Important Safety and Efficacy Information on IDHIFA® (Enasidenib Mesylate) – Market Withdrawal and Continued Access

Bristol Myers Squibb™

June 8, 2023

Audience
Healthcare professionals, including hematologists and hematologist-oncologists at hospitals and units specialized in the use of blood cancer treatments and community pharmacies currently dispensing Idhifa.

Key messages

- **IDHIFA will be withdrawn from the Canadian market on June 30, 2023.**
- **In 2019, IDHIFA (enasidenib mesylate) was authorized under a Notice of Compliance with conditions (NOC/c) for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with an isocitrate dehydrogenase-2 (IDH2) mutation.**
- **IDHIFA failed to demonstrate improved overall survival (OS) when compared to conventional care regimens in a Phase 3 confirmatory study. The safety profile remains unchanged.**
- **Healthcare professionals are advised to:**
    - **NOT initiate IDHIFA in new patients**
    - **Discuss with their patients whether to continue treatment with IDHIFA.**
    - **Apply to Health Canada's Special Access Program (SAP) to request IDHIFA for patients who require continued treatment.**

What is the issue?
IDHIFA failed to demonstrate improved OS in adult patients with late stage AML and an IDH2 mutation versus conventional care regimens in a Phase 3 confirmatory study evaluating efficacy and safety.

Do not initiate IDHIFA in new patients. IDHIFA is available through Health Canada's SAP for patients who require continued treatment.

Products affected
IDHIFA (enasidenib), 50 mg and 100 mg tablets

Background information
IDHIFA is an inhibitor of the IDH2 mutant enzyme. It is indicated for the treatment of adult patients with relapsed or refractory AML with an IDH2 mutation.

In 2019, IDHIFA was authorized under a NOC/c based on results from a Phase 2, open-label, single-arm, international, multicentre clinical trial of 105 adult patients with relapsed or refractory AML with an IDH2 mutation.

Continued authorization was contingent on verification of clinical benefit in a Phase 3, multicenter, open-label, randomized study (confirmatory study), comparing the efficacy and safety of IDHIFA versus conventional care regimens in older subjects with late stage AML and an IDH2 mutation. The Phase 3 confirmatory study did not demonstrate a statistically significant difference in the primary endpoint of OS.

At this time, the clinical benefit of IDHIFA for the treatment of adult patients with relapsed or refractory AML with an IDH2 mutation remains unconfirmed. The safety profile of IDHIFA remains unchanged. IDHIFA will be withdrawn from the Canadian market on June 30, 2023.

Information for consumers

IDHIFA is a prescription medicine used to treat acute myeloid leukemia (AML) in adults with a particular change (mutation) in the enzyme "IDH2". AML is a form of cancer which affects your bone marrow and can cause problems with producing normal blood cells.

IDHIFA was authorized with conditions based on promising evidence of clinical effectiveness following Health Canada's review. The manufacturer agreed to complete more studies to ensure that the drug works the way it was expected.

In a recent study, IDHIFA was given to patients whose AML came back (relapsed) or did not improve with another treatment (refractory). This study failed to show that IDHIFA prolonged the time these patients lived.

Patients should discuss any questions or concerns about this information with their healthcare professional. Patients should inform their healthcare professional if they are experiencing any side effects while receiving IDHIFA.

Information for healthcare professionals

IDHIFA will be withdrawn from the Canadian market on June 30, 2023.

Healthcare professionals are advised of the following:

- Do not initiate IDHIFA in new patients.
- Discuss this information with patients who are currently receiving IDHIFA and whether to continue their course of therapy. Consider providing 60 days of therapy to any patients continuing treatment to allow for transition to the SAP program.
- Apply to Health Canada's SAP to request IDHIFA for patients who require continued treatment.

Action taken by Health Canada
Health Canada is communicating this important information to healthcare professionals and Canadians via the Recalls and Safety Alerts Database on the Healthy Canadians Web Site. This communication will be further distributed through the MedEffect™ e-Notice email notification system, as well as through social media channels, including LinkedIn and Twitter.

Report health or safety concerns
Managing marketed health product-related side effects depends on healthcare professionals and consumers reporting them. Any case of serious or unexpected side effects in patients receiving IDHIFA should be reported to Celgene Inc., a Bristol-Myers Squibb company or Health Canada.

Celgene Inc., a Bristol-Myers Squibb company
2344 Alfred-Nobel Blvd
Suite 300
Saint-Laurent, QC
H4S 0A4

To correct your mailing address or fax number, contact Celgene Inc., a Bristol-Myers Squibb company.

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax.

For other health product inquiries related to this communication, contact Health Canada at:

Pharmaceutical Drugs Directorate
E-mail: pharma_drug_enquiries-renseignements_medicaments_pharma@hc-sc.gc.ca
Telephone: 613-957-0368
Fax: 613-952-7756

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Celgene Inc., a Bristol-Myers Squibb company