Polivy, in combination with bendamustine and rituximab is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified, who are not eligible for autologous stem cell transplant and have received at least one prior therapy has been issued marketing authorization with conditions, pending the results of trials to verify its clinical benefit. Patients should be advised of the nature of the authorization. For further information for Polivy please refer to Health Canada's Notice of Compliance with conditions - drug products web site.
This product has been authorized under the Notice of Compliance with Conditions (NOC/c) for one or all of its indicated uses.

What is a Notice of Compliance with Conditions (NOC/c)?

A NOC/c is a form of market approval granted to a product on the basis of promising evidence of clinical effectiveness following review of the submission by Health Canada.

Products authorized under Health Canada’s NOC/c policy are intended for the treatment, prevention or diagnosis of a serious, life-threatening or severely debilitating illness. They have demonstrated promising benefit, are of high quality and possess an acceptable safety profile based on a benefit/risk assessment. In addition, they either respond to a serious unmet medical need in Canada or have demonstrated a significant improvement in the benefit/risk profile over existing therapies. Health Canada has provided access to this product on the condition that sponsors carry out additional clinical trials to verify the anticipated benefit within an agreed upon time frame.

What will be different about this Product Monograph?

The following Product Monograph will contain boxed text at the beginning of each major section clearly stating the nature of the market authorization. Sections for which NOC/c status holds particular significance will be identified in the left margin by the symbol NOC/c. These sections may include, but are not limited to, the following:

- Indications;
- Action and Clinical Pharmacology;
- Warnings and Precautions;
- Adverse Reactions;
- Dosage and Administration; and
- Clinical Trials.

Adverse Drug Reaction Reporting and Re-Issuance of the Product Monograph

Health care providers are encouraged to report Adverse Drug Reactions associated with normal use of these and all drug products to Health Canada’s Canada Vigilance Program at 1-866-234-2345. The Product Monograph will be re-issued in the event of serious safety concerns previously unidentified or at such time as the sponsor provides the additional data in support of the product’s clinical benefit. Once the latter has occurred, and in accordance with the NOC/c policy, the conditions associated with market authorization will be removed.
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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Polivy (polatuzumab vedotin) in combination with bendamustine and rituximab is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified, who are not eligible for autologous stem cell transplant and have received at least one prior therapy.

1.1 Pediatrics

Pediatrics (< 18 years of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of Polivy in pediatric patients has not been established; therefore, Health Canada has not authorized an indication for pediatric use.

1.2 Geriatrics

Geriatrics (≥ 65 years of age): Patients age 65 and older had a higher incidence of adverse events ≥ Grade 3 and Polivy discontinuation compared with younger patients. There is insufficient evidence from clinical studies to determine if there are meaningful differences in response to Polivy in patients 65 years and older compared to a younger patient population (see sections 4.2 DOSAGE AND ADMINISTRATION, Recommended Dose and Dosage Adjustment and section 10.3 ACTION AND CLINICAL PHARMACOLOGY, Pharmacokinetics).

2 CONTRAINDICATIONS

Polivy is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see section 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

3 SERIOUS WARNINGS AND PRECAUTIONS BOX
Serious Warnings and Precautions

Clinically significant and/or life-threatening adverse events include:

Fatal, life threatening, or serious infections, including opportunistic infections have been reported in patients treated with Polivy (see section 7 WARNINGS AND PRECAUTIONS)

Serious and severe myelosuppression, including neutropenia, febrile neutropenia, thrombocytopenia and anemia have been reported in patients treated with Polivy (see section 7 WARNINGS AND PRECAUTIONS)

Polivy should only be administered by a qualified healthcare professional experienced in the use of antineoplastic therapy.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

In order to improve traceability of biological medicinal products, the trade name and the batch number of the administered product should be clearly recorded (or stated) in the patient file.

Health professionals should recognise the importance of recording both the brand name and the non-proprietary (active ingredient) name as well as other product-specific identifiers such as the Drug Identification Number (DIN) and the batch/lot number of the product supplied.

In order to prevent medication errors, it is important to check the vial labels to ensure that the drug being prepared and administered is Polivy.

Polivy therapy should only be administered under the supervision of a healthcare professional experienced in the treatment of cancer patients.

Polivy must be reconstituted and diluted using aseptic technique under the supervision of a healthcare professional. Polivy should be administered as an intravenous infusion through a dedicated infusion line equipped with a sterile, non-pyrogenic, low-protein binding in-line or add-on filter (0.2 or 0.22 µm pore size) and catheter (see section 4.3 DOSAGE AND ADMINISTRATION and section 4.4 Reconstitution). Do not administer as an IV push or bolus.

For information on rituximab or bendamustine, refer to their respective full Product Monographs. Refer to Table 3 for dose modification recommendations for neutropenia and thrombocytopenia.

4.2 Recommended Dose and Dosage Adjustment

The recommended dose of Polivy is 1.8 mg/kg given as an intravenous infusion every 21 days in combination with bendamustine and rituximab for 6 cycles. Polivy, bendamustine, and rituximab can be administered in any order on Day 1 of each cycle. The recommended dose of bendamustine is 90 mg/m²/day on Day 1 and 2 when administered with Polivy and rituximab. The recommended dose of rituximab is 375 mg/m² on Day 1 of each cycle.

If not already pre-medicated, administer premedication with an antihistamine and anti-pyretic to patients prior to administration of Polivy. The initial dose of Polivy should be administered as a
90-minute intravenous infusion. Patients should be monitored for infusion-related reactions (IRRs) during the infusion and for at least 90 minutes following completion of the initial dose. If the prior infusion was well tolerated, the subsequent dose of Polivy may be administered as a 30-minute infusion and patients should be monitored during the infusion and for at least 30 minutes after completion of the infusion.

**Dose Modifications**

*Infusion-Related Reaction*
For dose modifications for infusion-related reactions see **Table 1**.

**Table 1 Polivy Dose Modifications for Infusion-related reactions**

<table>
<thead>
<tr>
<th>Severity on Day 1 of any cycle</th>
<th>Dose modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1–3 Infusion-Related Reaction</td>
<td>Interrupt Polivy infusion and give supportive treatment. For the first instance of Grade 3 wheezing, bronchospasm, or generalized urticaria, permanently discontinue Polivy. For recurrent Grade 2 wheezing or urticaria, or for recurrence of any Grade 3 symptoms, permanently discontinue POLIVY. Otherwise, upon complete resolution of symptoms, infusion may be resumed at 50% of the rate achieved prior to interruption. In the absence of infusion related symptoms, the rate of infusion may be escalated in increments of 50 mg/hour every 30 minutes. For the next cycle, infuse POLIVY over 90 minutes. If no infusion related reaction occurs, subsequent infusions may be administered over 30 minutes. Administer premedication for all cycles.</td>
</tr>
<tr>
<td>Grade 4 Infusion-Related Reaction</td>
<td>Stop POLIVY infusion immediately. Give supportive treatment. Permanently discontinue POLIVY.</td>
</tr>
</tbody>
</table>

*Peripheral Neuropathy*
For dose modifications for peripheral neuropathy see **Table 2**.
### Table 2  Polivy Dose Modifications for Peripheral Neuropathy

<table>
<thead>
<tr>
<th>Severity on Day 1 of any cycle</th>
<th>Dose modification</th>
</tr>
</thead>
</table>
| Grade 2-3                       | Hold Polivy dosing until improvement to ≤ Grade 1.  
If recovered to Grade ≤1 on or before Day 14, restart Polivy at a permanently reduced dose of 1.4 mg/kg.  
If a prior dose reduction to 1.4 mg/kg has occurred, discontinue Polivy.  
If not recovered to Grade ≤1 on or before Day 14, discontinue Polivy. |
| Grade 4                         | Discontinue Polivy. |

Myelosuppression  
For dose modifications for myelosuppression see Table 3.

### Table 3  Polivy, Bendamustine, and Rituximab Dose Modifications for Myelosuppression

<table>
<thead>
<tr>
<th>Severity on Day 1 of any cycle</th>
<th>Dose modificationa</th>
</tr>
</thead>
</table>
| Grade 3-4                       | Hold all treatment until ANC recovers to >1000/µL.  
If ANC recovers to >1000/µL on or before Day 7, resume all treatment without any additional dose reductions. Prophylactic use of granulocyte colony stimulating factor (G-CSF) should be considered for subsequent cycles, if not previously administered.  
If ANC recovers to >1000/µL after Day 7:  
• restart all treatment, with a dose reduction of bendamustine from 90 mg/m² to 70 mg/m² or 70 mg/m² to 50 mg/m². Consider the use of prophylactic G-CSF, if not previously administered.  
• if a bendamustine dose reduction to 50 mg/m² has already occurred, discontinue all treatment. |
| Neutropenia                      |                    |
| Grade 3-4 Thrombocytopenia       | Hold all treatment until platelets recover to >75,000/µL.  
If platelets recover to >75,000/µL on or before Day 7, resume all treatment without any additional dose reductions.  
If platelets recover to >75,000/µL after Day 7:  
• restart all treatment, with a dose reduction of bendamustine from 90 mg/m² to 70 mg/m² or 70 mg/m² to 50 mg/m².  
• if a bendamustine dose reduction to 50 mg/m² has already occurred, discontinue all treatment. |

ANC: absolute neutrophil count  
aIf primary cause is due to lymphoma, the dose of bendamustine may not need to be reduced.
Dose Modifications for Special Populations

Pediatric use
The safety and efficacy of Polivy in patients (<18 years) have not been established.

