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Reimbursement Recommendation

Guanfacine Extended Release

Reimbursement request: For monotherapy of ADHD in children and adolescents aged 6 to 17 years

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 monotherapy of attention-deficit/hyperactivity disorder (ADHD) in children and adolescents aged 6 years to 17 years, provided certain conditions are met.

What Are the Conditions for Reimbursement?

Guanfacine XR may be reimbursed for monotherapy of ADHD in children and adolescents aged 6 years to 17 years, provided they meet the following conditions: the individual has experienced intolerable adverse events with at least 1 amphetamine-based psychostimulant and 1 methylphenidate-based psychostimulant that require discontinuation, or the individual has contraindications to the use of 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 — specifically 1 systematic review with network meta-analysis comparing monotherapy oral medications (i.e., amphetamines, methylphenidate, modafinil, atomoxetine, clonidine, guanfacine, or bupropion) and placebo for the treatment of ADHD in children and adolescents. The review also included 3 long-term extension studies of guanfacine XR as monotherapy for the treatment of ADHD in children and adolescents and a drug cost comparison of guanfacine XR and other treatment options in Canada. No input from external partners was received for this review.

Evidence from the systematic review with network meta-analysis suggests that guanfacine XR used as monotherapy for the treatment of children and adolescents with ADHD may result in improvement in ADHD core symptoms assessed by clinicians compared with placebo. Guanfacine XR may result in less improvement in ADHD core symptoms compared with amphetamines, with little to no difference compared with atomoxetine or methylphenidate. Guanfacine XR is available as a generic drug in Canada.

While FMEC concluded there was uncertainty in the clinical value, FMEC agreed that guanfacine XR addressed significant unmet clinical needs. The reimbursement conditions were further developed based on distinct

Summary

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. An adequate trial of both classes of long-acting psychostimulants (methylphenidate and amphetamines) is recommended before engaging in a trial of a second-line treatment. Second-line options may include short-acting psychostimulants or nonstimulant options such as atomoxetine 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 for the treatment of ADHD in children aged 6 years to 12 years as monotherapy due to insufficient evidence to assess the comparative clinical benefit of guanfacine XR as monotherapy relative to other less costly treatments.

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 as monotherapy for the treatment of ADHD in children and adolescents aged 6 years to 17 years. This request was prompted by the

emerging availability of evidence over the past decade 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 as monotherapy for the treatment of ADHD in children and adolescents aged 6 years to 17 years. 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 8 to 1, FMEC recommends that guanfacine XR for monotherapy of ADHD in children and adolescents aged 6 years to 17 years 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 as monotherapy for the treatment of ADHD in children and adolescents aged 6 years to 17 years if any of the following conditions are met: 1.1. they have experienced significant or intolerable adverse events with at least 1 amphetamine-based psychostimulant and 1 methylphenidate-based psychostimulant that require discontinuation 1.2. they have contraindications to the use of psychostimulants.	There is evidence based on 1 systematic review with network meta-analysis comparing monotherapy options (including amphetamines, methylphenidate, modafinil, atomoxetine, clonidine, guanfacine, bupropion, or placebo) for the treatment of ADHD in children and adolescents and 3 long-term extension studies that showed continued benefits with guanfacine XR, such as improvements in ADHD core symptoms at 24 months with no important safety signal. Based on input from guest specialists, guanfacine XR may offer benefits in addressing an unmet clinical need, particularly by providing options for individuals who are unable to tolerate psychostimulants or who have contraindications to psychostimulants. Further, guanfacine XR may be used in addition to nondrug interventions for individuals with the hyperactive-impulsive subtype of ADHD or with irritability, disruptive behaviour, or anxiety.	Please refer to the contraindications for individual psychostimulants as per their product monographs and Canadian clinical practice guidelines. The use of guanfacine XR may be reassessed when the patient turns 18 years of age to determine if the benefits of continuing treatment outweigh any potential risks.
Discontinuation and renewal		
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 XR will be associated with higher drug acquisition costs than that of its comparators based on publicly available list prices. Based on the available evidence, the clinical effectiveness of guanfacine XR against its relevant comparators is uncertain. The cost-effectiveness of guanfacine XR 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 it is uncertain whether 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 improvements in ADHD core symptoms are 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 family.
- FMEC members highlighted the following discussion points:
  - **Efficacy versus placebo or indirect treatment comparisons.** Based on the network meta-analysis by Cortese et al. (2018) included in the review, guanfacine XR may result in a decrease in ADHD core symptoms and an increase in clinical global functioning as rated by clinicians compared with placebo. Guanfacine may result in smaller improvements in ADHD core symptoms compared with amphetamines, with little to no difference compared with atomoxetine or methylphenidate. FMEC discussed the limitations of the evidence, including the potential for intransitivity and that the evidence for all comparisons to active treatments used in clinical practice was uncertain.
  - **Clinical importance of treatment effects.** Based on these findings, FMEC discussed that guanfacine may be less effective than the usual first-line options of amphetamines or methylphenidate-based psychostimulants. FMEC noted the evidence is limited to indirect evidence in which guanfacine is compared with other available treatment options. FMEC also discussed that in current clinical practice guidelines in Canada, guanfacine XR is recommended as a second-line option for monotherapy of ADHD.
  - **Specific populations.** FMEC noted that while guanfacine XR may offer clinical value in specific patient populations (namely, those who choose not to pursue first-line pharmacologic treatment options with psychostimulants, those who have an intolerance to psychostimulants, and those for whom psychostimulants are contraindicated), it did not have evidence to review specific to these populations.

