POLIVY- polatuzumab vedotin injection, powder, lyophilized, for solution
Genentech, Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use POLIVY safely and effectively. See full prescribing information for POLIVY.

POLIVY® (polatuzumab vedotin-piiq) for injection, for intravenous use
Initial U.S. Approval: 2019

RECENT MAJOR CHANGES

Dosage and Administration (2.4)	09/2020

INDICATIONS AND USAGE

POLIVY is a CD79b-directed antibody-drug conjugate indicated in combination with bendamustine and a rituximab product for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified, after at least two prior therapies. (1)
Accelerated approval was granted for this indication based on complete response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

DOSAGE AND ADMINISTRATION

- The recommended dose of POLIVY is 1.8 mg/kg as an intravenous infusion over 90 minutes every 21 days for 6 cycles in combination with bendamustine and a rituximab product. Subsequent infusions may be administered over 30 minutes if the previous infusion is tolerated. (2)
- Premedicate with an antihistamine and antipyretic before POLIVY. (2)
- See Full Prescribing Information for instructions on preparation and administration. (2.4)

DOSAGE FORMS AND STRENGTHS

For injection: 30 mg or 140 mg of polatuzumab vedotin-piiq as a lyophilized powder in a single-dose vial. (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Peripheral Neuropathy: Monitor patients for peripheral neuropathy and modify or discontinue dose accordingly. (5.1)
- Infusion-Related Reactions: Premedicate with an antihistamine and antipyretic. Monitor patients closely during infusions. Interrupt or discontinue infusion for reactions. (5.2)
- Myelosuppression: Monitor complete blood counts. Manage using dose delays or reductions and growth factor support. Monitor for signs of infection. (5.3)
- Serious and Opportunistic Infections: Closely monitor patients for signs of bacterial, fungal, or viral infections. (5.4)
- Progressive Multifocal Leukoencephalopathy (PML): Monitor patients for new or worsening neurological, cognitive, or behavioral changes suggestive of PML. (5.5)
- Tumor Lysis Syndrome: Closely monitor patients with high tumor burden or rapidly proliferative tumors. (5.6)
- Hepatotoxicity: Monitor liver enzymes and bilirubin. (5.7)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment and for 3 months after the last dose. (5.8)

ADVERSE REACTIONS

The most common adverse reactions (≥20%) included neutropenia, thrombocytopenia, anemia, peripheral neuropathy, fatigue, diarrhea, pyrexia, decreased appetite, and pneumonia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genentech at 1-888-835-2555 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Concomitant use of strong CYP3A inhibitors or inducers has the potential to affect the exposure to unconjugated monomethyl auristatin E (MMAE). (7.1)

USE IN SPECIFIC POPULATIONS

- Hepatic impairment has the potential to increase exposure to MMAE. Monitor patients for adverse reactions. (8.6)
- Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 9/2020

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

POLIVY in combination with bendamustine and a rituximab product is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, after at least two prior therapies.

Accelerated approval was granted for this indication based on complete response rate *[see Clinical Studies (14.1)]*. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

The recommended dose of POLIVY is 1.8 mg/kg administered as an intravenous infusion every 21 days for 6 cycles in combination with bendamustine and a rituximab product. Administer POLIVY, bendamustine, and a rituximab product in any order on Day 1 of each cycle. The recommended dose of bendamustine is 90 mg/m^2/day on Days 1 and 2 when administered with POLIVY and a rituximab product. The recommended dose of rituximab product is 375 mg/m^2 intravenously on Day 1 of each cycle.

If not already premedicated, administer an antihistamine and antipyretic at least 30 minutes prior to POLIVY. Administer the initial dose of POLIVY over 90 minutes. Monitor patients for infusion-related reactions during the infusion and for a minimum of 90 minutes following completion of the initial dose. If the previous 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.

If a planned dose of POLIVY is missed, administer as soon as possible. Adjust the schedule of administration to maintain a 21-day interval between doses.

2.2 Management of Adverse Reactions

Table 1 provides management guidelines for peripheral neuropathy, infusion-related reaction, and myelosuppression.