Geriatric use
No dose adjustment of Polivy is required in patients ≥ 65 years of age (see section 10.3 ACTION AND CLINICAL PHARMACOLOGY, Pharmacokinetics, Special Populations and Conditions, Geriatrics).

Renal Impairment
No dose adjustment of Polivy is required in patients with creatinine clearance (CrCL) ≥30mL/min. Polivy has not been studied in patients with severe renal impairment (CrCL 15 to 29 mL/min, n=3). No data are available in patients with end-stage renal disease with or without dialysis. A recommended dose has not been determined for patients with CrCL <30mL/min. (see section 10.3 ACTION AND CLINICAL PHARMACOLOGY, Pharmacokinetics, Special Populations and Conditions, Renal Impairment).

Hepatic Impairment
The administration of Polivy in patients with moderate or severe hepatic impairment (total bilirubin >1.5×ULN) should be avoided. Patients with moderate or severe hepatic impairment are likely to have increased exposure to MMAE, potentially increasing their risk of adverse reactions. Polivy has not been studied in patients with moderate or severe hepatic impairment (see section 10.3 ACTION AND CLINICAL PHARMACOLOGY, Pharmacokinetics, Special Populations and Conditions, Hepatic Impairment).

No dose adjustment of Polivy is required for patients with mild hepatic impairment (total bilirubin greater than ULN to less than or equal to 1.5 × ULN or aspartate transaminase [AST] greater than ULN).

4.3 Administration

Polivy is administered as an intravenous infusion only.

Polivy must be reconstituted using sterile water for injection and diluted into an IV infusion bag containing 0.9% sodium chloride, 0.45% sodium chloride, or 5% dextrose by a healthcare professional prior to administration.

Polivy should be reconstituted immediately before dilution.

Use aseptic technique for reconstitution and dilution of Polivy. Appropriate procedures for the preparation of antineoplastic products should be used.

The reconstituted product contains no preservative and is intended for single use only. Discard any unused portion.

A dedicated infusion line equipped with a sterile, non-pyrogenic, low-protein binding in-line or add-on filter (0.2 or 0.22 µm pore size) and catheter must be used to administer diluted Polivy.
4.4 Reconstitution

1. Using a sterile syringe, slowly inject 1.8 mL of sterile water for injection into the 30 mg Polivy vial or 7.2 mL of sterile water for injection into the 140 mg Polivy vial to yield a single-dose solution containing 20 mg/mL polatuzumab vedotin. Direct the stream toward the wall of the vial and not directly on the lyophilized cake.

2. Swirl the vial gently until completely dissolved. Do not shake.

3. Inspect the reconstituted solution for discolouration and particulate matter. The reconstituted solution should appear colourless to slightly brown, clear to slightly opalescent, and free of visible particulates. Do not use if the reconstituted solution is discoloured, cloudy, or contains visible particulates.

From a microbiological point of view, the reconstituted solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C to 8°C, unless reconstitution has taken place in controlled and validated aseptic conditions.

Chemical and physical in-use stability of the reconstituted solution has been demonstrated for up to 72 hours at 2°C to 8°C and up to 24 hours at room temperature (9°C to 25°C).

Dilution

1. Polatuzumab vedotin must be diluted to a final concentration of 0.72 – 2.7 mg/mL in an IV infusion bag with a minimum volume of 50mL containing 0.9% sodium chloride, 0.45% sodium chloride, or 5% dextrose.

2. Determine the volume of 20 mg/mL reconstituted solution needed based on the required dose:

   \[ \text{Volume} = \frac{\text{Polivy dose (1.8 or 1.4 mg/kg)} \times \text{patient’s weight (kg)}}{\text{Reconstituted vial concentration (20 mg/mL)}} \]

3. Withdraw the required volume of reconstituted solution from the Polivy vial using a sterile syringe and dilute into the IV infusion bag. Discard any unused portion left in the vial.

4. Gently mix the IV bag by slowly inverting the bag. Do not shake.

5. Inspect the IV bag for particulates and discard if present.

From a microbiological point of view, the prepared solution for infusion should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C to 8°C, unless dilution has taken place in controlled and validated aseptic conditions. Acceptable chemical and physical stability of the prepared solution for infusion has been demonstrated for the durations listed in Table 4. Discard if storage time exceeds these limits. Do not freeze or expose to direct sunlight.
### Table 4  Durations for which Acceptable Chemical and Physical Stability of the Prepared Solution for Infusion have been Demonstrated

<table>
<thead>
<tr>
<th>Diluent used to prepare solution for infusion</th>
<th>Solution for infusion storage conditions¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.9% Sodium Chloride</td>
<td>Up to 72 hours at 2°C to 8°C or up to 4 hours at room temperature (9°C to 25°C)</td>
</tr>
<tr>
<td>0.45% Sodium Chloride</td>
<td>Up to 72 hours at 2°C to 8°C or up to 8 hours at room temperature (9°C to 25°C)</td>
</tr>
<tr>
<td>5% Dextrose</td>
<td>Up to 72 hours at 2°C to 8°C or up to 8 hours at room temperature (9°C to 25°C)</td>
</tr>
</tbody>
</table>

¹To ensure product stability, do not exceed specified storage durations.

Avoid transportation of the prepared solution for infusion as agitation stress can result in aggregation. If the prepared solution for infusion will be transported, remove air from the infusion bag and limit transportation to 30 minutes at 9°C to 25°C or 24 hours at 2°C to 8°C. If air is removed, an infusion set with a vented spike is required to ensure accurate dosing during the infusion.

#### Incompatibilities

- Do not mix Polivy with, or administer through the same infusion line, as other medicinal products.
- No incompatibilities have been observed between Polivy and IV infusion bags with product contacting materials of polyvinyl chloride (PVC), or polyolefins (PO) such as polyethylene (PE) and polypropylene (PP). In addition, no incompatibilities have been observed with infusion sets or infusion aids with product contacting materials of PVC, PE, polyurethane (PU), polybutadiene (PBD), acrylonitrile butadiene styrene (ABS), polycarbonate (PC), polyetherurethane (PEU), or fluorinated ethylene propylene (FEP), or polytetrafluorethylene (PTFE), or with filter membranes composed of polyether sulfone (PES) or polysulfone (PSU).

### 4.5 Missed Dose

If a planned dose of Polivy is missed, it should be administered as soon as possible and the schedule of administration should be adjusted to maintain a 21-day interval between doses.

### 5 OVERDOSE

There is no experience with overdose in human clinical trials. Patients who experience overdose should have immediate interruption of their infusion and be closely monitored.

For management of a suspected drug overdose, contact your regional poison control centre.
6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

To help ensure the traceability of biologic products, including biosimilars, health professionals should recognise the importance of recording both the brand name and the non-proprietary (active ingredient) name as well as other product-specific identifiers such as the Drug Identification Number (DIN) and the batch/lot number of the product supplied.

Table 5 Dosage Forms, Strengths, Composition and Packaging

<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>Dosage Form / Strength/Composition</th>
<th>Non-medicinal Ingredients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous infusion</td>
<td>Powder for concentrate for solution for infusion / 20 mg per mL</td>
<td>polysorbate 20, sodium hydroxide, succinic acid, sucrose</td>
</tr>
</tbody>
</table>

Polivy is a sterile, preservative-free, white to grayish-white, lyophilized cake supplied in single-use 6 mL vial containing 30 mg and 20 mL vial containing 140 mg of polatuzumab vedotin. Upon reconstitution Polivy concentrate contains 20 mg/mL of polatuzumab vedotin for intravenous infusion only.

7 WARNINGS AND PRECAUTIONS

General

Infusion-Related Reactions
Infusion-related reactions, including severe cases have been observed with Polivy. Infusion-related reactions can occur as late as 24 hours after receiving Polivy. Patients should be administered premedication with an antihistamine and anti-pyretic to patients prior to administration of Polivy. Patients should be monitored closely during administration for infusion-related reactions. Symptoms include fever, chills, flushing, dyspnea, hypotension, or urticaria. If an infusion-related reaction occurs, the infusion should be interrupted and appropriate management followed (see section 4.2 DOSAGE AND ADMINISTRATION, Recommended Dose and Dosage Adjustment and section 8 ADVERSE REACTIONS Description of Selected Adverse Drug Reactions from Clinical Trials, Infusion-Related Reactions).

