Canadian Journal of Health Technologies

Canada's Drug Agency
L'Agence des médicaments du Canada

February 2026 Volume 6 Issue 2

Drugs Health Technologies Health Systems

Reimbursement Recommendation

Guanfacine Extended Release

Reimbursement request: For the adjunct therapy to psychostimulants for the treatment of ADHD in children and adolescents, aged 6 to 17 years, with a sub-optimal response to psychostimulants

Requester: Public drug programs

Final recommendation: Reimburse with conditions

Summary

What Is the Reimbursement Recommendation for Guanfacine Extended Release?

The Formulary Management Expert Committee (FMEC) recommends that guanfacine extended release (XR) be reimbursed for the adjunct therapy to psychostimulants for the treatment of attention-deficit/hyperactivity disorder (ADHD) in children and adolescents, aged 6 years to 17 years, whose disease has responded suboptimally to psychostimulants, provided certain conditions are met.

What Are the Conditions for Reimbursement?

Guanfacine XR may be reimbursed for the adjunct therapy to psychostimulants for the treatment of ADHD in children and adolescents, aged 6 years to 17 years, whose disease has responded suboptimally to psychostimulants. Guanfacine XR should be discontinued if there are unacceptable toxicities. Guanfacine XR must represent good value to the drug plans.

Why Did Canada's Drug Agency Make This Recommendation?

FMEC reviewed the report by Canada's Drug Agency (CDA-AMC), which included a review of the clinical evidence from 2 randomized controlled trials (RCTs) comparing guanfacine XR plus psychostimulant to placebo plus psychostimulant (studies by van Stralen [2020] and Wilens et al. [2012]) and a cost comparison of guanfacine XR versus other treatments used in Canada. No input from external partners was received for this review.

Evidence from 2 RCTs comparing guanfacine XR plus a psychostimulant to placebo plus a psychostimulant suggests that guanfacine XR may result in greater improvements in ADHD core symptoms in children and adolescents. Guanfacine XR is available as a generic drug in Canada.

FMEC concluded that guanfacine XR demonstrates acceptable clinical value, and the reimbursement conditions were further developed based on an unmet clinical need, distinct social and ethical considerations, economic considerations, and impacts on health systems.

Review Background

What Is ADHD?

ADHD is a neurodevelopmental disorder most commonly identified in children and adolescents that often continues into adulthood. It is an impairment of the ability to regulate attention or focus. ADHD can present differently in different people. Some symptoms may include forgetfulness, impulsivity, disorganization, distracted behaviour, and restlessness. People with ADHD can also experience emotional dysregulation. These factors may contribute to learning challenges, problems with self-esteem, and difficulties with relationships.

In Canada, the prevalence of ADHD in children and adolescents combined is estimated to range from 2.6% to 8.6%. The prevalence is thought to be higher in males (range, 3.7% to 13.3%) than in females (range, 1.5% to 7.0%).

What Are the Current Treatment Options?

The treatment goals for children and adolescents with ADHD are to reduce hyperactivity, impulsivity (including aggressive impulsive actions), inattention, oppositional behaviours, and emotional dysregulation to enhance their development (e.g., learning, social development, cognitive outcomes, and health-related quality of life [HRQoL]). According to a tool the Canadian ADHD Resource Alliance (CADDRA) published, the CADDRA Guide to ADHD Pharmacological Treatments in Canada, first-line treatment options for ADHD may include long-acting psychostimulants such as amphetamine-based psychostimulants or methylphenidate-based psychostimulants. Second-line options may include short-acting psychostimulants or nonstimulant options such as atomoxetine (monotherapy) or guanfacine XR.

What Is the Treatment Under Review?

Guanfacine XR is an alpha-2a agonist available as an oral tablet. Health Canada has approved guanfacine XR as monotherapy for the treatment of ADHD in children and adolescents aged 6 years to 17 years, and as adjunctive therapy to psychostimulants for the treatment of ADHD in children and adolescents aged 6 years to 17 years, with a sub-optimal response to psychostimulants.

In 2015, the Canadian Drug Expert Committee recommended that guanfacine XR not be listed as adjunctive therapy to psychostimulants for ADHD due to limited evidence from 1 RCT of only 9 weeks' duration.

Why Did We Conduct This Review?

Participating public drug programs have requested that a non-sponsored reimbursement review be conducted to inform whether guanfacine hydrochloride XR should be reimbursed for the adjunct therapy to psychostimulants for the treatment of ADHD in children and adolescents, aged 6 years to 17 years, with a sub-optimal response to psychostimulants. This request was prompted by the emerging availability of evidence over the past decade for a treatment regimen with the potential to fulfill an unmet need in patients with ADHD. Guanfacine XR is noted to be funded in some but not all jurisdictions.

