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

Drug	**nintedanib**
Brand Name	Ofev®
Dosage Form	100 mg and 150 mg oral capsule
Manufacturer	Boehringer Ingelheim (Canada) Ltd.
Submission Type	**New Submission**
Use Reviewed	For the treatment of Chronic Fibrosing Interstitial Lung Diseases (ILDs) with a Progressive Phenotype also known as progressive fibrosing ILD (PF-ILD) or progressive pulmonary fibrosis (PPF).
Common Drug Review (CDR)	Yes, CDR recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CDR website for more details: https://www.cadth.ca/sites/default/files/attachments/2021-07/SR0654%20Ofev%20-%20Final%20CDEC%20Recommendation%20February%2026%2C%202021_For%20Posting.pdf
Drug Benefit Council (DBC)	The DBC met on March 1, 2021. In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on February 24, 2021, which included clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Drug Expert Committee (CDEC). The DBC also considered Patient Input Questionnaire responses from 49 Patients, 17 Caregivers, and 3 Patient Groups, patient input provided to the CDR, a Clinical Practice Review from a specialist, and a Budget Impact Assessment.
Drug Coverage Decision	**Limited Coverage Benefit** **Access the nintedanib criteria from www.gov.bc.ca/pharmacarespecialauthority**

Date	**June 7, 2022**
Reasons	**Drug coverage decision is consistent with the CDEC recommendation but is inconsistent with the DBC recommendation.** • In one double-blind, randomized, placebo-controlled trial of patients with PF-ILD treatment with nintedanib was associated with a slower annual rate of decline in forced vital capacity (FVC) compared with placebo in patients with PF-ILD. • Based on this trial results, CDEC recommended covering the medication with criteria but on the condition that the cost not exceed best supportive care (BSC). BSC was assumed to consist of immunosuppressant therapy. The trials showed no statistically significant differences between nintedanib and placebo in mortality or quality of life related outcomes. Therefore, the DBC recommended that this drug not be listed. • Based on economic considerations and the submitted product price, the drug was not cost-effective and did not offer optimal value for money. • The Ministry participated in the pan-Canadian Pharmaceutical Alliance (pCPA) negotiations with the manufacturer of nintedanib and the participating jurisdictions were able to reach an agreement with the manufacturer. • Considering the improvements observed on pulmonary function outcomes in clinical studies, the severity of the disease, the unmet clinical need and the agreement that was reached between the manufacturer and the pCPA, the decision was made to list nintedanib as a Limited Coverage benefit for the treatment of PPF or PF-ILD.
Other Information	None

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 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.

Appendix

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

Nintedanib (Ofev)
Boehringer Ingelheim Canada Inc.

Description:

Drug review of **nintedanib (Ofev)** for the following Health Canada approved indications:

> For the treatment of adult patients with other chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype (also known as progressive fibrosing ILD) [PF-ILD].

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on February 24, 2021, which included clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Drug Expert Committee (CDEC). The DBC also considered Patient Input Questionnaire responses from 49 Patients, 17 Caregivers, and 3 Patient Groups, patient input provided to the CDR, a Clinical Practice Review from a specialist, and a Budget Impact Assessment.

Dosage Forms:

Ofev is available as nintedanib 100 mg and 150 mg capsules.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list nintedanib (Ofev) for the treatment of PF-ILD.

Reasons for the Recommendation:

1. Summary

- In one double-blind, randomized, placebo-controlled trial of patients with PF-ILD treatment with nintedanib was associated with a slower annual rate of decline in forced vital capacity (FVC) compared with placebo in patients with PF-ILD.
- There was no statistically significant decrease in mortality between nintedanib and placebo or in the combined end point of acute interstitial lung disease exacerbation or death in the trial.
- There were no statistically significant differences in health-related quality of life (HRQoL) between nintedanib and placebo.
- Gastrointestinal effects, particularly diarrhea, were common in the nintedanib group and led to a higher percentage of patients who discontinued treatment.

- A higher percentage of patients treated with nintedanib experienced elevated liver enzymes, increased bilirubin, and serious drug-induced liver injury compared to placebo.
- The decision of the DBC to recommend not to list nintedanib followed a rigorous and complete and respectful discussion regarding the merits of arguments for and against listing before coming to this conclusion.