Driving and Operating Machinery
Polivy may affect one’s ability to drive and use machines.

Infusion-related reactions, peripheral neuropathy, fatigue, and dizziness may occur during treatment with Polivy (see section 7 WARNINGS AND PRECAUTIONS and section 8 ADVERSE REACTIONS).

Endocrine and Metabolism

Tumour Lysis Syndrome (TLS)
Tumour lysis syndrome has been reported in patients treated with Polivy. Patients with high tumour burden and rapidly proliferative tumour may be at increased risk of tumour lysis syndrome. Appropriate measures in accordance with local guidelines should be taken prior to treatment with Polivy.
treatment with Polivy. Patients should be monitored closely for tumour lysis syndrome during treatment with Polivy.

**Hematologic**

**Myelosuppression**
Serious and severe neutropenia and febrile neutropenia have been reported in patients treated with Polivy as early as the first cycle of treatment. Prophylactic G-CSF (granulocyte colony stimulating factor) administration should be considered. Grade 3 or 4 thrombocytopenia or anemia can also occur with Polivy. Complete blood counts should be monitored prior to each dose of Polivy. More frequent lab monitoring and/or Polivy delays or discontinuation should be considered in patients with Grade 3 or Grade 4 neutropenia and thrombocytopenia (see section 4.2 DOSAGE AND ADMINISTRATION, Recommended Dose and Dosage Adjustment and section 8 ADVERSE REACTIONS Description of Selected Adverse Drug Reactions from Clinical Trials, Myelosuppression).

**Hepatic/Biliary/Pancreatic**

**Hepatic Toxicity**
Serious cases of hepatic toxicity that were consistent with hepatocellular injury, including elevations of transaminases (AST/ALT) and/or bilirubin, have occurred in patients treated with Polivy (see section 8 ADVERSE REACTIONS). Preexisting liver disease, elevated baseline liver enzymes, and concomitant medications may increase the risk of hepatotoxicity. Liver enzymes and bilirubin level should be monitored.

**Immune**

**Infections**
Fatal, life threatening, or serious infections, including opportunistic infections, such as pneumonia (including *pneumocystis jirovecii* and other fungal pneumonia), bacteremia, sepsis, herpes zoster infection, and cytomegalovirus infection have been reported in patients treated with Polivy (see section 8 ADVERSE REACTIONS). Patients should be closely monitored during treatment for signs of bacterial, fungal, or viral infections. Anti-infective prophylaxis and/or treatment should be considered. Polivy and any concomitant chemotherapy should be discontinued in patients who develop serious infections.

**Neurologic**

**Peripheral Neuropathy**
Peripheral neuropathy has been reported in patients treated with Polivy as early as the first cycle of treatment, and the risk increases with sequential doses (see section 8 ADVERSE REACTIONS). Patients with pre-existing peripheral neuropathy may experience worsening of this condition. Peripheral neuropathy reported with Polivy treatment is predominantly sensory peripheral neuropathy; however, motor and sensorimotor peripheral neuropathy have also been reported. Patients should be monitored for symptoms of peripheral neuropathy such as hypoesthesia, hyperesthesia, paresthesia, dysesthesia, neuropathic pain, burning sensation, weakness, or gait disturbance. Patients experiencing new or worsening peripheral neuropathy may require a delay, dose reduction, or discontinuation of Polivy (see section 4.2 DOSAGE AND ADMINISTRATION, Recommended Dose and Dosage Adjustment).
Progressive Multifocal Leukoencephalopathy (PML)
PML has been reported with Polivy treatment (see section 8 ADVERSE REACTIONS). Patients should be monitored closely for new or worsening neurological, cognitive, or behavioral changes suggestive of PML. Polivy and any concomitant chemotherapy should be held if PML is suspected and permanently discontinued if the diagnosis is confirmed.

Sexual Health

Reproduction

Pregnancy testing
The pregnancy status of female patients of reproductive potential should be verified prior to initiating Polivy (see section 7.1.1 WARNINGS AND PRECAUTIONS, Special Populations, Pregnant Women).

Contraception
Female patients of reproductive potential should be advised of the potential harm to the fetus. Female patients of reproductive potential should be advised to use effective contraception during treatment with Polivy and for at least 9 months after the last dose (see sections 7.1.1 WARNINGS AND PRECAUTIONS, Special Populations, Pregnant Women and 16 NON-CLINICAL TOXICOLOGY).

Based on genotoxicity findings, male patients with female partners of reproductive potential should be advised to use effective contraception during treatment with Polivy and for at least 6 months after the last dose (see section 16 NON-CLINICAL TOXICOLOGY).

Fertility
Based on findings from animal studies, Polivy may impair male reproductive function and fertility (see section 16 NON-CLINICAL TOXICOLOGY).

7.1 Special Populations

7.1.1 Pregnant Women

There are no human data on the use of Polivy during pregnancy. In animal studies, administration of MMAE to pregnant rats during organogenesis caused embryo-fetal death and fetal malformations at exposures below those occurring clinically at the recommended dose (see section 16 NON-CLINICAL TOXICOLOGY). Based on the findings in animal studies and its mechanism of action, Polivy can cause fetal harm when administered to a pregnant woman.

Polivy should not be used in women who are pregnant. If Polivy is used in pregnancy, or if the patient becomes pregnant while taking Polivy, the patient should be apprised of potential hazard to the fetus.

7.1.2 Breast-feeding

It is not known whether polatuzumab vedotin is excreted in human breast milk. No studies have been conducted to assess the impact of Polivy on milk production or its presence in breast milk. Since many drugs are excreted in human milk and because of the potential for serious adverse reactions in breastfeeding infants due to Polivy, nursing women should be advised not to breastfeed during treatment with Polivy and for at least 3 months after the last dose.
7.1.3 Pediatrics

**Pediatrics (< 18 years of age):** Based on the data submitted and reviewed by Health Canada, the safety and efficacy of Polivy in pediatric patients has not been established; therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4 Geriatrics

**Geriatrics (≥ 65 years of age):** There is insufficient evidence, from clinical studies, to determine if there are meaningful differences in response to Polivy in patients 65 years and older compared to a younger patient population (see 4.2 DOSAGE AND ADMINISTRATION, Recommended Dose and Dosage Adjustment and 10.3 ACTION AND CLINICAL PHARMACOLOGY, Pharmacokinetics).

Renal Impairment

The safety and efficacy of Polivy in patients with CrCL <30 mL/min has not been formally studied (see 4.2 DOSAGE AND ADMINISTRATION, Recommended Dose and Dosage Adjustment and 10.3 ACTION AND CLINICAL PHARMACOLOGY, Pharmacokinetics).

Hepatic Impairment

The safety and efficacy of Polivy in patients with AST>2.5×ULN, ALT>2.5×ULN or total bilirubin>1.5×ULN has not been formally studied (see 4.2 Recommended Dose and Dosage Adjustment and 10.3 Pharmacokinetics).

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

For the clinical development program of Polivy as a whole, an estimated total of 588 patients have received Polivy. In the GO29365 study, the most frequently-reported (≥20%) adverse drug reactions (ADRs) in patients with DLBCL treated with Polivy in combination with bendamustine (B) and rituximab (R) were anemia, thrombocytopenia, neutropenia, decreased appetite, neuropathy peripheral, fatigue, diarrhea, nausea, and pyrexia.

Serious adverse events were reported in 64.4% of Polivy plus BR treated patients which included febrile neutropenia (11.1%), pyrexia (8.9%), pneumonia (8.9%), anemia (4.4%), duodenal ulcer hemorrhage (4.4%), sepsis (4.4%), and thrombocytopenia (4.4%).

Four patients (8.9%) experienced fatal ADRs which included pneumonia (6.7%) and meningoencephalitis herpetic (2.2%).

ADRs leading to treatment regimen discontinuation in >5% of patients were thrombocytopenia (8.9%) and neutropenia (6.7%).

8.2 Clinical Trial Adverse Reactions

Because clinical trials are conducted under very specific conditions, the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be
compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

The adverse drug reactions (ADRs) described in this section were identified during treatment and follow-up of previously treated relapsed / refractory diffuse large B-cell lymphoma (DLBCL) adult patients from the pivotal Phase Ib/II clinical trial GO29365. See Table 6 below.

In patients with relapsed or refractory DLBCL, the trial included a single-arm safety evaluation of Polivy in combination with bendamustine and rituximab (BR) (n = 6), followed by an open-label randomization to Polivy in combination with BR versus BR alone (n = 39 treated per arm).

Randomized patients in the Polivy treatment arm received a median of 5 cycles of treatment while randomized patients in the comparator arm received a median of 3 cycles of treatment.