Table 1 Management of Peripheral Neuropathy, Infusion-Related Reaction, and Myelosuppression

Event	Dose Modification
Grade 2–3 Peripheral Neuropathy	Hold POLIVY dosing until improvement to Grade 1 or lower. If recovered to Grade 1 or lower on or before Day 14, restart POLIVY with the next cycle 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 or lower on or before Day 14, discontinue POLIVY.
Grade 4 Peripheral Neuropathy	Discontinue POLIVY.
Grade 1–3 Infusion-Related Reaction	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.
Grade 4 Infusion-Related Reaction	Stop POLIVY infusion immediately. Give supportive treatment. Permanently discontinue POLIVY.
	Hold all treatment until ANC recovers to greater than 1000/microliter. If ANC recovers to greater than 1000/microliter on or before Day 7, resume all treatment without any additional dose reductions. Consider granulocyte colony-stimulating factor prophylaxis for subsequent cycles, if not

Grade 3–4 Neutropenia*,†	previously given. If ANC recovers to greater than 1000/microliter after Day 7: • restart all treatment. Consider granulocyte colony-stimulating factor prophylaxis for subsequent cycles, if not previously given. If prophylaxis was given, consider dose reduction of bendamustine. • if dose reduction of bendamustine has already occurred, consider dose reduction of POLIVY to 1.4 mg/kg.
Grade 3–4 Thrombocytopenia*,†	Hold all treatment until platelets recover to greater than 75,000/microliter. If platelets recover to greater than 75,000/microliter on or before Day 7, resume all treatment without any additional dose reductions. If platelets recover to greater than 75,000/microliter after Day 7: • restart all treatment, with dose reduction of bendamustine. • if dose reduction of bendamustine has already occurred, consider dose reduction of POLIVY to 1.4 mg/kg.

* Severity on Day 1 of any cycle.
† If primary cause is due to lymphoma, dose delay or reduction may not be needed.

2.3 Recommended Prophylactic Medications

If not already premedicated for a rituximab product, administer an antihistamine and antipyretic at least 30 to 60 minutes prior to POLIVY for potential infusion-related reactions *[see Warnings and Precautions (5.2)]*.

Administer prophylaxis for *Pneumocystis jiroveci* pneumonia and herpesvirus throughout treatment with POLIVY.

Consider prophylactic granulocyte colony stimulating factor administration for neutropenia *[see Warnings and Precautions (5.3)]*.

Administer tumor lysis syndrome prophylaxis for patients at increased risk of tumor lysis syndrome *[see Warnings and Precautions (5.6)]*.

2.4 Instructions for Preparation and Administration

Reconstitute and further dilute POLIVY prior to intravenous infusion.

POLIVY is a cytotoxic drug. Follow applicable special handling and disposal procedures.[1]

Parenteral drug products should be inspected visually for particulate matter and

discoloration prior to administration, whenever solution and container permit.

Reconstitution

- Reconstitute immediately before dilution.
- More than one vial may be needed for a full dose. Calculate the dose, the total volume of reconstituted POLIVY solution required, and the number of POLIVY vials needed.
- Using a sterile syringe, slowly inject Sterile Water for Injection, USP, using the volume provided in Table 2, into the POLIVY vial, with the stream directed toward the inside wall of the vial to obtain a concentration of 20 mg/mL of polatuzumab vedotin-piiq.

Table 2 Reconstitution Volumes

Strength	Volume of Sterile Water for Injection, USP required for reconstitution
30 mg vial	1.8 mL
140 mg vial	7.2 mL

- Swirl the vial gently until completely dissolved. *Do not shake*.
- Inspect the reconstituted solution for discoloration and particulate matter. The reconstituted solution should appear colorless to slightly brown, clear to slightly opalescent, and free of visible particulates. Do not use if the reconstituted solution is discolored, is cloudy, or contains visible particulates. *Do not freeze or expose to direct sunlight.*
- If needed, store unused reconstituted POLIVY solution refrigerated at 2°C to 8°C (36°F to 46°F) for up to 48 hours or at room temperature (9°C to 25°C, 47°F to 77°F) up to a maximum of 8 hours prior to dilution. Discard vial when cumulative storage time prior to dilution exceeds 48 hours.

