Reimbursement Recommendation

Mepolizumab

Reimbursement request: For the treatment of eosinophilic granulomatosis with polyangiitis, with or without oral corticosteroids and/or immunosuppressive therapy

Requester: Public drug programs

Recommendation: Reimburse with conditions

Summary

The Formulary Management Expert Committee (FMEC) recommends that mepolizumab should be reimbursed for individuals diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA), provided certain clinical conditions are met.

FMEC reviewed 2 phase III, randomized, double-blind trials: the MIRRA trial and the MANDARA trial. FMEC concluded that mepolizumab meets unmet medical need and achieves important outcomes for persons with EGPA, specifically improved remission rates and reductions in oral corticosteroid (OCS) exposure.

In comparison with current treatment options, mepolizumab poses incremental costs to the health care system, and the cost-effectiveness is presently unknown.

Therapeutic Landscape

What Is Eosinophilic Granulomatosis With Polyangiitis?

EGPA is a rare disease, characterized by asthma, vasculitis, and eosinophilia. Patients with EPGA experience acute relapses followed with periods of remission. Recurrent relapses increase the risk of end organ (e.g., heart, kidney) damage complications. As a result, treatment goals of EGPA are focused on achieving remission, preventing relapses, and minimizing other treatment-related harms.

Why Did We Conduct This Review?

This review was driven by the clinical need to provide an effective treatment option for patients with EGPA. The manufacturer of mepolizumab has previously declined to file through the reimbursement review process; therefore, publicly funded drug programs have requested a reimbursement review and recommendation.

Person With Lived Experience

A person with lived experience from urban Ontario was diagnosed with EGPA in April 2022, shortly after retiring. He described his symptoms initially manifested with respiratory issues and progressed to severe joint pain, acid reflux, weight loss, and nerve damage affecting mobility. Treatment began with high-dose IV prednisone followed by cyclophosphamide and later azathioprine. He highlighted concerns about the long-term toxicity and potential risks and expressed apprehension about the potential dependency on these drugs to maintain remission. Despite initial challenges, including severe nerve pain and mobility issues, he has responded well to treatment and is currently in remission. In March, he started mepolizumab at the lower dose of 100 mg to ensure coverage to manage respiratory symptoms, noting a benefit in stabilizing his condition without observable adverse effects. He views mepolizumab as a promising alternative to traditional treatments, emphasizing its potential for long-term use and reduced toxicity risks for patients living with EGPA.

Input From Community Partners

What Did We Hear From Persons Living With EGPA?

One patient group noted that patients with EGPA frequently experience lengthy hospitalizations and require high-dose IV steroids and immunosuppressants to induce remission. Most patients remain on maintenance therapy (e.g., prednisone). Patients wish to reduce the need for repeated steroid treatments to mitigate toxicity and long-term side effects. They wish to have equitable access to treatments.

What Did We Hear From Clinicians?

Clinicians emphasized the lack of approved treatments for EGPA in Canada. Current treatments are insufficient for individuals with refractory eosinophilic symptoms requiring high-dose glucocorticoids. Glucocorticoids are also associated with both short-term and long-term complications. Clinicians emphasized that individuals with EGPA often continue to experience sinopulmonary symptoms that worsen health-related quality of life.

What Did We Hear From the Pharmaceutical Industry?

One industry group noted that treatment for EGPA is tailored based on symptom severity; individuals with more severe disease receive more intense immunosuppressive agents. Glucocorticoids are the foundation in the standard of care for EGPA. Industry highlighted similar concerns as those raised by persons living with EGPA and treating clinicians.

What Did We Hear From Public Drug Programs?

Public drug plans inquired about considerations for initiation, continuation, and duration of therapy.

► Refer to the Input section of the full report.

Deliberation

With a unanimous vote of 6 to 0, FMEC concluded that mepolizumab at a dosage of 300 mg every 4 weeks addresses several unmet needs and achieves important outcomes for persons with EGPA, specifically improved remission rates and reduced OCS exposure. Mepolizumab represents incremental costs to the health care system, and the cost-effectiveness of this intervention is presently unknown.

FMEC deliberated on the following domains as illustrated in the deliberative framework:

- Clinical value: Whether the drug under review provides clinical value.
- Unmet clinical need: Whether there is an unmet clinical need that available treatment(s) is/are not currently addressing.
- Comparable efficacy: Whether the drug under review shows at least similar efficacy to other available treatment(s) for the condition.
- Patient perspective: Whether the drug under review addresses patients' specific unmet needs and values.
- Economic implications: What are the economic implications of reimbursing the drug under review based on public list prices.
- Health system and social considerations: Whether there are health system or social considerations (e.g., administration, testing, equity, access, ethical) for the drug under review.