Following premedication with an antihistamine and antipyretic, Polivy 1.8 mg/kg was administered by intravenous infusion on Day 2 of Cycle 1 and on Day 1 of Cycles 2–6, with a cycle length of 21 days. Bendamustine 90 mg/m² daily was administered intravenously on Days 2 and 3 of Cycle 1 and on Days 1 and 2 of Cycles 2–6. Rituximab dosed at 375 mg/m² was administered intravenously on Day 1 of each cycle.

In Polivy treated patients (n = 45), the median age was 67 years (range 33 – 86) with 58% being ≥ age 65, 69% were male, 69% were white, and 87% had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. The trial required an absolute neutrophil count ≥1500/μL, platelet count ≥75000/μL, creatinine clearance (CrCL) ≥40 mL/min, hepatic transaminases ≤2.5 times ULN, and bilirubin <1.5 times ULN, unless abnormalities were from the underlying disease. Patients with Grade 2 or higher peripheral neuropathy or prior allogeneic hematopoietic stem cell transplantation (HSCT) were excluded.

ADRs are listed by MedDRA system organ class in Table 6.

Table 6  Adverse Drug Reactions Reported in ≥5% of Relapsed or Refractory DLBCL Patients Treated with Polivy in Combination with Bendamustine and Rituximab Compared with Patients Treated with Bendamustine and Rituximab in Study GO29365

<table>
<thead>
<tr>
<th>Adverse Drug Reactions System Organ Class Preferred Term</th>
<th>Polivy + Bendamustine + Rituximab N = 45</th>
<th>Bendamustine + Rituximab N = 39</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All grades (%)</td>
<td>Grades 3-4 (%)</td>
</tr>
<tr>
<td>Blood and Lymphatic System Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>46.7</td>
<td>24.4</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>46.7</td>
<td>40.0</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>46.7</td>
<td>37.8</td>
</tr>
<tr>
<td>Febrile Neutropenia</td>
<td>11.1</td>
<td>11.1</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>11.1</td>
<td>6.7</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>11.1</td>
<td>11.1</td>
</tr>
<tr>
<td>Pancytopenia</td>
<td>6.7</td>
<td>4.4</td>
</tr>
<tr>
<td>Cardiac Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tachycardia</td>
<td>8.9</td>
<td>2.2</td>
</tr>
<tr>
<td>Adverse Drug Reactions System Organ Class Preferred Term</td>
<td>Polivy + Bendamustine + Rituximab N = 45</td>
<td>Bendamustine + Rituximab N = 39</td>
</tr>
<tr>
<td>--------------------------------------------------------</td>
<td>-------------------------------------------</td>
<td>---------------------------------</td>
</tr>
<tr>
<td></td>
<td>All grades (%)</td>
<td>Grades 3-4 (%)</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>37.8</td>
<td>4.4</td>
</tr>
<tr>
<td>Nausea</td>
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<td>0</td>
</tr>
<tr>
<td>Constipation</td>
<td>17.8</td>
<td>0</td>
</tr>
<tr>
<td>Vomiting</td>
<td>17.8</td>
<td>2.2</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>11.1</td>
<td>4.4</td>
</tr>
<tr>
<td>Abdominal Pain Upper</td>
<td>11.1</td>
<td>2.2</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>6.7</td>
<td>0</td>
</tr>
<tr>
<td>Gastroesophageal reflux disease</td>
<td>6.7</td>
<td>0</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>6.7</td>
<td>0</td>
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<tr>
<td>General Disorders and Administration Site Conditions</td>
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<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>40.0</td>
<td>4.4</td>
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<tr>
<td>Pyrexia</td>
<td>33.3</td>
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<tr>
<td>Asthenia</td>
<td>11.1</td>
<td>0</td>
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<tr>
<td>Chills</td>
<td>11.1</td>
<td>0</td>
</tr>
<tr>
<td>Infections and Infestations</td>
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<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>15.6</td>
<td>6.7</td>
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<tr>
<td>Upper respiratory tract infection</td>
<td>8.9</td>
<td>0</td>
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<tr>
<td>Herpes virus infection</td>
<td>6.7</td>
<td>2.2</td>
</tr>
<tr>
<td>Sepsis</td>
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<td>4.4</td>
</tr>
<tr>
<td>Injury, Poisoning, and Procedural</td>
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<tr>
<td>Infusion-related reaction</td>
<td>33.3</td>
<td>6.7</td>
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<td>Investigations</td>
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<td></td>
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<tr>
<td>Weight decreased</td>
<td>15.6</td>
<td>2.2</td>
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<tr>
<td>Hypophosphatemia</td>
<td>9</td>
<td>4.4</td>
</tr>
<tr>
<td>Blood creatinine increased</td>
<td>8.9</td>
<td>0</td>
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<tr>
<td>Transaminase elevation</td>
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<td>Lipase increase</td>
<td>6.7</td>
<td>2.2</td>
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<tr>
<td>Metabolism and Nutrition Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>26.7</td>
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<tr>
<td>Hypokalemia</td>
<td>15.6</td>
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<tr>
<td>Hypoalbuminemia</td>
<td>13.3</td>
<td>2.2</td>
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<tr>
<td>Hypocalcemia</td>
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<tr>
<td>Dehydration</td>
<td>8.9</td>
<td>0</td>
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<tr>
<td>Musculoskeletal and Connective Tissue Disorders</td>
<td></td>
<td></td>
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<tr>
<td>Arthralgia</td>
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<tr>
<td>Nervous System Disorders</td>
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<tr>
<td>Neuropathy Peripheral</td>
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<tr>
<td>Dizziness</td>
<td>13.3</td>
<td>0</td>
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<tr>
<td>Peripheral Sensory neuropathy</td>
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<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>8.9</td>
<td>2.2</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>6.7</td>
<td>0</td>
</tr>
<tr>
<td>Hypoesthesia</td>
<td>6.7</td>
<td>0</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia</td>
<td>8.9</td>
<td>0</td>
</tr>
<tr>
<td>Anxiety</td>
<td>6.7</td>
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</table>
### Adverse Drug Reactions

#### Respiratory, Thoracic and Mediastinal Disorders

<table>
<thead>
<tr>
<th>Term</th>
<th>All grades (%)</th>
<th>Grades 3-4 (%)</th>
<th>All grades (%)</th>
<th>Grades 3-4 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>15.6</td>
<td>0</td>
<td>20.5</td>
<td>0</td>
</tr>
<tr>
<td>Productive cough</td>
<td>8.9</td>
<td>0</td>
<td>5.1</td>
<td>0</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>6.7</td>
<td>0</td>
<td>5.1</td>
<td>0</td>
</tr>
</tbody>
</table>

#### Skin and Subcutaneous Tissue Disorders

<table>
<thead>
<tr>
<th>Term</th>
<th>All grades (%)</th>
<th>Grades 3-4 (%)</th>
<th>All grades (%)</th>
<th>Grades 3-4 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pruritis</td>
<td>13.3</td>
<td>0</td>
<td>10.3</td>
<td>2.6</td>
</tr>
<tr>
<td>Rash</td>
<td>6.7</td>
<td>0</td>
<td>12.8</td>
<td>7.7</td>
</tr>
</tbody>
</table>

#### Vascular Disorders

<table>
<thead>
<tr>
<th>Term</th>
<th>All grades (%)</th>
<th>Grades 3-4 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>8.9</td>
<td>4.4</td>
</tr>
</tbody>
</table>

---

**Description of Selected Adverse Drug Reactions from Clinical Trials**

**Tumor Lysis syndrome (TLS)**

TLS has been reported in polatuzumab vedotin clinical trials..

**Myelosuppression**

The incidence of Grade 3-4 neutropenia was higher in the Polivy plus BR arm (40%) compared to the BR arm (33.3%). The incidence of febrile neutropenia was 11.1% in the Polivy plus BR arm compared to 12.8% in the BR arm. 8.9% of patients in the Polivy plus BR arm discontinued Polivy due to neutropenia compared to 2.6% of patients in the BR arm who discontinued treatment due to neutropenia.

The incidence of Grade 3-4 thrombocytopenia was higher in the Polivy plus BR arm (37.8%) compared to the BR arm (23.1%). Thrombocytopenia events led to discontinuation of treatment in 11.1% of patients in the Polivy plus BR arm and 5.1% of patients in the BR arm.

The incidence of Grade 3-4 anemia was higher in the Polivy plus BR arm (24.4%) compared to the BR arm (17.9%). No patients discontinued treatment due to anemia in either the Polivy plus BR arm or BR arm.