Dilution

- Dilute polatuzumab vedotin-piiq to a final concentration of 0.72–2.7 mg/mL in an intravenous infusion bag with a minimum volume of 50 mL containing 0.9% Sodium Chloride Injection, USP, 0.45% Sodium Chloride Injection, USP, or 5% Dextrose Injection, USP.
- Determine the volume of 20 mg/mL reconstituted solution needed based on the required dose.
- Withdraw the required volume of reconstituted solution from the POLIVY vial using a sterile syringe and dilute into the intravenous infusion bag. Discard any unused portion left in the vial.
- Gently mix the intravenous bag by slowly inverting the bag. *Do not shake*.
- Inspect the intravenous bag for particulates and discard if present.
- If not used immediately, store the diluted POLIVY solution as specified in Table 3. Discard if storage time exceeds these limits. *Do not freeze or expose to direct sunlight.*

Table 3 Diluted POLIVY Solution Storage Conditions

Diluent Used to Prepare Solution	Diluted POLIVY Solution Storage Conditions*

for Infusion	Conditions
0.9% Sodium Chloride Injection, USP	Up to 36 hours at 2°C to 8°C (36°F to 46°F) or up to 4 hours at room temperature (9 to 25°C, 47 to 77°F)
0.45% Sodium Chloride Injection, USP	Up to 18 hours at 2°C to 8°C (36°F to 46°F) or up to 4 hours at room temperature (9 to 25°C, 47 to 77°F)
5% Dextrose Injection, USP	Up to 36 hours at 2°C to 8°C (36°F to 46°F) or up to 6 hours at room temperature (9 to 25°C, 47 to 77°F)

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

- Limit transportation to 30 minutes at 9°C to 25°C or 24 hours at 2°C to 8°C (refer to instructions below). The total storage plus transportation times of the diluted product should not exceed the storage duration specified in Table 3.
- Agitation stress can result in aggregation. Limit agitation of diluted product during preparation and transportation to administration site. Do not transport diluted product through an automated system (e.g., pneumatic tube or automated cart). If the prepared solution will be transported to a separate facility, remove air from the infusion bag to prevent aggregation. If air is removed, an infusion set with a vented spike is required to ensure accurate dosing during the infusion.
- No incompatibilities have been observed between POLIVY and intravenous infusion bags with product-contacting materials of polyvinyl chloride (PVC) or polyolefins (PO) such as polyethylene (PE) and polypropylene (PP). 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), fluorinated ethylene propylene (FEP), or polytetrafluorethylene (PTFE), or with filter membranes composed of polyether sulfone (PES) or polysulfone (PSU).

Administration

- Administer POLIVY as an intravenous infusion only.
- POLIVY must be administered using a dedicated infusion line equipped with a sterile, non-pyrogenic, low-protein-binding in-line or add-on filter (0.2- or 0.22-micron pore size) and a catheter.
- Do not mix POLIVY with or administer as an infusion with other drugs.

3 DOSAGE FORMS AND STRENGTHS

For Injection: 30 mg/vial or 140 mg/vial of polatuzumab vedotin-piiq as a white to grayish-white lyophilized powder in a single-dose vial for reconstitution and further dilution.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Peripheral Neuropathy

POLIVY can cause peripheral neuropathy, including severe cases. Peripheral neuropathy occurs as early as the first cycle of treatment and is a cumulative effect *[see Adverse Reactions (6.1)]*. POLIVY may exacerbate pre-existing peripheral neuropathy.

In Study GO29365, of 173 patients treated with POLIVY, 40% reported new or worsening peripheral neuropathy, with a median time to onset of 2.1 months. The peripheral neuropathy was Grade 1 in 26% of cases, Grade 2 in 12%, and Grade 3 in 2.3%. Peripheral neuropathy resulted in POLIVY dose reduction in 2.9% of treated patients, dose delay in 1.2%, and permanent discontinuation in 2.9%. Sixty-five percent of patients reported improvement or resolution of peripheral neuropathy after a median of 1 month, and 48% reported complete resolution.