Decision Summary

Table 1: Why Did FMEC Make This Recommendation?

Domains	Reason
Patient perspective: Whether the drug under review addresses patients' specific unmet needs and values.	• FMEC agreed that mepolizumab meets some unmet needs and achieves important outcomes identified by persons with EGPA, such as providing an effective treatment for management of acute symptoms of EGPA and reducing the risks associated with OCS and immunosuppressive therapies. • The committee also expressed a desire to reduce the risks of end organ damage, which was identified as an important patient need. However, the clinical trials for mepolizumab, namely the MIRRA and MANDARA trials which were considered during the deliberative process, did not address this outcome, nor did they include long-term evaluations (past 52 weeks) required for assessing chronic complications. • Clinical experts and patients shared that, from their experience, persons with EGPA under treatment particularly value the reduction in steroid use, which can be associated with serious adverse events.
Clinical value: Whether the drug under review provides clinical value.	• Based on the MIRRA and MANDARA trials, FMEC concluded that mepolizumab improves remission rates while also reducing steroid exposure compared to placebo. • FMEC also highlighted the exclusion of organ-threatening or life-threatening EGPA within 3 months prior to screening in both the MIRRA and MANDARA trials and the lack of long-term data to inform mepolizumab's long-term effectiveness and ability to prevent end organ damage. • The committee noted that some included patients did not benefit from the treatment. It is important to identify the characteristics of these patients and understand how they differ in terms of eligibility for treatment as well as their response or lack of response to treatment with mepolizumab. • Given the rarity of the disease, FMEC concluded that there should be greater allowance for uncertainty with the clinical evidence.
Unmet clinical need: Whether there is an unmet clinical need that available treatment(s) is/are not currently addressing.	• FMEC discussed that the severe condition of EGPA with life-threatening implications and available treatments including standard of care and immunosuppressive therapies are inadequate. • FMEC also highlighted that mepolizumab has a different harm profile than current therapy and might lead to better tolerance for patients. • Current treatments are not effective for all patients in inducing or sustaining remission and may often require prolonged treatment, which presents with a range of adverse effects. • Although rare, EGPA presents with disease heterogeneity, manifesting a spectrum of adverse effects. Asthma and respiratory issues are of primary concern that often drive treatment decisions. However, issues with the heart, kidneys, and nervous system, may bear more long-term effects and consequence to the health and quality of life.
Comparable efficacy: Whether the drug under review shows at least similar efficacy to other available treatment(s) for the condition.	• FMEC agreed that mepolizumab demonstrates an improved effect on EGPA outcomes compared to available therapies, including total accrued weeks of remission, proportion of patients in remission, OCS dosing considerations, and time to first relapse.
Health system and social considerations: Whether there are health system or social considerations for the drug under review.	• FMEC discussed that the clinician input received highlighted that some patients in Canada who receive mepolizumab receive reimbursement from private drug insurance, which reflects inequity in access across Canada.

Domains	Reason
Economic implications: What are the economic implications of reimbursing the drug under review based on public list price.	• The committee noted that using publicly available pricing information, mepolizumab is more costly than OCS and immunosuppressive therapies. Consequently, mepolizumab results in incremental costs relative to all relevant comparators. • The committee observed that a comprehensive economic assessment would need to consider potential cost savings and impact on health-related quality of life over a lifetime, taking into account efficacy and the prevention of adverse events associated with standard of care treatments. However, the lack of robust clinical evidence reduces the feasibility of conducting a cost-effectiveness analysis. The absence of evidence for long-term treatment benefits of mepolizumab beyond 52 weeks limits the availability of data needed to assess its cost-effectiveness.

EPGA = eosinophilic granulomatosis with polyangiitis; FMEC = Formulary Management Expert Committee; OCS = oral corticosteroid.

Reconsideration Request From Public Drug Programs

- A subpanel of FMEC members was convened to address implementation considerations highlighted by public drug programs. Both patient groups and industry also had the opportunity to provide their comments as part of the reconsideration requested by the public payors.
- The FMEC subpanel discussed the initiation criteria for mepolizumab and made revisions to improve clarity, including allowing patients on glucocorticoids at an equivalent dose to be eligible. In addition, the FMEC subpanel added the relapsing and refractory EGPA definition from the MIRRA trial to provide guidance on implementation. The FMEC subpanel also emphasized that patients must meet the relapsing and refractory EGPA definition and be receiving prednisone as outlined in the Table 1 to qualify for mepolizumab.
- The FMEC subpanel discussed the discontinuation and renewal criteria. The initial recommended reimbursement period was changed from 26 weeks to 6 months as proposed by public drug programs. The reimbursement renewal period of every 6 months was added. It was also discussed that clinical improvement must be demonstrated as evidenced by a reduction in the dosing of concomitant OCS as described in Table 2 to qualify for renewal.
- The FMEC subpanel discussed the prescribing and cost conditions and concluded that no change is required.