**Peripheral Neuropathy (PN)**

In the Polivy plus BR arm, Grade 1 and 2 PN events were reported in 26.7% and 13.3% of patients, respectively. In the BR arm, Grade 1 and 2 PN events were reported in 2.6% and 5.1% of patients, respectively. No Grade 3-5 PN events were reported in either the Polivy plus BR arm or BR arm. 2.2% of patients discontinued Polivy treatment due to PN and 4.4% of patients had Polivy dose reduction due to PN. No patients in the BR arm discontinued treatment or had dose reductions due to PN. In the Polivy plus BR arm, the median onset to first event of PN was 1.8 months, and 61.1% of patients with PN events reported event resolution (see 7 WARNINGS AND PRECAUTIONS).

**Infections**

Infections, including pneumonia and other types of infections, were reported in 53.3% of patients in the Polivy plus BR arm and 51.3% of patients in the BR arm. In the Polivy plus BR arm, opportunistic infections were reported in 8.9% of patients, serious infections were reported.
in 28.9% of patients and fatal infections were reported in 8.9% of patients. In the BR arm, opportunistic infections were reported in 5.1% of patients, serious infections were reported in 30.8% of patients and fatal infections were reported in 10.3% of patients. One patient (2.2%) discontinued treatment in the Polivy plus BR arm due to infection compared to 5.1% of patients in the BR arm (see section 7 WARNINGS AND PRECAUTIONS).

Progressive Multifocal Leukoencephalopathy (PML)
One case of PML, which was fatal, occurred in a patient treated with Polivy plus bendamustine and obinutuzumab. This patient had three prior lines of therapy that included anti-CD20 antibodies (see section 7 WARNINGS AND PRECAUTIONS).

Hepatic toxicity
Hepatic toxicity events were reported in 20% of patients in the Polivy plus BR arm and 12.8% of patients in the BR arm. Grade 3-4 were reported in 4.4% of patients in the Polivy plus BR arm compared to 2.6% of patients in the BR arm. Most events were low grade laboratory abnormalities that were reversible. In another study, two cases of serious hepatic toxicity (hepatocellular injury and hepatic steatosis) were reported and were reversible (see section 7 WARNINGS AND PRECAUTIONS).

Gastrointestinal Toxicity
Gastrointestinal toxicity events were reported in 80.0% of patients in the Polivy plus BR arm compared to 64.1% of patients in the BR arm. Most events were Grade 1-2, and Grade 3-4 events were reported in 22.2% of patients in the Polivy plus BR arm compared to 12.8% of patients in the BR arm. The most common gastrointestinal toxicity events were diarrhea and nausea.

8.3 Less Common Clinical Trial Adverse Reactions
Other clinically relevant adverse reactions in recipients of Polivy plus BR included:

Infections and infestations: cytomegalovirus infection (2.2%)
Respiratory disorders: pneumonitis (4.4%)

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Table 7 Significant Laboratory Abnormalities Worsening from Baseline in Patients with Relapsed or Refractory DLBCL and ≥ 5% More in the Polivy Plus Bendamustine and Rituximab Product Group

<table>
<thead>
<tr>
<th>Laboratory Parametera</th>
<th>Polivy + Bendamustine + Rituximab N = 45</th>
<th>Bendamustine + Rituximab N = 39</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades, N (%)</td>
<td>Grade 3-4, N (%)</td>
</tr>
<tr>
<td>Hematologic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin decreased</td>
<td>78</td>
<td>18</td>
</tr>
<tr>
<td>Lymphocyte count</td>
<td>87</td>
<td>87</td>
</tr>
<tr>
<td>Neutrophil count</td>
<td>78</td>
<td>61</td>
</tr>
<tr>
<td>Platelet count</td>
<td>76</td>
<td>31</td>
</tr>
</tbody>
</table>
| Laboratory Parametera | Polivy + Bendamustine + Rituximab  
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 45</td>
</tr>
<tr>
<td></td>
<td>All Grades, N (%)</td>
</tr>
<tr>
<td>Amylase increased</td>
<td>24 (0.07)</td>
</tr>
<tr>
<td>Calcium decreased</td>
<td>44 (0.14)</td>
</tr>
<tr>
<td>Creatinine increased</td>
<td>87 (0.25)</td>
</tr>
<tr>
<td>Lipase increased</td>
<td>36 (0.10)</td>
</tr>
<tr>
<td>Phosphorus decreased</td>
<td>33 (0.09)</td>
</tr>
<tr>
<td>Potassium decreased</td>
<td>24 (0.07)</td>
</tr>
<tr>
<td>SGPT/ALT increased</td>
<td>36 (0.10)</td>
</tr>
<tr>
<td>SGOT/AST increased</td>
<td>36 (0.10)</td>
</tr>
<tr>
<td>Calcium decreased</td>
<td>44 (0.14)</td>
</tr>
<tr>
<td>Creatinine increased</td>
<td>87 (0.25)</td>
</tr>
<tr>
<td>Lipase increased</td>
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<td>Phosphorus decreased</td>
<td>33 (0.09)</td>
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<td>36 (0.10)</td>
</tr>
<tr>
<td>SGOT/AST increased</td>
<td>36 (0.10)</td>
</tr>
</tbody>
</table>

aIncludes laboratory abnormalities that are new or worsening in grade or with worsening from baseline unknown.

8.5 Clinical Trial Adverse Reactions (Pediatrics)

The safety and efficacy of Polivy in pediatric patients below the age of 18 years have not been established.

8.6 Post-Market Adverse Reactions

Not applicable.

9 DRUG INTERACTIONS

9.1 Overview

No dedicated clinical drug-drug interaction studies with Polivy in humans have been conducted.

9.2 Drug-Drug Interactions

Drug interactions with co-medications that are CYP3A inhibitors, inducers or substrates

Based on physiological-based pharmacokinetic (PBPK) model simulations of monomethyl auristatin E (MMAE) released from polatuzumab vedotin, strong CYP3A inhibitors (e.g., ketoconazole) may increase the area under the concentration-time curve (AUC) of unconjugated MMAE by 48%. Monitor patients receiving concomitant strong CYP3A inhibitors more closely for signs of toxicities. Strong CYP3A inducers (e.g., rifampin) may decrease the AUC of unconjugated MMAE.

Unconjugated MMAE is not predicted to alter the AUC of concomitant drugs that are CYP3A substrates (e.g., midazolam).

Drug interactions of rituximab and bendamustine in combination with polatuzumab vedotin

The pharmacokinetics (PK) of rituximab and bendamustine are not affected by co-administration with Polivy. Concomitant rituximab is associated with increased antibody conjugated MMAE (acMMAE) plasma AUC by 24% and decreased unconjugated MMAE plasma AUC by 37%, based on population PK analysis. No dose adjustment is required.

Bendamustine does not affect acMMAE and unconjugated MMAE plasma AUC.
9.3 Drug-Food Interactions

Interactions with food have not been specifically studied with Polivy. Grapefruit has CYP3A4 inhibitory activity. Therefore, ingestion of grapefruit while on Polivy therapy may increase MMAE plasma concentrations. However, Patients consuming grapefruit, grapefruit containing products, or other foods known to inhibit CYP3A4 should be monitored more closely for signs of toxicity during treatment with Polivy.

9.4 Drug-Herb Interactions

Interactions with herbs have not been established.

9.5 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

9.6 Drug-Lifestyle Interactions

Polivy may affect one’s ability to drive and use machines (see section 7 WARNINGS AND PRECAUTIONS).

10 ACTION AND CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Polatuzumab vedotin is a CD79b-targeted antibody-drug conjugate that preferentially delivers an anti-mitotic agent (monomethyl auristatin E, or MMAE) to B-cells, which results in the killing of malignant B-cells. The polatuzumab vedotin molecule consists of MMAE covalently attached via a cleavable linker to a humanized immunoglobulin G1 (IgG1) monoclonal antibody, which is produced by recombinant DNA technology in Chinese hamster ovary (CHO) cells. The monoclonal antibody binds with nanomolar affinity and selectivity to CD79b, a cell surface component of the B-cell receptor. CD79b expression is restricted to normal cells within the B cell lineage (with the exception of plasma cells) and malignant B-cells; it is expressed in >95% of DLBCL. Upon binding CD79b, polatuzumab vedotin is rapidly internalized and the linker is cleaved by lysosomal proteases to enable intracellular delivery of MMAE. MMAE binds to microtubules and kills dividing cells by inhibiting cell division and inducing apoptosis.

10.2 Pharmacodynamics

Cardiac Electrophysiology
The effect of polatuzumab vedotin on the QTc interval was evaluated based on triplicate ECG data from two open-label studies in 209 patients (102 patients at 1.8 mg/kg) with previously treated B-cell malignancies. Administration of polatuzumab vedotin did not prolong the mean QTc interval >20 ms from baseline. Increases in the mean QTc interval of <10 ms cannot be excluded because this study did not include a placebo arm and a positive control arm.