As of September 2025, Health Canada had reviewed 4 generic versions of guanfacine XR (2 are marketed and 2 are approved) and the data protection for guanfacine expired on January 5, 2022, making this drug eligible for a non-sponsored reimbursement review as per the Procedures for Reimbursement Reviews.

Highlights of Input From Interested Parties

- CDA-AMC did not receive input from clinician groups, patient groups, or industry.
- Public drug plans inquired about the evidence for guanfacine XR to inform a recommendation on whether it should be reimbursed for the adjunct therapy to psychostimulants for the treatment of ADHD in children and adolescents, aged 6 years to 17 years, with a sub-optimal response to psychostimulants. The public drug plans outlined implementation issues related to relevant comparators, considerations for treatment initiation, and considerations for renewal or discontinuation of therapy.

► **Refer to the main report and the supplemental material document for this review.**

Person With Lived Experience

A parent from Western Canada shared her experience as a caregiver to her 8-year-old child. A history of hyperactivity and dysregulated behaviour in her son prompted a referral to a pediatrician and a diagnosis of ADHD when he was aged 3 years. Different medications were trialled, including Adderall, which was discontinued due to intolerable side effects. Her son now takes methylphenidate hydrochloride twice daily plus guanfacine XR, introduced when he was aged 4 years. The addition of guanfacine in the evening significantly improves her son's ability to focus, control impulses, and regulate emotions the next day without any associated side effects like drowsiness. He is aware of how guanfacine XR benefits him. He quickly learned how to swallow pills, so there have been no administration challenges. The parent has private drug coverage and no access issues. Though her son's medications suppress appetite, she ensures he maximizes his intake when he is hungry to maintain his health and weight, so this is not problematic. Her son attends a private school where he has access to psychological services and occupational therapy for ADHD. Weekly ADHD-targeted equine therapy is also part of his treatment regimen. She feels confident supporting her son's management with the parental resources she has obtained from his care team and all she has learned over the years.

Disclaimer: The perspectives shared by people with lived experience who present to the committee reflect their individual experiences and are not necessarily representative of all people with the same condition or course of treatment. Their insights provide valuable context about what a patient, support person, or caregiver might go through when facing this condition or treatment, helping to inform the committee's deliberations. These narratives complement other forms of evidence and input and should be considered as part of a broader understanding of the condition and treatment under review. When gender or gendered pronouns are used in these narratives, they are included with the permission of the individual.

Recommendation

With a vote of 9 to 0, FMEC recommends that guanfacine XR for the adjunct therapy to psychostimulants for the treatment of ADHD in children and adolescents, aged 6 years to 17 years, whose disease has responded suboptimally to psychostimulants, be reimbursed if the conditions presented in Table 1 are met.

Table 1: Conditions, Reasons, and Guidance

Reimbursement condition	Reason	Implementation guidance
Initiation		
1. Guanfacine XR may be initiated for the adjunct therapy to psychostimulants for the treatment of ADHD in children and adolescents, aged 6 years to 17 years, if the following condition is met: 1.1. their disease has responded suboptimally to psychostimulants for the treatment of ADHD.	There is evidence from 2 randomized controlled trials (studies by van Stralen [2020] and Wilens et al. [2012]) comparing guanfacine XR plus psychostimulant to placebo plus psychostimulant that suggests guanfacine XR as adjunctive therapy to a psychostimulant may result in greater improvement in ADHD core symptoms in children and adolescents.	The patient may have a suboptimal disease response and be unable to titrate or tolerate a full dose of psychostimulant due to intolerance or adverse events. The suboptimal disease response should include a trial of at least 1 amphetamine-based psychostimulant and 1 methylphenidate-based psychostimulant. The use of guanfacine XR may be reassessed when the patient turns 18 years old to determine if the benefits of continuing treatment outweigh any potential risks.
Discontinuation		
2. Guanfacine XR should be discontinued if there are unacceptable toxicities.	Consistent with clinical practice, patients may discontinue treatment upon unacceptable toxicities.	—
Pricing		
3. Guanfacine XR must represent good value to the drug plans.	FMEC concluded that reimbursement of guanfacine as adjunctive therapy to psychostimulants is associated with higher drug acquisition costs than those of comparators based on publicly available list prices. Based on the available evidence, guanfacine XR may improve multiple clinical outcomes when compared to placebo plus a psychostimulant, with unknown benefit when compared to atomoxetine or clonidine. The cost-effectiveness of guanfacine XR as adjunct therapy to psychostimulants compared to relevant comparators is unknown.	Guanfacine XR is available as a generic drug in Canada, and its cost is therefore subject to the pCPA tiered pricing framework for generic drugs.

ADHD = attention-deficit/hyperactivity disorder; FMEC = Formulary Management Expert Committee; pCPA = pan-Canadian Pharmaceutical Alliance; XR = extended release.