The peripheral neuropathy is predominantly sensory; however, motor and sensorimotor peripheral neuropathy also occur. Monitor 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 Dosage and Administration (2.2)]*.

5.2 Infusion-Related Reactions

POLIVY can cause infusion-related reactions, including severe cases. Delayed infusion-related reactions as late as 24 hours after receiving POLIVY have occurred. With premedication, 7% of patients (12/173) in Study GO29365 reported infusion-related reactions after the administration of POLIVY. The reactions were Grade 1 in 67%, Grade 2 in 25%, and Grade 3 in 8%. Symptoms included fever, chills, flushing, dyspnea, hypotension, and urticaria.

Administer an antihistamine and antipyretic prior to the administration of POLIVY, and monitor patients closely throughout the infusion. If an infusion-related reaction occurs, interrupt the infusion and institute appropriate medical management *[see Dosage and Administration (2.2)]*.

5.3 Myelosuppression

Treatment with POLIVY can cause serious or severe myelosuppression, including neutropenia, thrombocytopenia, and anemia. In patients treated with POLIVY plus BR (n = 45), 42% received primary prophylaxis with granulocyte colony-stimulating factor. Grade 3 or higher hematologic adverse reactions included neutropenia (42%), thrombocytopenia (40%), anemia (24%), lymphopenia (13%), and febrile neutropenia (11%) *[see Adverse Reactions (6.1)]*. Grade 4 hematologic adverse reactions included neutropenia (24%), thrombocytopenia (16%), lymphopenia (9%), and febrile neutropenia (4.4%). Cytopenias were the most common reason for treatment discontinuation (18% of all patients).

Monitor complete blood counts throughout treatment. Cytopenias may require a delay, dose reduction, or discontinuation of POLIVY *[see Dosage and Administration (2.2)]*. Consider prophylactic granulocyte colony-stimulating factor administration.

5.4 Serious and Opportunistic Infections

Fatal and/or serious infections, including opportunistic infections such as sepsis, pneumonia (including *Pneumocystis jiroveci* and other fungal pneumonia), herpesvirus infection, and cytomegalovirus infection have occurred in patients treated with POLIVY *[see Adverse Reactions (6.1)]*.

Grade 3 or higher infections occurred in 32% (55/173) of patients treated with POLIVY. Infection-related deaths were reported in 2.9% of patients within 90 days of last treatment.

Closely monitor patients during treatment for signs of infection. Administer prophylaxis for *Pneumocystis jiroveci* pneumonia and herpesvirus.

5.5 Progressive Multifocal Leukoencephalopathy (PML)

PML has been reported after treatment with POLIVY (0.6%, 1/173). Monitor for new or worsening neurological, cognitive, or behavioral changes. Hold POLIVY and any concomitant chemotherapy if PML is suspected, and permanently discontinue if the diagnosis is confirmed.

5.6 Tumor Lysis Syndrome

POLIVY may cause tumor lysis syndrome. Patients with high tumor burden and rapidly proliferative tumor may be at increased risk of tumor lysis syndrome. Monitor closely and take appropriate measures, including tumor lysis syndrome prophylaxis.

5.7 Hepatotoxicity

Serious cases of hepatotoxicity that were consistent with hepatocellular injury, including elevations of transaminases and/or bilirubin, have occurred in patients treated with POLIVY.

In recipients of POLIVY in Study GO29365 (n = 173), Grade 3 and 4 transaminase elevations developed in 1.9% and 1.9%, respectively. Laboratory values suggestive of drug-induced liver injury (both an ALT or AST greater than 3 times upper limit of normal [ULN] and total bilirubin greater than 2 times ULN) occurred in 2.3% of patients.

Preexisting liver disease, elevated baseline liver enzymes, and concomitant medications may increase the risk of hepatotoxicity. Monitor liver enzymes and bilirubin level.

5.8 Embryo-Fetal Toxicity

Based on the mechanism of action and findings from animal studies, POLIVY can cause fetal harm when administered to a pregnant woman. The small molecule component of POLIVY, MMAE, administered to rats caused adverse developmental outcomes, including embryo-fetal mortality and structural abnormalities, at exposures below those occurring clinically at the recommended dose.

Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with POLIVY and for at least 3 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with POLIVY and for at least 5 months after the last dose *[see Use in Specific Populations (8.1, 8.3), Clinical Pharmacology (12.1)]*.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are discussed in greater detail in other sections of the label:

- Peripheral Neuropathy *[see Warnings and Precautions (5.1)]*
- Infusion-Related Reactions *[see Warnings and Precautions (5.2)]*
- Myelosuppression *[see Warnings and Precautions (5.3)]*
- Serious and Opportunistic Infections *[see Warnings and Precautions (5.4)]*
- Progressive Multifocal Leukoencephalopathy *[see Warnings and Precautions (5.5)]*
- Tumor Lysis Syndrome *[see Warnings and Precautions (5.6)]*
- Hepatotoxicity *[see Warnings and Precautions (5.7)]*

6.1 Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described in this section reflect exposure to POLIVY in Study GO29365, a multicenter clinical trial for adult patients with relapsed or refractory B-cell lymphomas *[see Clinical Studies (14)]*. In patients with relapsed or refractory DLBCL, the trial included a single-arm safety evaluation of POLIVY in combination with bendamustine and a rituximab product (BR) (n = 6), followed by an open-label randomization to POLIVY in combination with BR versus BR alone (n = 39 treated per arm).

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/m^2 daily was administered intravenously on Days 2 and 3 of Cycle 1 and on Days 1 and 2 of Cycles 2–6. A rituximab product dosed at 375 mg/m^2 was administered intravenously on Day 1 of each cycle. Granulocyte colony-stimulating factor primary prophylaxis was optional and administered to 42% of recipients of POLIVY plus BR.

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 ≥75/µL, creatinine clearance (CLcr) ≥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.

Patients treated with POLIVY plus BR received a median of 5 cycles, with 49% receiving 6 cycles. Patients treated with BR alone received a median of 3 cycles, with 23% receiving 6 cycles.

Fatal adverse reactions occurred in 7% of recipients of POLIVY plus BR within 90 days of last treatment. Serious adverse reactions occurred in 64%, most often from infection. Serious adverse reactions in ≥5% of recipients of POLIVY plus BR included pneumonia (16%), febrile neutropenia (11%), pyrexia (9%), and sepsis (7%).

In recipients of POLIVY plus BR, adverse reactions led to dose reduction in 18%, dose interruption in 51%, and permanent discontinuation of all treatment in 31%. The most

common adverse reactions leading to treatment discontinuation were thrombocytopenia and/or neutropenia.

Table 4 summarizes commonly reported adverse reactions. In recipients of POLIVY plus BR, adverse reactions in ≥20% of patients included neutropenia, thrombocytopenia, anemia, peripheral neuropathy, fatigue, diarrhea, pyrexia, decreased appetite, and pneumonia.

Table 4 Adverse Reactions Occurring in >10% of Patients with Relapsed or Refractory DLBCL and ≥5% More in the POLIVY Plus Bendamustine and Rituximab Product Group

Adverse Reactions by Body System	POLIVY + BR n = 45		BR n = 39	
	All Grades, %	Grade 3 or Higher, %	All Grades, %	Grade 3 or Higher, %
Blood and Lymphatic System Disorders				
Neutropenia	49	42	44	36
Thrombocytopenia	49	40	33	26
Anemia	47	24	28	18
Lymphopenia	13	13	8	8
Nervous System Disorders				
Peripheral neuropathy	40	0	8	0
Dizziness	13	0	8	0
Gastrointestinal Disorders				
Diarrhea	38	4.4	28	5
Vomiting	18	2.2	13	0
General Disorders				
Infusion-related reaction	18	2.2	8	0
Pyrexia	33	2.2	23	0
Decreased appetite	27	2.2	21	0
Infections				
Pneumonia	22	16*	15	2.6†
Upper respiratory tract infection	13	0	8	0
Investigations				
Weight decreased	16	2.2	8	2.6
Metabolism and Nutrition Disorders				
Hypokalemia	16	9	10	2.6
Hypoalbuminemia	13	2.2	8	0
Hypocalcemia	11	2.2	5	0

The table includes a combination of grouped and ungrouped terms. Events were graded using NCI CTCAE version 4.

