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

# Mepolizumab

## Formulary Management Expert Committee Responses to Drug Programs' Questions

### Table 1: Response Summary

| Drug program implementation questions | Clinical expert response | FMEC response |
|---|---|---|
| **Considerations for relevant comparators** | | |
| Mepolizumab is the only IL-5 with the HC-approved indication for treatment of EGPA. Is there evidence to suggest other IL-5 inhibitors (benralizumab, reslizumab) are effective for the treatment of EGPA? | In the recently published MANDARA trial, benralizumab was found to be noninferior to mepolizumab for remission at 36 and 48 weeks, as well as accrued duration of remission and time to first relapse. Both groups also experienced a reduction in oral corticosteroid use during the trial. However, benralizumab is not currently indicated for EGPA in Canada.<br><br>There is no RCT evidence for the use of Cinqair in patients with EGPA. | FMEC defers to the experts. |
| **Policy considerations for reimbursing the drug** | | |
| When is it appropriate to add mepolizumab therapy to corticosteroids? At what stage in the disease process should mepolizumab be added to the treatment regimen for EGPA? | Mepolizumab should be added to corticosteroids for severe EGPA, such as those with neurological or cardiac disease. Patients would receive cyclophosphamide or rituximab induction therapy to induce remission, and mepolizumab could then be used for maintenance of remission. | Refer to the initiation criteria for mepolizumab for more information. |
| What is the anticipated duration of therapy for mepolizumab for EGPA? Is this long-term therapy? Do drug plans have quantity limits in place to limit dosing to those appropriate for asthma? | The anticipated duration of therapy for mepolizumab for EGPA is suggested to be long-term, potentially extending beyond 5 years, based on the need to maintain EGPA remission and minimize the use of corticosteroids. The experts highlighted that stopping mepolizumab after 1 year tends to lead to a loss of benefits within 3 months, indicating the necessity for prolonged treatment.<br><br>Patients may experience partial responses to the lower dosage (100 mg every 4 weeks compared to the recommended dosage of 300 mg every 4 weeks for EGPA), which may be insufficient for optimal management of EGPA. The lower dose is being investigated after a patient has been stable on mepolizumab for at | FMEC agrees that long-term therapy may be necessary for certain conditions, although the feasibility of downward dosage titration remains unknown. |

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| | least 2 years, but this is in the early stages of evaluation. It is too early to recommend reducing the dose of mepolizumab after 2 years.<br><br>Patients require a trial of 6 months to determine if mepolizumab is effective. If patients have not experienced an adequate response by 6 months, the clinical expert stated that they would discontinue mepolizumab and switch to another biologic such as benralizumab. | |
| Standard of care in the clinical trial was glucocorticoids with or without immunosuppressive therapy. Are there other therapies that should be trialled (other than steroids) before mepolizumab for treatment of EGPA? | Corticosteroids and immunosuppressive therapies are the only currently available therapies for EGPA; however, the clinical experts noted that immunosuppressive therapies such as azathioprine are often ineffective and offer no benefit for eosinophilic asthma. For patients with severe EGPA, they would first need cyclophosphamide or rituximab induction therapy to induce remission, then they could be started on mepolizumab for maintenance of remission. | FMEC acknowledges the response from the experts. However, it was noted that not all trial participants were receiving immunosuppressive therapy in the MIRRA and MANDARA trials (the number was lower in the MANDARA trial). |
| How is loss of response to mepolizumab in EGPA defined? | Loss of response would be based on EGPA relapse, including the need for corticosteroids (initiating in those who were not using corticosteroids or increasing the dose), symptoms of vasculitis, asthma, and/or sinonasal disease, or the need for an increase in immunosuppressive therapy. | FMEC agrees with the experts regarding the loss of response consideration. Difficulty in the assessment of the lack of initial response was noted as more challenging to determine.<br><br>Refer to the discontinuation and renewal criteria for additional information. |
| Are patients able to discontinue treatment with mepolizumab for EGPA? | If mepolizumab is stopped before 5 years of use, most patients will experience an EGPA relapse. The clinical expert also noted that there is early evidence that some patients who have been maintained on mepolizumab for more than 5 years may be able to discontinue therapy without experiencing relapse; however, it is unclear at this time which patients will not experience a relapse after discontinuation. | The lack of long-term evidence limits the answer to this question.<br><br>Refer to the discontinuation and renewal criteria for additional information. |

EGPA = eosinophilic granulomatosis with polyangiitis; FMEC = Formulary Management Expert Committee; HC = Health Canada; IL-5 = interleukin-5; RCT = randomized controlled trial.