Summary of Deliberation

FMEC deliberated on 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, please refer to the Expert Committee Deliberation at Canada's Drug Agency document.

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

Clinical Value

- **FMEC concluded that guanfacine XR demonstrates acceptable clinical value versus appropriate comparators in the Canadian setting.**
- Through reflection on the insights shared by people with lived experience, FMEC members noted that improvement in ADHD core symptoms is important to patients and families.
- In addition, child-specific HRQoL and effects on their family are also important. Specifically, parents whose children have ADHD must navigate additional parental support and emotional regulation support for their children. Patients with ADHD may request special accommodations or other interventions at schools that may not always be readily available, which can be challenging for both patients and their families.
- FMEC members highlighted the following discussion points:
  - **Appropriate comparators.** FMEC discussed that the comparator in the included studies was placebo as add-on therapy. Given that there are limited options in the adjunctive setting, the use of placebo as a comparator was considered appropriate.
  - **Efficacy and clinical importance of treatment effects.** In both studies (by van Stralen [2020] and Wilens et al. [2012]), the reductions (improvements) in ADHD symptoms at the end of treatment compared to placebo met the minimal important difference in ADHD Rating Scale–IV total scores for adjunctive therapy (a 4-point difference) among patients who had already experienced a reduction (improvement) in ADHD symptoms while taking a psychostimulant alone.
  - **Safety.** FMEC also discussed the harms data. Although it was noted that there was an increase in adverse events among the group receiving the guanfacine XR plus psychostimulant combination as compared to the group receiving a psychostimulant alone, there was no strong safety signal related to serious adverse events or the need for discontinuation of therapy. The clinical experts suggested that guanfacine XR should be discontinued if benefits are not clear and/or if there are prominent adverse effects such as drowsiness, headaches, or blood pressure issues. The decision to discontinue guanfacine XR upon unacceptable toxicities would be left to the discretion of the treating clinician and shared decision-making with the patient and their family.
  - **Evidence generation is needed.** There is a need for additional research to generate evidence in pediatric settings. FMEC highlighted that while ADHD is not classified as a rare condition, there may be systemic barriers to participation in clinical trials. While evidence generation in the

pediatric setting is needed, FMEC acknowledged that the additional monitoring and follow-up required for clinical trial participation may add to the burden of caregivers. FMEC acknowledged the need for more initiatives and better infrastructure to support research in the pediatric population and on ADHD (e.g., related to HRQoL and long-term effects).

- **Importance of HRQoL and other outcomes.** FMEC noted that evidence related to HRQoL is limited. FMEC discussed the importance of HRQoL data in this setting to consider how this treatment may improve HRQoL outcomes and the potential benefits from the perspectives of patients and their caregivers. Further, outcomes related to individuals' life-course development, school performance, ability to form meaningful social circles, and interactions with peers and families are important outcome measures for ADHD treatments.

Unmet Clinical Need

- **FMEC concluded that there is a significant clinical need arising from ADHD despite available treatments.**
- Through reflection on the insights shared by people with lived experience, FMEC members noted the following important patient values or perspectives:
  - There are short- and long-term effects and consequences of undertreatment for children and their families despite available options.
  - Undertreatment may affect a child's ability to focus and to regulate emotions, both of which can be challenging for parents and school systems to manage.
  - Nonmedical supports are an important part of treatment; however, some interventions and resources may not be affordable or accessible to all patients and families.
- FMEC members highlighted the following discussion points:
  - **Availability of treatment options.** FMEC noted that currently available therapies are predominately for first-line use. There are limited adjunctive options — guanfacine XR or clonidine. Based on guest specialists' input, clonidine is not used because patients do not tolerate this treatment well.
  - **Severity of the disease.** FMEC noted ADHD may lead to short-term morbidities including difficulties with focus and concentration in school and challenges with interpersonal relationships. ADHD may also lead to long-term morbidities such as difficulties with social relationships and negative effects on employment and career prospects.
  - **Significant unmet clinical need.**
    - FMEC discussed that there would be individuals who do not respond fully to first-line treatment options with psychostimulants and who would require an adjunct treatment option to meet treatment goals. Suboptimal response may be limited by the inability to further titrate doses due to intolerance (e.g., insomnia or weight loss due to a psychostimulant interfering with quality of life or growth development).

- FMEC also heard from the guest specialists that guanfacine XR is particularly helpful for individuals with the hyperactive-impulsive subtype of ADHD, with irritability, disruptive behaviour, or anxiety.
- FMEC also heard from 1 guest specialist that knowledge of genetics and of how an individual's genetics may affect their disease response to treatment is evolving. There is a growing understanding of the role of genetics in determining individuals' disease responses to and metabolism of psychostimulants, and there is growing recognition that adding an adjunct therapy may complement the treatment of individuals whose disease responds suboptimally to monotherapy with a psychostimulant.

