

# Drug Coverage Decision for B.C. PharmaCare

## About PharmaCare

B.C. PharmaCare is a government-funded drug plan. It helps British Columbians with the cost of eligible prescription drugs and specific medical supplies.

## Details of Drug Reviewed

<b>Drug</b>	<b>mepolizumab</b>
Brand Name	<b>Nucala™</b>
Dosage Form(s)	lyophilized powder for subcutaneous injection
Manufacturer	GlaxoSmithKline Inc.
<b>Submission Type</b>	<b>New Submission</b>
Use Reviewed	Asthma
Common Drug Review (CDR)	Yes, CDR recommended: <b>to Reimburse with clinical criteria and/or conditions</b> . Visit the CDR website for more details: <a href="http://www.cadth.ca/sites/default/files/cdr/complete/SR0461_complete_Nucala_June-20-16_e.pdf">www.cadth.ca/sites/default/files/cdr/complete/SR0461_complete_Nucala_June-20-16_e.pdf</a>
Drug Benefit Council (DBC)	DBC met on July 4, 2016. DBC considered various inputs including: clinical and pharmacoeconomic evidence review material and the recommendation from the Canadian Drug Expert Committee (CDEC). DBC also considered Clinical Practice Reviews from two specialists. The DBC received no Patient Input Questionnaire responses from patients, caregivers, or Patient Groups.
<b>Drug Coverage Decision</b>	<b>Limited Coverage Benefit</b> . Access the mepolizumab criteria from: <a href="http://www.gov.bc.ca/pharmacarespecialauthority">www.gov.bc.ca/pharmacarespecialauthority</a>
Date	November 13, 2018
Reasons	<b>Drug coverage decision is consistent with the DBC recommendation. See complete DBC Recommendation and Reasons below.</b> <ul style="list-style-type: none"> <li>Two double blind randomised controlled trials demonstrated that mepolizumab reduced the rate of clinically significant exacerbations, daily oral corticosteroids dose, and improved quality of life compared to placebo.</li> <li>At the submitted price mepolizumab was not considered cost-effective by DBC.</li> <li>BC participated in the pan-Canadian Pharmaceutical Alliance (pCPA) negotiations with manufacturer and an agreement was reached.</li> </ul>
Other Information	None

**Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation**  
**FINAL**  
**Mepolizumab (Nucala®)**  
**GlaxoSmithKline Inc.**

**Description**

Drug review of mepolizumab (Nucala®) for the following Health Canada approved indication:

For the treatment of severe eosinophilic asthma.

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on June 16, 2016, which included clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Drug Expert Committee (CDEC). The DBC also considered CDR Patient Group input, Clinical Practice Reviews from two specialists, and a Budget Impact Assessment. The DBC received no Patient Input Questionnaire responses from patients, caregivers, or Patient Groups.

**Dosage Forms**

Nucala® is available as mepolizumab 100 mg/mL lyophilized powder for subcutaneous (SC) injection.

**Recommendations**

The Drug Benefit Council (DBC) recommends that mepolizumab (Nucala®) not be listed at the submitted price.

**Reasons for the Recommendation**

**1. Summary**

- Two phase 3, multi-centre, double-blind, placebo-controlled randomized controlled trials (RCTs) provided evidence mepolizumab was associated with a statistically significant reduction in the rate of clinically significant exacerbations, a greater likelihood of a reduction in daily oral corticosteroids (OCS) dose, and improvements in quality of life compared to placebo.
- At the manufacturer submitted price, the annual cost of mepolizumab is very high.

**2. Clinical Efficacy**

- The DBC considered the CDR systematic review, which included two phase 3, multi-centre, double-blind, placebo-controlled RCTs. MENSA was a 32-week study that evaluated the efficacy and safety of mepolizumab SC administration at 100 mg and mepolizumab intravenous (IV) administration at 75 mg once every 4 weeks as adjunctive therapy in patients with severe eosinophilic asthma. The primary end point was the rate of clinically significant exacerbations at week 32. Secondary end points included the change from baseline in pre-bronchodilator forced expiratory volume in one second (FEV1) and the change from baseline in St. George's Respiratory Questionnaire (SGRQ) at week 32.
- SIRIUS was a 24-week corticosteroid sparing study that evaluated the effect of mepolizumab SC 100 mg once every 4 weeks in reducing OCS use in patients with severe eosinophilic asthma. The primary end point was the percentage reduction of OCS dose during weeks 20 to 24 compared with baseline dose, while maintaining asthma control. Secondary end points included the proportion of patients achieving specific OCS dose reductions and median percentage reduction in OCS dose from baseline. Both studies enrolled patients at least 12 years of age with documented asthma who met specific peripheral blood eosinophil counts and were treated with high-dose inhaled corticosteroids (ICS) and an additional controller medication.