10.3 Pharmacokinetics

Antibody-conjugated MMAE (acMMAE) plasma exposure increased dose-proportionally over the 0.1 to 2.4 mg/kg polatuzumab vedotin dose range. After the first 1.8 mg/kg polatuzumab
vedotin dose, the acMMAE mean maximum concentration ($C_{\text{max}}$) was 803 (± 233) ng/mL and
the area under the concentration-time curve from time zero to infinity ($\text{AUC}_{\text{inf}}$) was 1860 (± 966)
day*ng/mL. Based on the population PK analysis, Cycle 3 acMMAE AUC increased by
approximately 30% over cycle 1 AUC, and achieved more than 90% of the Cycle 6 AUC. The
terminal half-life at cycle 6 was approximately 12 days (95% CI of 8.1-19.5 days) for acMMAE.

Exposures of unconjugated MMAE, the cytotoxic component of polatuzumab vedotin, increased
dose proportionally over the 0.1 to 2.4 mg/kg polatuzumab vedotin dose range. MMAE plasma
concentrations followed formation rate limited kinetics. After the first 1.8 mg/kg polatuzumab
vedotin dose, the $C_{\text{max}}$ was 6.82 (± 4.73) ng/mL, the time to maximum plasma concentration is
approximately 2.5 days, and the terminal half-life is approximately 4 days. Plasma exposures of
unconjugated MMAE are <3% of acMMAE exposures. Based on the population PK analysis,
there is a decrease of plasma unconjugated MMAE exposure ($\text{AUC}$ and $C_{\text{max}}$) after repeated
every-three-week dosing.

Absorption: Polivy is administered as an IV infusion. There have been no studies performed
with other routes of administration.

Distribution: The population estimate of central volume of distribution for acMMAE was 3.15 L,
which approximated plasma volume. In vitro, MMAE is moderately bound (71% - 77%) to
human plasma proteins. MMAE does not significantly partition into human red blood cells in
vitro; the blood to plasma ratio is 0.79 to 0.98. In vitro data indicate that MMAE is a P-gp
substrate but does not inhibit P-gp at clinically relevant concentrations.

Metabolism: Polatuzumab vedotin is expected to undergo catabolism in patients, resulting in
the production of small peptides, amino acids, unconjugated MMAE, and unconjugated MMAE
related catabolites. In vitro studies indicate that MMAE is a substrate for CYP 3A4/5 but does
not induce major CYP enzymes. MMAE is a weak time-dependent inhibitor of CYP3A4/5 but
does not competitively inhibit CYP3A4/5 at clinically relevant concentrations. MMAE does not
inhibit CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, or CYP2D6.

Elimination: Based on a population pharmacokinetic analysis, the conjugate (acMMAE) is
primarily eliminated by non-specific linear clearance pathway with a value of 0.9 L/day.
In vivo studies in rats dosed with polatuzumab vedotin (radiolabel on MMAE) demonstrate that
the majority of radioactivity is excreted in feces and the minority of radioactivity is excreted in
urine.

Special Populations and Conditions

Pediatrics: No studies have been conducted to investigate the pharmacokinetics of Polivy in
pediatric patients (<18 years old).

Geriatrics: Age did not have an effect on the pharmacokinetics of acMMAE and unconjugated
MMAE based on a population PK analysis with patients aged 20-89 years. No significant
difference was observed in the pharmacokinetics of acMMAE and unconjugated MMAE among
patients <65 years of age (n=187) and patients ≥65 years of age (n=273).

Hepatic Impairment: In patients with mild hepatic impairment [AST >1.0 - 2.5×ULN or ALT >1.0
- 2.5×ULN or total bilirubin >1.0 - 1.5×ULN, n=54], acMMAE exposures are similar whereas
unconjugated MMAE AUC are 40% higher compared to patients with normal hepatic function
(n=399), based on a population pharmacokinetic analysis. There are insufficient data to assess
the impact of moderate hepatic impairment (total bilirubin >1.5 - 3×ULN, n=2) on PK. No data are available in patients with severe hepatic impairment or liver transplantation (see 4 DOSAGE AND ADMINISTRATION).

**Renal Impairment:** In patients with mild (CrCL 60-89 mL/min, n=161) or moderate (CrCL 30-59 mL/min, n=109) renal impairment, acMMAE and unconjugated MMAE exposures are similar to patients with normal renal function (CrCL ≥ 90 mL/min, n=185), based on a population pharmacokinetic analysis. There are insufficient data to assess the impact of severe renal impairment (CrCL 15-29 mL/min, n=3) on PK. No data are available in patients with end-stage renal disease and/or who are on dialysis (see 4 DOSAGE AND ADMINISTRATION).

11 STORAGE, STABILITY AND DISPOSAL

**Vials**
Store unopened vials at 2°C to 8°C.

Keep vial in the outer carton in order to protect from light.

Do not freeze. Do not shake.

**Shelf life**
This medicine should not be used after the expiry date (EXP) shown on the pack.

**Shelf life of reconstituted product and solution for infusion**
See section 4.4 DOSAGE AND ADMINISTRATION, Reconstitution.

The reconstituted solution and solution for infusion should not be frozen or exposed to direct sunlight.

**Disposal of unused/expired medicines**
The release of pharmaceuticals in the environment should be minimized. Medicines should not be disposed of via wastewater and disposal through household waste should be avoided. The following points should be strictly adhered to regarding the use and disposal of syringes and other medicinal sharps:
- Needles and syringes should never be reused.
- Place all used needles and syringes into a sharps container (puncture-proof disposable container).

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

12 SPECIAL HANDLING INSTRUCTIONS

Not applicable.
PART II: SCIENTIFIC INFORMATION

Polivy, in combination with bendamustine and rituximab is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified, who are not eligible for autologous stem cell transplant and have received at least one prior therapy has been issued marketing authorization with conditions, pending the results of trials to verify its clinical benefit. Patients should be advised of the nature of the authorization. For further information for Polivy please refer to Health Canada’s Notice of Compliance with conditions - drug products web site.

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: polatuzumab vedotin

Chemical name: Immunoglobulin G1, anti-(human antigen CD79b) (human-Mus musculus monoclonal MCDS4409A heavy chain), disulfide with human-Mus musculus monoclonal MCDS4409A κ-chain, dimer, thioether with maleimidocaproyl-valine-citrulline- p-aminobenzyloxycarbonyl monomethylauristatin E

Molecular formula and molecular mass: \( C_{68}H_{108}N_{11}O_{15} \)
Polatuzumab vedotin has an average molecular mass of 1316.63 Da.

Structural formula:
14  CLINICAL TRIALS

14.1  Trial Design and Study Demographics

The efficacy of Polivy was evaluated in Study GO29365, an international, multicenter, open-label, Phase Ib/II trial which included a randomized cohort of 80 patients with previously treated DLBCL. Patients were randomized 1:1 to receive Polivy plus bendamustine and rituximab (BR) or BR alone for six 21-day cycles. Patients were stratified by duration of response to last prior treatment of ≤12 months or >12 months.

Eligible patients were not candidates for autologous hematopoietic stem cell transplant (HSCT) at study entry, had relapsed or refractory disease after receiving at least one prior systemic chemotherapy regimen, and had an ECOG PS ≤2. The study excluded patients with prior allogeneic HSCT, central nervous system lymphoma, transformed follicular lymphoma (FL), grade 3b FL, Grade >1 peripheral neuropathy, significant cardiovascular or pulmonary disease, active infections. In addition, patients with abnormal creatinine >1.5×ULN (or CrCl < 40 mL/min), and AST or ALT >2.5×ULN or total bilirubin ≥1.5×ULN were also excluded, unless abnormal laboratory values were due to underlying lymphoma per the investigator.

Polivy was given intravenously at 1.8 mg/kg administered on Day 2 of Cycle 1 and on Day 1 of Cycles 2-6. Bendamustine was administered at 90 mg/m² intravenously daily on Days 2 and 3 of Cycle 1 and on Days 1 and 2 of Cycles 2-6. Rituximab was administered at 375 mg/m² intravenously on Day 1 of Cycles 1-6.

In study GO29365, 80 patients were randomized to receive Polivy plus BR (n=40) or BR alone (n=40). The median age was 69 years (range 30 to 86 years) and 71% of patients were white and 66% were male. The majority of patients (98%) had DLBCL not otherwise specified (NOS). Overall, 48% of patients had activated B-cell (ABC) DLBCL and 40% of patients had germinal center B-cell like (GCB) DLBCL. Primary reasons patients were not candidates for HSCT included age (40%), insufficient response to salvage therapy (26%) and prior transplant failure (20%). The median number of prior therapies was 2 (range: 1-7) with 29% (n=23) receiving one prior therapy, 25% (n=20) receiving 2 prior therapies, and 46% (n=37) receiving 3 or more prior therapies. Eighty (80%) of patients had refractory disease.