Distinct Social and Ethical Considerations

- **FMEC concluded that guanfacine XR would potentially address a significant nonclinical need arising from ADHD despite available treatments. FMEC did not identify any important measures that should be implemented to ensure that the use of guanfacine XR addresses relevant social and ethical implications.**
- Through reflection on the insights shared by people with lived experience, FMEC members noted the following important patient values or perspectives:
  - While there are treatment options available for ADHD, the stigma associated with the condition may continue to play a role as individuals and families decide on the best treatment options for them.
- FMEC members highlighted the following discussion points:
  - FMEC discussed that there are nonclinical needs arising from the impact of ADHD on individuals' families and classmates in school (e.g., disruption from the individual affecting others such that their home situation or ability to learn is affected). The adjunct therapy of guanfacine XR may help address these nonclinical needs.
  - FMEC also discussed that there is a disparity across jurisdictions in access to nonpharmacologic interventions, and this may lead to the overuse of or reliance on medications for the management of ADHD.
  - FMEC heard from a guest specialist that comprehensive management of ADHD includes effective nonpharmacologic interventions. FMEC discussed and agreed with the need for improved access to these nonpharmacologic interventions for patients and families affected by ADHD.

Economic Considerations

- **FMEC concluded there are economic considerations that are important to address when implementing guanfacine XR as adjunct therapy to psychostimulants for ADHD.**
- FMEC members highlighted the following discussion points:

- At publicly available prices, the reimbursement of guanfacine XR as adjunct therapy to psychostimulants is expected to increase overall drug acquisition costs compared with all relevant comparators.
- Based on the available evidence, guanfacine XR as adjunct therapy may improve multiple clinical outcomes when compared to placebo plus a psychostimulant, with unknown benefit when compared to atomoxetine (monotherapy) or clonidine.
- The cost-effectiveness of guanfacine XR as adjunct therapy to psychostimulants compared with relevant comparators is unknown.
- Guanfacine XR is available as a generic drug in Canada and its cost is therefore subject to the pan-Canadian Pharmaceutical Alliance tiered pricing framework for generic drugs.

Impacts on Health Systems

- **FMEC did not identify any impacts on health systems that are important to address when implementing guanfacine XR as adjunct therapy to psychostimulants for ADHD.**
- FMEC members highlighted the following discussion points:
  - FMEC discussed that there may be a disparity in access to the diagnosis of ADHD, as a comprehensive evaluation and assessment may be costly and inaccessible to some individuals and their families. In addition, specialized nonpharmacologic care may not be accessible or affordable to individuals and their families.

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 related to guanfacine XR (refer to the Main Report and the Supplemental Material document)
- input from a person with lived experience who delivered a brief presentation and answered questions from the committee (refer to the Person With Lived Experience section earlier in this document)
- input from public drug programs that participate in the reimbursement review process (refer to the *FMEC Responses to Questions From the Drug Program* document)
- input from 2 clinical experts with expertise in the management of ADHD consulted by CDA-AMC
- a pilot data utilization analysis of guanfacine XR.

Feedback on Draft Recommendation

CDA-AMC received feedback from the public drug programs. The public drug programs agreed with the recommendation. The public drug programs requested editorial revisions to improve readability and clarity and for clarification regarding atomoxetine.

All feedback received in response to the draft recommendation is available on the CDA-AMC project web page.

FMEC Information

Members of the committee: Dr. Emily Reynen (Chair), Dr. Zaina Albalawi, Dr. Hardit Khuman, Ms. Valerie McDonald, Ms. Marilyn Barrett, Dr. Bill Semchuk, Dr. Jim Silvius, Dr. Marianne Taylor, Dr. Maureen Trudeau, and Dr. Dominika Wranik. Two guest specialists (clinical experts) from Ontario and British Columbia participated in this review.

Meeting date: November 20, 2025

Regrets: One guest specialist did not attend the meeting. While 2 clinical experts were consulted for the clinical and pharmacoeconomic report, 1 clinical expert was unable to attend the meeting.

Conflicts of interest: None

Special thanks: CDA-AMC extends special thanks to the individuals who presented directly to FMEC and to patient organizations representing and supporting the community of people living with ADHD, including Brooke Bradley and Sterling Bradley.

Note: CDA-AMC makes every attempt to engage with people with lived experience as closely to the indication and treatments under review as possible; however, at times, CDA-AMC is unable to do so and instead engages with individuals with similar treatment journeys or experience with comparators under review to ensure lived experience perspectives are included and considered in Reimbursement Reviews. CDA-AMC is fortunate to be able to engage with individuals who are willing to share their treatment journeys with FMEC.

ISSN: 2563-6596

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