Full Recommendation

With a unanimous 6 to 0 vote, FMEC recommends that mepolizumab be conditionally reimbursed for the treatment of adult persons with EGPA if the conditions presented in Table 2 are met.

Table 2: Conditions, Reasons, and Guidance

Reimbursement condition	Reason	Implementation guidance
Initiation		
Mepolizumab should be reimbursed in persons with a diagnosis of EGPA and who meet the following conditions: • have relapsing or refractory EGPA and are at least 6 months since the last flare • receiving prednisone at a dose of 7.5 mg/day or higher, or another glucocorticoid at equivalent dose, with or without additional immunosuppressive therapies (i.e., azathioprine or methotrexate).	Treatment with mepolizumab should be reimbursed for persons with EGPA whose disease characteristics are consistent with those of patients included in the MIRRA clinical trial. The initiation criteria reflect current practice.	Treatment with mepolizumab should be reimbursed for patients with EGPA whose disease characteristics are consistent with those of patients included in the MIRRA clinical trial. Relapsing and refractory EGPA is defined as having active vasculitis (BVAS greater than 0), active asthma symptoms, and other criteria as specified in the MIRRA trial.
Discontinuation and renewal		
Mepolizumab should be discontinued after a trial of 6 months of therapy if there is no clinical improvement as demonstrated by 1 of the following: • inability to reduce the daily dosage of prednisone to less than 7.5 mg per day, or another glucocorticoid at an equivalent dose • inability to have a clinically significant reduction in the daily maintenance dosage of OCS. Therapy with mepolizumab should be reviewed every 6 months.	Treatment should be continued for 6 months, at which time effectiveness should be assessed. Expert opinion suggests that mepolizumab therapy must demonstrate a benefit and/or clinical improvement as evidenced by a clinically significant reduction in the dosing of concomitant OCS to qualify for renewal. The recurrent need to increase or resume oral corticosteroid therapy constitutes a treatment failure according to the clinical experts.	Clinically significant reduction of the maintenance oral corticosteroid dose as determined by the prescribing clinical specialist in consultation with the patient.
Prescribing		
Mepolizumab must be initiated by a clinician with expertise in the management of EGPA.	Persons with EGPA are expected to be under the care of an experienced clinical team to address the complexity of treatment, maximize potential benefits, and mitigate adverse events.	—
Cost		
A price reduction may be required.	Based on publicly available pricing information, mepolizumab is more costly than OCS and immunosuppressive therapies, leading to incremental costs to the health care system. The cost-effectiveness of mepolizumab relative to SOC is currently unknown. Because of the degree of uncertainty and price of mepolizumab relative to SOC, a price reduction may be required.	—

BVAS = Birmingham Vasculitis Activity Score; EGPA = eosinophilic granulomatosis with polyangiitis; OCS = oral corticosteroid; SOC = standard of care.

Feedback on Draft Recommendation

Vasculitis Foundation Canada, GlaxoSmithKline, and the drug plans provided feedback on the draft recommendation. The drug plans requested a minor reconsideration of the reimbursement conditions to help with implementation, specifically requesting clarity around criteria to initiate treatment as well as discontinuation and renewal criteria. Both Vasculitis Foundation Canada and GlaxoSmithKline have also expressed some concerns for the prescribing conditions and provided other editorial suggestions on the report. As such, a subcommittee panel met to discuss all feedback and to revise the reimbursement conditions, as described in Table 2.

FMEC Information

Members of the committee: Dr. Emily Reynen (Chair), Dr. Alun Edwards, Ms. Valerie McDonald, Dr. Jim Silvius, Dr. Marianne Taylor, Dr. Maureen Trudeau, Dr. Dominika Wranik, and 2 guest clinical immunology, rheumatology, and internal medicine expert specialists from Ontario and Alberta.

Meeting date: July 4, 2024

Reconsideration meeting date: October 9, 2024

Conflicts of interest: None

Special thanks: Canada's Drug Agency extends our special thanks to the individuals who presented directly to FMEC on behalf of people with lived experience and to the patient organizations representing the community of those living with EGPA, notably Vasculitis Foundation Canada, which includes Jon Stewart and Craig Taylor.

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