14.2  Study Results

The primary endpoint of the study was complete response (CR) rate at end of treatment (6-8 weeks after day 1 of cycle 6 or last study treatment) as assessed by independent review committee (IRC). Efficacy was based on the primary endpoint, complete response (CR) rate at the end of treatment as assessed by IRC. Key supportive efficacy endpoints were objective response rate at the end of treatment and best overall response rate. Duration of response was also assessed in the study.
Table 8  Summary of Efficacy in Patients with Previously Treated DLBCL from study GO29365

<table>
<thead>
<tr>
<th></th>
<th>Polivy + Bendamustine + Rituximab N= 40</th>
<th>Bendamustine + Rituximab N= 40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Endpoint</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Complete Response Rate</strong> (IRC-assessed) at End of treatment**</td>
<td>Responders (%)</td>
<td>16 (40.0)</td>
</tr>
<tr>
<td></td>
<td>Difference in response rate (%) [95% CI]</td>
<td>22.5 [2.6, 40.2]</td>
</tr>
<tr>
<td>Key Secondary Endpoints</td>
<td>Objective Response Rate** (IRC-assessed) at End of Treatment</td>
<td>Responders (%) (CR, PR)</td>
</tr>
<tr>
<td></td>
<td>Difference in response rate (%) [95% CI]</td>
<td>27.5 [7.2, 45.0]</td>
</tr>
<tr>
<td><strong>Best Overall Response Rate</strong> (IRC-assessed)</td>
<td>Responders (%) [CR, PR]</td>
<td>25 (62.5)</td>
</tr>
<tr>
<td></td>
<td>Complete Response (%) [CR]***</td>
<td>20 (50.0)</td>
</tr>
</tbody>
</table>

IRC: Independent Review Committee; CI: Confidence Interval

*Per modified Lugano 2014 criteria: Bone marrow confirmation of PET-CT CR required. PET-CT PR required meeting both PET-CT criteria and CT criteria.

**6-8 weeks after day 1 of cycle 6 or last study treatment

***95% CI Clopper-Pearson: [33.8, 66.2] versus [10.8, 38.5]

In the Polivy plus BR arm 25 patients achieved a complete or partial response versus 10 in the BR arm. The median duration of response was 12.6 months for patients in the Polivy plus BR arm versus 7.7 months for patients in the BR arm.

Immunogenicity

As with all therapeutic proteins, there is the potential for an immune response in patients treated with polatuzumab vedotin. Across all arms of study GO29365, 8 out of 134 (6.0%) patients tested positive for anti-polatuzumab vedotin antibodies at one or more post-baseline time points. Across all seven clinical studies, 14 out of 536 (2.6%) patients tested positive for anti-polatuzumab vedotin antibodies at one or more post-baseline time points. Due to the limited number of anti-polatuzumab vedotin antibody positive patients, no conclusions can be drawn concerning a potential effect of immunogenicity on efficacy or safety.

15 MICROBIOLOGY

Not applicable.
General toxicology

**Repeat dose toxicity**

Repeat dose toxicity studies were conducted in rats (non-binding species) intravenously administered 2, 6, or 10 mg/kg polatuzumab vedotin, given once weekly (QW) for 4 total doses, followed by a 6-week recovery period. Bone marrow (decreased cellularity), thymus (decreased cellularity and increased apoptosis/mitoses), liver (focal necrosis and increased apoptosis/mitoses), and gastrointestinal tract (increased apoptosis/mitoses in the epithelium of the small and large intestines) toxicities were observed primarily at the 6 and 10 mg/kg dose levels. Testes toxicity was observed across all dose levels. All changes were reversible following a 6 week recovery period except for testes toxicity and residual histologic findings observed in single individual animals. The AUC for total antibody in rats at 2 mg/kg QW was similar to the AUC in patients at the recommended dose of 1.8 mg/kg every 21 days (Q3W). The AUC for unconjugated MMAE in rats at 2 mg/kg QW was below the exposure in patients at the recommended dose.

Repeat dose toxicity studies were also conducted in cynomolgus monkeys intravenously administered polatuzumab vedotin at 1, 3 or 5 mg/kg or a surrogate antibody-drug conjugate (ADC) at 3 or 5 mg/kg, given once every 3 weeks for 4 total doses, followed by a 9-week recovery period. The surrogate ADC binds to CD79b on monkey B-cells, whereas polatuzumab vedotin does not. Reversible, dose-dependent bone marrow hypocellularity was observed in both polatuzumab vedotin and surrogate ADC groups. Pharmacologically anticipated decreases in circulating B-lymphocytes and depletion of lymphoid follicular germinal centers in the spleen were observed in all animals administered the surrogate ADC. The AUC for total antibody in monkeys receiving 3 mg/kg Q3W of the surrogate ADC was 2.2-fold higher compared to patients at the 1.8 mg/kg Q3W dose. The AUC for unconjugated MMAE in monkeys receiving 3 mg/kg Q3W of the surrogate ADC was below the exposure in patients at the 1.8 mg/kg Q3W dose.

In both rats and monkeys, the predominant systemic toxicities associated with repeated administration of MMAE and polatuzumab vedotin included reversible bone marrow toxicity and associated peripheral blood cell effects.

**Carcinogenicity**

No carcinogenicity studies in animals have been performed with polatuzumab vedotin or MMAE.

**Genotoxicity**

No genotoxicity studies have been performed with polatuzumab vedotin. MMAE was genotoxic in the rat bone marrow micronucleus study through an aneugenic mechanism. This mechanism is consistent with the pharmacological effect of MMAE as a microtubule disrupting agent. MMAE was not mutagenic in vitro in the bacterial reverse mutation assay (Ames test) or the L5178Y mouse lymphoma forward mutation assay.
Reproductive and Developmental Toxicology

Impairment of Fertility
No dedicated fertility studies in animals have been performed with polatuzumab vedotin. However, results of repeat-dose toxicity in rats indicate the potential for polatuzumab vedotin to impair male reproductive function and fertility. In the 4-week repeat-dose toxicity study in rats with weekly dosing of 2, 6, or 10 mg/kg polatuzumab vedotin, dose-dependent testicular seminiferous tubule degeneration with abnormal lumen contents in the epididymis was observed. Findings in the testes and epididymis did not reverse and correlated with decreased testes weight and gross findings of small and/or soft testes at recovery necropsy in males given doses ≥ 2 mg/kg (below the exposure in patients at the recommended dose based on unconjugated MMAE AUC).

Developmental Toxicity
No teratogenicity studies in animals have been performed with polatuzumab vedotin. However, MMAE was evaluated in rats in an embryo-fetal developmental and toxicokinetic study, in which pregnant rats received 2 intravenous doses of 0.2 mg/kg MMAE during the period of organogenesis on gestational day 6 and 13. Treatment with MMAE at 0.2 mg/kg caused fetal external malformations including protruding tongue, malrotated limbs, gastroschisis, and agnathia. Systemic exposure (AUC) in rats at a dose of 0.2 mg/kg MMAE is approximately 50% of the AUC in patients who received the recommended dose of 1.8 mg/kg Polivy every 21-days.
READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

(pO - liv - ee)

POLIVY®

polatuzumab vedotin for injection

Read this carefully before you start taking Polivy and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about Polivy.

Serious Warnings and Precautions

- Infections: Fatal, life threatening, or serious infections have been reported in patients treated with Polivy (see section What are possible side effects from using Polivy?)
- Decreased production of blood cells: Serious and severe reduction in blood cells have been reported in patients treated with Polivy (see section What are possible side effects from using Polivy?)

What is Polivy used for?

For the following indication Polivy has been approved with conditions (NOC/c). This means it has passed Health Canada’s review and can be bought and sold in Canada, but the manufacturer has agreed to complete studies to make sure the drug works the way it should. For more information, talk to your healthcare professional.

Polivy is given to adults to treat “relapsed or refractory diffuse large B-cell lymphoma” that has come back or has not responded to at least one previous therapy and who cannot receive a stem cell transplant. Diffuse large B-cell lymphoma is a cancer that develops from “B-lymphocytes”; a type of blood cell in the lymphatic system. Polivy is given in combination with two other medicines for cancer called rituximab and bendamustine.

What is a Notice of Compliance with Conditions (NOC/c)?

A Notice of Compliance with Conditions (NOC/c) is a type of approval to sell a drug in Canada.

Health Canada only gives a NOC/c to a drug that treats, prevents, or helps identify a serious or life-threatening illness. The drug must show promising proof that it works well, is of high quality, and is reasonably safe. Also, the drug must either respond to a serious medical need in Canada, or be much safer than existing treatments.

Drug makers must agree in writing to clearly state on the label that the drug was given a NOC/c, to complete more testing to make sure the drug works the way it should, to actively monitor the drug’s performance after it has been sold, and to report their findings to Health Canada.
How does Polivy work?
Polivy contains the active substance polatuzumab vedotin, an anti-cancer agent, which is made up of a monoclonal antibody linked to a substance intended to kill cancer cells. The monoclonal antibody part allows the drug to find the cancer cell in the body. This substance is delivered to cancer cells by the monoclonal antibody. A monoclonal antibody is a protein that recognizes certain cancer cells.

