Important Safety Information on BENVYON (Bendamustine Hydrochloride for Injection) concentrated solution dosage and administration

26 January 2023

Audience
Healthcare professionals including physicians, pharmacists, nurses and oncologists.

Key messages

- **BENVYON (Bendamustine Hydrochloride for Injection) was authorized by Health Canada. BENVYON is indicated for treatment of patients with relapsed indolent B-cell non-Hodgkin lymphoma (NHL) who did not respond to or progressed during or shortly following treatment with a rituximab regimen and symptomatic chronic lymphocytic leukemia (CLL) who have received no prior treatment.**
- **Healthcare professionals are advised that BENVYON is a concentrated formulation and must be diluted directly in infusion solution before administration. There is no reconstitution for BENVYON.**
- **Dosing information is available in the Canadian Product Monograph (CPM). The CPM is available in French and English on Health Canada's Drug Product Database or at pfizer.ca.**

What is the issue?
BENVYON (Bendamustine Hydrochloride for Injection) was authorized by Health Canada on January 14, 2022. BENVYON is a concentrated formulation and must be diluted directly in infusion solution before administration. This risk communication is to mitigate any potential dosing errors since there is no reconstitution for BENVYON.

Products affected
Bendamustine Hydrochloride for Injection 25 mg/mL, sterile solution, intravenous
(in vials containing 25 mg/1 mL, 100 mg/4 mL and 200 mg/8 mL)
Drug Identification Number (DIN): 02524309

Background information
BENVYON is indicated for treatment of patients with relapsed indolent B-cell non-Hodgkin lymphoma (NHL) who did not respond to or progressed during or shortly following treatment with a rituximab regimen and symptomatic chronic lymphocytic leukemia (CLL) who have received no prior treatment.

Information for healthcare professionals
There is no reconstitution for BENVYON. Dilution for Intravenous Infusion: **CAUTION: BENVYON is a concentrated formulation and must be diluted directly in infusion solution before administration.**

Aseptically withdraw the volume needed for the required dose (based on 25 mg/mL concentration, refer to Table 1) and immediately transfer to a 500 mL infusion bag of 0.9% Sodium Chloride Injection, USP (normal saline). As an alternative to 0.9% Sodium Chloride Injection, USP (normal saline), a 500 mL infusion bag of 2.5% Dextrose/0.45% Sodium Chloride Injection, USP, may be considered. Both polyvinyl chloride (PVC) and polyethylene (PE) lined PVC infusion bags may be used. The resulting final concentration of bendamustine hydrochloride in the infusion bag should be within 0.2 – 0.6 mg/mL. After transferring, thoroughly mix the contents of the infusion bag. The admixture should be a clear and colorless to slightly yellow solution.

Use either 0.9% Sodium Chloride Injection, USP, or 2.5% Dextrose/0.45% Sodium Chloride Injection, USP, for dilution, as outlined in Table 1. No other diluents have been shown to be compatible.

Table 1: BENVYON volume (mL) required for dilution into 500 mL of 0.9% Sodium Chloride Injection USP (normal saline), or alternate 2.5% Dextrose/0.45% Sodium Chloride Injection USP for a given Body Surface Area (m2) and dose (mg/m2)

Body Surface Area (m^2)	Volume of BENVYON to withdraw (mL)					
	120 mg/m^2	100 mg/m^2	90 mg/m^2	60 mg/m^2	50 mg/m^2	25 mg/m^2
1	4.8	4	3.6	2.4	2	1
1.1	5.3	4.4	4	2.6	2.2	1.1
1.2	5.8	4.8	4.3	2.9	2.4	1.2
1.3	6.2	5.2	4.7	3.1	2.6	1.3
1.4	6.7	5.6	5	3.4	2.8	1.4
1.5	7.2	6	5.4	3.6	3.0	1.5
1.6	7.7	6.4	5.8	3.8	3.2	1.6
1.7	8.2	6.8	6.1	4.1	3.4	1.7
1.8	8.6	7.2	6.5	4.3	3.6	1.8
1.9	9.1	7.6	6.8	4.6	3.8	1.9
2	9.6	8	7.2	4.8	4	2.0
2.1	10.1	8.4	7.6	5	4.2	2.1
2.2	10.6	8.8	7.9	5.3	4.4	2.2
2.3	11	9.2	8.3	5.5	4.6	2.3
2.4	11.5	9.6	8.6	5.8	4.8	2.4
2.5	12	10	9	6	5	2.5
2.6	12.5	10.4	9.4	6.2	5.2	2.6
2.7	13.0	10.8	9.7	6.5	5.4	2.7
2.8	13.4	11.2	10.1	6.7	5.6	2.8
2.9	13.9	11.6	10.4	7	5.8	2.9
3	14.4	12	10.8	7.2	6	3.0

Note: shaded areas are typically outside the recommended product concentration 0.2 – 0.6 mg/mL.

The CPM should be referenced for complete product information. The CPM is available in French and English on Health Canada's Drug Product Database, or at pfizer.ca.

For any medical questions, contact **Pfizer Canada ULC Medical Information** at www.pfizermedicalinformation.ca or 1-800-463-6001. For any other general inquiries, contact **Pfizer Canada ULC Customer Service** at 1-888-888-9221.

Report health or safety concerns

Adverse drug reactions associated with the use of Benvyon should be reported to Pfizer Canada ULC by calling 1-866-723-7111, online at Pfizer's Adverse Event Reporting Portal (pfizersafetyreporting.com) or to Health Canada at https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html or by calling toll-free at 1-866-234-2345.

Sincerely,

Vratislav Hadrava M.D., Ph.D.
Vice President & Medical Director
Pfizer Canada ULC