year time horizon.
- **Key findings of the economic evaluation:** Based on the submitted evidence using the sponsor's cost-utility analysis, the CDA-AMC base case estimated that both ubrogepant 50 mg and 100 mg were slightly less effective ( $-0.001$  quality-adjusted life-year difference) and more costly than rizatriptan 10 mg and eletriptan 40 mg.
- **Certainty of the evidence:** The CDA-AMC analysis was informed by the sponsor-submitted NMA, which was deemed uncertain.
- **Other considerations:** CDA-AMC analyses were unable to account for potential reductions in MOHs in patients who may require triptans frequently enough to experience them. Patients who experienced more than 8 migraine attacks per month were excluded from the sponsor's model.



## Impacts on Health Systems

- **Anticipated budget impact:** CDA-AMC estimates that the budget impact of reimbursing ubrogepant for the treatment of adults with acute migraine with or without aura will be approximately \$543.5 million over the first 3 years of reimbursement compared to the amount currently spent on triptans, with an estimated expenditure of \$575.7 million on ubrogepant over this period. The CDA-AMC budget impact analysis base-case population did not limit the population to only those with moderate to severe headache pain. Therefore, the anticipated budget impact of reimbursing

ubrogepant in the recommended population may be lower than estimated in the CDA-AMC base case. The actual budget impact of reimbursing ubrogepant will depend on the size of the eligible population, the uptake of ubrogepant, the current market shares and displacement of the comparators, and the frequency of use of all comparators.

## Sources of Information Used by the Committee

To make its recommendation, the committee considered the following information (links to the full documents for the review can be found on the [project web page](#)):

- the CDA-AMC review of the clinical and pharmacoeconomic evidence submitted by the sponsor related to ubrogepant (refer to the Main Report and the Supplemental Material document)
- the sponsor's comments on the draft report and the responses by CDA-AMC
- patients' perspectives gathered by 2 patient groups — the Canadian Migraine Society and Migraine Canada (refer to the Patient and Clinician Group Input document)
- input from 2 clinician groups — the Canadian Headache Society Advocacy Committee and the National General Neurology Group (refer to the Patient and Clinician Group Input document)
- input from public drug programs that participate in the reimbursement review process (refer to the Supplemental Material document)
- input from 2 clinical experts with expertise in the management of migraine consulted by CDA-AMC.

## CDEC Information

### Members of the Committee

Dr. Peter Jamieson (Chair), Dr. Kerry Mansell (Vice-Chair), Sally Bean, Daryl Bell, Dan Dunskey, Dr. Ran Goldman, Dr. Trudy Huyghebaert, Dr. Dennis Ko, Dr. Christine Leong, Alicia McCallum, Dr. Srinivas Murthy, Dr. Nicholas Myers, Dr. Krishnan Ramanathan, Dr. Marco Solmi, Carla Velastegui, Dr. Edward Xie, and Dr. Peter Zed.

**Meeting date:** May 28, 2026

**Regrets:** None

**Conflicts of interest:** One expert committee member did not participate due to considerations of conflict of interest.



**Canada's Drug Agency**  
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Drugs. Health Technologies and Systems. Médicaments, technologies de la santé et systèmes.

**ISSN:** 2563-6596

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