What are the ingredients in Polivy?
Medicinal ingredients: polatuzumab vedotin
Non-medicinal ingredients: polysorbate 20, sodium hydroxide, succinic acid, sucrose

Polivy comes in the following dosage forms:
Powder for concentrate for solution for infusion in a single-use vial containing 30 mg or 140 mg (20 mg per mL).

Do not use Polivy if:
- you are allergic of polatuzumab or any of the other ingredients of this medicine or components of the container

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Polivy. Talk about any health conditions or problems you may have, including the following:
- you have fever, cough, chest pain, fatigue, painful rash, sore throat, burning pain when passing urine, feeling weak or generally unwell
- you are receiving treatment with other medications
- you are taking, have recently taken or are planning to take grapefruit and grapefruit containing products
- you sometimes feel sharp, jabbing, burning pain, prickling or tingling in your arms or legs
- you have any history of liver problems. Your doctor will check your blood to test your liver function before and regularly during treatment.
- you are pregnant, think you may be pregnant or are planning to have a baby

Warnings you should know about:
Polivy can make some existing conditions worse, or cause side effects. Also see section What are possible side effects from using Polivy?
- Infusion reactions can occur, which include fever, chills, rash or breathing problems within 24 hours of infusion. Patients should contact their healthcare professional if they experience signs and/or symptoms of infusion reactions.
- Liver toxicity (inflammation or damage to cells in the liver that can affect the normal function of the liver).
  - Injured liver cells may leak higher than normal amounts of certain substances (liver enzymes and bilirubin) into the bloodstream, resulting in elevated values in blood tests. In most cases, you will not have any symptoms but tell your healthcare professional straight away if you get yellowing of your skin and whites of your eyes (jaundice). Your healthcare professional will check your blood to test your liver function before and regularly during treatment.
- Infections
  - Signs and symptoms of infections vary between individuals, tell your healthcare professional immediately if you develop symptoms of an infection such as fever,
cough, chest pain, fatigue, painful rash, sore throat, burning pain when passing urine, feeling weak or generally unwell.

- **Myelosuppression** (a condition in which the production of normal blood cells is decreased, resulting in fewer red blood cells, white blood cells, and platelets). Your healthcare professional will do blood tests to check your blood cell count.
  - Tell your healthcare professional immediately if you develop chills or shivering, have a fever, have headaches, feel tired, experience dizziness, look pale, have unusual bleeding, bruising under the skin, longer than usual bleeding after your blood has been drawn, or bleeding from your gums.

- **Peripheral neuropathy** (problems with a change in the sensitivity of your skin).
  - Tell your healthcare professional immediately if you have any problems with a change in the sensitivity of your skin, especially in your hands or feet, such as numbness, tingling, a burning sensation, pain, or discomfort or weakness.
  - If you had any of these symptoms before treatment with Polivy, tell your doctor straight away if you notice any changes in them. You may need an adjustment to your dose (see Section “Usual dose”)

- **Progressive Multifocal Leukoencephalopathy (PML)** (a very rare and life threatening infection in the brain, that has been reported in one patient having treatment with Polivy together with bendamustine and another medicine called obinutuzumab).
  - Tell your healthcare professional immediately if you have memory loss, trouble speaking, difficulty walking, problems with your eyesight. If you had any of these symptoms before treatment with Polivy, tell your doctor straight away if you notice any changes in them. You may need medical treatment.

- **Sexual Health**
  - Women must use contraception during treatment and for 9 months following the last dose of Polivy.
  - Men must use contraception during treatment and for 6 months following the last dose of Polivy.
  - Polivy may impair a man’s ability to have children.

- **Tumour Lysis Syndrome** (also called TLS) (the development of unusual levels of some chemicals, such as potassium and uric acid, in the blood caused by the fast breakdown of cancer cells during treatment)
  - Your healthcare professional will do blood tests to check for TLS.

- **Driving and Operating Machinery**
  - Polivy may affect your ability to drive, cycle or use any tools or machines. If you get infusion related reactions or nerve damage, or if you feel tired, weak or dizzy, do not drive, cycle or use any tools or machines until the reaction stops.

- **Pregnancy**
  - It is important to tell your doctor before and during treatment if you are pregnant, think you may be pregnant, or are planning to get pregnant. This is because Polivy can affect your baby’s health. You should not use this medicine if you are pregnant unless you and your doctor decide that the benefit to you outweighs the potential risk to the unborn baby.

- **Breast-feeding**
  - Do not breast-feed while receiving Polivy and for at least 3 months after the last dose.

- **Children and adolescents**
  - This medicine should not be used in children or young people under the age of 18. This is because there is no information about its use in this age group.
Tell your healthcare professional about all the medicines you take, have recently taken or might start taking, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Polivy:
- Grapefruit and grapefruit containing products

How to take Polivy:
Polivy is given under the supervision of a healthcare professional experienced in the administration of treatments for cancer patients. Polivy is given into a vein, as a drip over 90 minutes for the initial dose and over 30 minutes for subsequent doses.

Usual dose:
The dose of this medicine depends on your body weight. The usual starting dose of this medicine is 1.8 mg for each kilogram of your body weight. You will be given 6 treatment cycles of Polivy in combination with two other medicines called rituximab and bendamustine. Each cycle lasts 21 days. If you have symptoms of peripheral neuropathy, your doctor may lower your dose to 1.4 mg for each kilogram of your body weight.

Overdose:
If you think you have taken too much Polivy, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:
If you miss an appointment to have Polivy administered, make another one straight away. For the treatment to be fully effective, it is very important to not miss a dose.

What are possible side effects from using Polivy?
These are not all the possible side effects you may feel when taking Polivy. If you experience any side effects not listed here, contact your healthcare professional.

<table>
<thead>
<tr>
<th>Serious side effects and what to do about them</th>
<th>Talk to your healthcare professional</th>
<th>Stop taking drug and get immediate medical help</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom / effect</td>
<td>Only if severe</td>
<td>In all cases</td>
</tr>
<tr>
<td>VERY COMMON</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduced number of white blood cells may lead to an increase chance of infection - symptoms may include: fever, chills, sore throat, cough</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>COMMON</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever - symptoms include: fever, chills, headache, muscle aches, loss of appetite</td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>
### Serious side effects and what to do about them

<table>
<thead>
<tr>
<th>Symptom / effect</th>
<th>Talk to your healthcare professional</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Only if severe</td>
<td>In all cases</td>
</tr>
<tr>
<td><strong>Lung Infection</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- symptoms may include: cough, fever, chills, shortness of breath, trouble breathing, chest pain</td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td><strong>Low Red Blood Cell Count</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- symptoms may include: tiredness, unusually fast heartbeat, shortness of breath, difficulty concentrating, dizziness, pale skin, leg cramps</td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td><strong>Digestive Tract Bleeding</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- symptoms may include: tiredness, unusually fast heartbeat, shortness of breath, difficulty concentrating, dizziness, pale skin, leg cramps, blood in your stool, vomiting up blood</td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td><strong>Severe Infection</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- symptoms may include: rapid breathing, confusion, fever, chills, very low body temperature, urinating less than normal, rapid pulse, feeling sick (nausea), vomiting, diarrhea</td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td><strong>Low Blood Platelet Count</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- symptoms may include: bleeding in the skin that looks like tiny red or purple spots on the skin, bleeding outside or inside your body, blood in your urine or stool</td>
<td></td>
<td>✔</td>
</tr>
</tbody>
</table>

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.
Reporting Side Effects

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

- Visiting the 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; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Reporting Suspected Side Effects Following Immunization

For the general public: Should you experience a side effect following immunization, please report it to your doctor, nurse, or pharmacist.

Should you require information related to the management of the side effect, please contact your healthcare provider. The Public Health Agency of Canada, Health Canada and Hoffmann-La Roche Limited cannot provide medical advice.

For healthcare professionals: If a patient experiences a side effect following immunization, please complete the Adverse Events Following Immunization (AEFI) Form appropriate for your province/territory (http://www.phac-aspc.gc.ca/im/aefi-essi-form-eng.php) and send it to your local Health Unit.

Storage:

Polivy will be stored by the healthcare professionals at the hospital or clinic. The storage details are as follows:
- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the carton after “EXP”. The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C to 8°C).
- Do not freeze.
- Do not shake.
- Keep the container in the outer carton in order to protect from light.

Medicines should not be disposed of via wastewater or household waste. Your healthcare professional will properly dispose of any medicines that are no longer being used. These measures will help protect the environment.

If you want more information about Polivy:
- Talk to your healthcare professional
• Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website; the manufacturer’s website www.rochecanada.com, or by calling 1-888-762-4388.

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