2. Clinical Efficacy

- The DBC considered the CDEC Clinical Review, which included one double-blind, randomized, placebo-controlled trial of patients with PF-ILD. INBUILD was a 52-week study that compared nintedanib 150 mg twice daily to matched placebo in 663 patients.
- INBUILD's primary outcome was annual rate of decline in forced vital capacity (FVC) over 52 weeks, expressed in milliliters. The main secondary outcomes included: change from baseline to week 52 in King's Brief Interstitial Lung Disease Questionnaire (K-BILD, a validated HRQoL measure); time to first acute ILD exacerbation or death over the 52 weeks; and time to death over 52 weeks.
- Limitations of INBUILD were the large number of patients who discontinued treatment in the nintedanib group (20%) compared with the placebo group (10%) by week 52.
- The 52-week study duration was not long enough to assess the impact of nintedanib on mortality, hospitalizations, and HRQoL, key outcomes for patients. An adequately powered trial with a longer term follow-up is likely required in order to demonstrate a survival benefit.
- Treatment with nintedanib was associated with a slower annual rate of decline in FVC compared with placebo in patients PF-ILD. The adjusted mean difference between groups in FVC at 52 weeks was 107 mL per year.
- Although decreases in percent predicted FVC are correlated with mortality in patients with interstitial lung diseases, it is unclear whether the mean difference in the annual rate of decline in FVC observed in INBUILD was clinically meaningful.
- INBUILD was a placebo-controlled trial, and there were no indirect comparisons available that compared nintedanib to other treatments for PF-ILD.
- A slower annualized decline in FVC over the 52 weeks, the primary outcome of INBUILD, was also seen in pre-defined subgroups of patients with UIP-like fibrosis on high resolution computed tomography (HRCT) and in those with other fibrotic patterns, although the latter subgroup was outside of the statistical hierarchy and should be viewed as supportive evidence only
- No long term extensions of INBUILD were available, and this limits any conclusions that can be drawn about the long term balance of efficacy and harms of nintedanib.
- For detailed information on the systematic review of nintedanib for PF-ILD, please see the CDEC Final Recommendation at: https://www.cadth.ca/nintedanib-0.

3. Safety

- Gastrointestinal effects, particularly diarrhea, were common in the nintedanib group (67% versus 24% with placebo) and led to a higher percentage of patients who discontinued treatment (7% with nintedanib versus less than 1% with placebo).
- A higher percentage of patients treated with nintedanib experienced elevated liver enzymes, increased bilirubin, and serious drug-induced liver injury.
- Drug-induced liver injury was categorized as a serious adverse event in 2% of patients in the nintedanib group and in no patients in the placebo group.

- For detailed information on the safety and tolerability of nintedanib, please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- The Canadian Agency for Drugs and Technologies in Health (CADTH) reanalysis of the sponsor-submitted economic model reported an incremental cost-effectiveness ratio (ICER) for nintedanib with best supportive care (BSC, assumed to consist of immunosuppressant therapy) compared with BSC alone of $154,688 per quality-adjusted life-year (QALY) gained.
- A price reduction of more than 77% for nintedanib would be required to achieve an ICER of $50,000 per QALY.
- CADTH was unable to validate the survival benefit modelled in the manufacturer's submission. In the CADTH scenario analysis where no survival benefit for nintedanib was assumed, the ICER for nintedanib plus BSC versus BSC alone increased to $317,832 per QALY gained.

5. Of Note

- The DBC considered Patient Input Questionnaire responses from 49 Patients, 17 Caregivers, and 3 Patient Groups. Patients indicated that PF-ILD is a debilitating, progressively worsening disease characterized by a breathing difficulties that leaves them unable to carry out activities of daily living and makes them dependent on assistance from caregivers. PF-ILD has a very high mortality rate.
- The physical deterioration from PF-ILD has a significant impact on the emotional and mental health and quality of life of patients and caregivers.
- Thirteen of forty-nine patients who completed the questionnaire reported trying nintedanib. Some, but not all, of the patients reported that treatment with nintedanib had slowed the progression of their PF-ILD. A few patients reported they discontinued nintedanib after experiencing side effects such as nausea and diarrhea.
- Patient with PF-ILD are usually prescribed multiple other drugs (e.g. mycophenolate, azathioprine, rituximab, or tocilizumab). Most patients reported these drugs either did not slow the progression or were hard to tolerate. Patient input indicated there is an unmet need for a drug that can either slow or halt disease progression.
- The DBC noted that nintedanib is the first drug approved for the treatment of PF-ILD.