- Results from MENSA suggested that mepolizumab is associated with a statistically significant reduction in the rate of clinically significant asthma exacerbations compared to placebo in patients currently on high-dose ICS and an additional asthma controller who meet screening eosinophil criteria of  $\geq 150$  cells/ $\mu\text{L}$  at screening or  $\geq 300$  cells/ $\mu\text{L}$  in the past year. There was a statistically significantly greater improvement in SGRQ total score at week 32 in the mepolizumab group compared with the placebo group.
- Results from SIRIUS suggested that mepolizumab is associated with a greater likelihood of a reduction in daily OCS dose compared to placebo in patients with SEA who were taking OCS at a dose of 5 to 35 mg per day. There was a greater improvement in SGRQ total score at week 24 in the mepolizumab group compared with the placebo group.
- For detailed information on the systematic review of mepolizumab, please see the CDEC Final Recommendation at: [https://www.cadth.ca/sites/default/files/cdr/complete/SR0461\\_complete\\_Nucala\\_June-20-16\\_e.pdf](https://www.cadth.ca/sites/default/files/cdr/complete/SR0461_complete_Nucala_June-20-16_e.pdf).

### 3. Safety

- In both MENSA and SIRIUS, the number of patients reporting an adverse event (AE) was similar in the mepolizumab and placebo groups. Common AEs included nasopharyngitis, headache, upper respiratory tract infections, asthma, sinusitis, bronchitis, and fatigue.
- In both trials, the proportion of patients reporting a serious adverse event (SAE) was higher in the placebo groups compared with the mepolizumab groups.
- In MENSA, one patient in the mepolizumab group and four patients in the placebo group withdrew due to an adverse event. In SIRIUS, three patients in each group withdrew due to an adverse event.
- Injection site reactions occurred infrequently, but were numerically more common in the mepolizumab group compared with the placebo group. All injection site reactions were reported as mild or moderate in intensity. Systemic allergic reactions were infrequent and balanced across the mepolizumab and placebo groups in both trials.
- For detailed information on the safety and tolerability of mepolizumab, please see the CDEC Final Recommendations at the link above.

### 4. Economic Considerations

- At manufacturer submitted prices, the annual cost of mepolizumab is slightly less than that of omalizumab. Because omalizumab is not a PharmaCare benefit, adding mepolizumab to the formulary would be a significant cost impact.
- The CDR reanalysis of the manufacturer submission found an incremental cost-effectiveness ratio (ICER) for mepolizumab plus standard of care (SOC) versus SOC alone was \$521,000 per quality-adjusted life year (QALY). A price reduction of 80% and 89% would be required for mepolizumab plus SOC to achieve ICERs of \$100,000 per QALY and \$50,000 per QALY, respectively, versus SOC alone.

### 5. Of Note

- The DBC received no Patient Input Questionnaire responses from patients, caregivers, or Patient Groups. Patient group input submissions received by the CDR emphasized that severe eosinophilic asthma significantly limits patient daily activities and exercise, and significantly interferes with social activity, including school and work attendance. Half of the patients surveyed had visited an emergency room in the previous year, one third more than once, and one fifth had been hospitalized. Many patients reported having tried all available treatment options. Many patients reported not filling prescriptions or skipping doses due to the cost of medications. Patients wanted a new medication to reduce asthma exacerbations, reduce airway symptoms, and reduce their use of corticosteroids.

### The Drug Review Process in B.C.

A manufacturer submits a request to the Ministry of Health (Ministry).

An independent group called the [Drug Benefit Council \(DBC\)](#) gives advice to the Ministry. The DBC looks at:

- whether the drug is safe and effective
- advice from a national group called the [Common Drug Review \(CDR\)](#)
- what the drug costs and whether it is a good value for the people of B.C.
- ethical considerations involved with covering or not covering the drug
- input from physicians, patients, caregivers, patient groups and drug submission sponsors

The Ministry makes PharmaCare coverage decisions by taking into account:

- the existing PharmaCare policies, programs and resources
- the evidence-informed advice of the DBC
- the drugs already covered by PharmaCare that are used to treat similar medical conditions
- the overall cost of covering the drug

Visit the [The Drug Review Process in B.C. - Overview](#) and [Ministry of Health - PharmaCare](#) for more information.

**This document is intended for information only.**

It does not take the place of advice from a physician or other qualified health care provider.