- For individuals who choose not to pursue first-line pharmacologic treatment options with psychostimulants, FMEC discussed the concern of recommending a potentially less effective treatment and the short- and long-term risks of worse outcomes with undertreatment. FMEC also heard from the guest specialists that undertreatment can lead to incomplete management of ADHD core symptoms and negatively affect social and educational functions. FMEC noted that treatment with guanfacine XR is not intended for individuals or parents who choose not to pursue first-line treatment options with psychostimulants. For these scenarios, nonpharmacologic interventions should be encouraged, which the guest specialist also supported.
- For individuals with an intolerance to first-line treatment options, FMEC discussed there are existing strategies to explore depending on the type of intolerance. Dose reduction is an option. Nonetheless, there will be scenarios in which individuals who are intolerant to first-line options may need to consider alternative options.
- For individuals who have contraindications to psychostimulants, FMEC discussed that the implications of absolute versus relative contraindications need to be understood. As per the current CADDRA *Canadian ADHD Practice Guidelines*, relative contraindications to psychostimulants include cardiac concerns but may also include precautions for use in patients with psychosis, bipolar disorder, or anxiety disorders. According to 1 guest specialist, the restricting subtype of anorexia nervosa would be a contraindication to the use of psychostimulants for the treatment of ADHD.

◦ **Importance of HRQoL and other outcomes.** FMEC also noted that evidence related to HRQoL is lacking and evidence generation related to child-specific HRQoL would be helpful for future assessments related to pharmacologic management of ADHD. FMEC discussed the importance of HRQoL data in this setting to consider how this treatment may improve HRQoL outcomes and potential benefits from the perspectives of patients and their caregivers. Further, outcomes related to individuals' abilities to participate in school, form meaningful social connections, and interact with peers and family are important outcome measures for ADHD treatments.

◦ **Evidence generation is needed.** FMEC discussed that the evidence available is limited to indirect treatment comparisons. There is a need for additional research through direct comparison of guanfacine XR with other drugs, including psychostimulants, which would provide higher-quality evidence to inform guanfacine's role in ADHD as a monotherapy for this pediatric population. 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).

Unmet Clinical Need

- **FMEC concluded that there is a significant unmet 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 discussed potential scenarios in which individuals with intolerance of or contraindications to psychostimulants may require nonstimulant treatment options for ADHD. Currently, nonstimulant pharmacologic treatment options are guanfacine XR, atomoxetine, or clonidine, although clonidine is rarely used in practice.
  - **Severity of the disease.** ADHD may lead to long-term morbidities such as difficulties with social relationships and negative effects on employment and career prospects. Effective treatment of core symptoms would potentially have a positive benefit on life-course development; however, the evidence presented focused on core symptoms and did not evaluate outcomes related to life-course development.
  - **Significant unmet clinical need.**
    - FMEC also heard from the guest specialists that guanfacine XR may offer synergistic benefits with nonmedication interventions, particularly in individuals with the hyperactive-impulsive subtype of ADHD, with irritability, disruptive behaviour, or anxiety. In these scenarios, the guest specialists indicated that the use of guanfacine along with parental or family intervention can be very helpful.
    - FMEC also heard from 1 guest specialist that while monotherapy with psychostimulants has demonstrated benefits for the treatment of ADHD, our 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. For individuals who may have genetic predispositions that explain a lack of disease response to psychostimulants, a nonstimulant treatment option such as guanfacine XR may be a treatment option.
    - FMEC agreed that there is an unmet clinical need for patients who have experienced substantial or intolerable adverse events with at least 1 amphetamine-based psychostimulant

and 1 methylphenidate-based psychostimulant that require discontinuation, and for patients who have contraindications to the use of psychostimulants.

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 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 when 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 their ability to learn is affected). Guanfacine XR may help address these nonclinical needs.
  - FMEC discussed that while treatment of ADHD may be associated with stigma, the choice of drug treatment does not change this. That said, there may be ethical implications related to individuals and families choosing a less effective treatment option. FMEC discussed that there is a delicate balance between respecting a patient's treatment choice and advocating for the most effective treatment option.
  - FMEC also discussed 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 the 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 monotherapy for ADHD.**
- FMEC members highlighted the following discussion points:
  - At publicly available prices, the reimbursement of guanfacine XR as monotherapy is expected to increase overall drug acquisition costs compared with all relevant comparators.

- Based on the available evidence, the clinical effectiveness of guanfacine XR as monotherapy versus its relevant comparators is uncertain.
- The cost-effectiveness of guanfacine XR as monotherapy versus 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 monotherapy 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 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 of 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 minor editorial revisions to improve readability and clarity, as well as minor corrections to punctuation and formatting.

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: Canada's Drug Agency (CDA-AMC) extends special thanks to the individuals who presented directly to FMEC and to patient organizations representing and supporting the community of those 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 journey with FMEC.

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Questions or requests for information about this report can be directed to Requests@cda-amc.ca.