* Includes 2 events with fatal outcome.

† Includes 1 event with fatal outcome.

Other clinically relevant adverse reactions (<10% or with a <5% difference) in recipients of POLIVY plus BR included:

- **Blood and lymphatic system disorders:** pancytopenia (7%)
- **Musculoskeletal disorders:** arthralgia (7%)
- **Investigations:** hypophosphatemia (9%), transaminase elevation (7%), lipase increase (7%)
- **Respiratory disorders:** pneumonitis (4.4%)

Selected treatment-emergent laboratory abnormalities are summarized in Table 5. In recipients of POLIVY plus BR, >20% of patients developed Grade 3 or 4 neutropenia, leukopenia, or thrombocytopenia, and >10% developed Grade 4 neutropenia (13%) or Grade 4 thrombocytopenia (11%).

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

Laboratory Parameter*	POLIVY + BR n = 45		BR n = 39	
	All Grades, (%)	Grade 3–4, (%)	All Grades, (%)	Grade 3–4, (%)
Hematologic				
Lymphocyte count decreased	87	87	90	82
Neutrophil count decreased	78	61	56	33
Hemoglobin decreased	78	18	62	10
Platelet count decreased	76	31	64	26
Chemistry				
Creatinine increased	87	4.4	77	5
Calcium decreased	44	9	26	0
SGPT/ALT increased	38	0	8	2.6
SGOT/AST increased	36	0	26	2.6
Lipase increased	36	9	13	5
Phosphorus decreased	33	7	28	8
Amylase increased	24	0	18	2.6
Potassium decreased	24	11	28	5

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

Safety was also evaluated in 173 adult patients with relapsed or refractory lymphoma who received POLIVY, bendamustine, and either a rituximab product or obinutuzumab in

Study GO29365, including the 45 patients with DLBCL described above. In the expanded safety population, the median age was 66 years (range 27 – 86), 57% were male, 91% had an ECOG performance status of 0-1, and 32% had a history of peripheral neuropathy at baseline.

Fatal adverse reactions occurred in 4.6% of recipients of POLIVY within 90 days of last treatment, with infection as a leading cause. Serious adverse reactions occurred in 60%, most often from infection.

Table 6 summarizes the most common adverse reactions in the expanded safety population. The overall safety profile was similar to that described above. Adverse reactions in ≥20% of patients were diarrhea, neutropenia, peripheral neuropathy, fatigue, thrombocytopenia, pyrexia, decreased appetite, anemia, and vomiting. Infection-related adverse reactions in >10% of patients included upper respiratory tract infection, febrile neutropenia, pneumonia, and herpesvirus infection.

Table 6 Most Common Adverse Reactions (≥20% Any Grade or ≥5% Grade 3 or Higher) in Recipients of POLIVY and Chemoimmunotherapy for Relapsed or Refractory Lymphoma

Adverse Reaction by Body System	POLIVY + Bendamustine + Rituximab Product or Obinutuzumab n = 173	
	All Grades, %	Grade 3 or Higher, %
Blood and Lymphatic System Disorders		
Neutropenia	44	39
Thrombocytopenia	31	23
Anemia	28	14
Febrile neutropenia*	13	13
Leukopenia	13	8
Lymphopenia	12	12
Nervous System Disorders		
Peripheral neuropathy	40	2.3
Gastrointestinal Disorders		
Diarrhea	45	8
Vomiting	27	2.9
General Disorders		
Fatigue	40	5
Pyrexia	30	2.9
Decreased appetite	29	1.7
Infections		
Pneumonia	13	10†
Sepsis	6	6‡
Metabolism and Nutrition Disorders		

Hypokalemia	18	6

The table includes a combination of grouped and ungrouped terms.

* Primary prophylaxis with granulocyte colony-stimulating factor was given to 46% of all patients.
† Includes 5 events with fatal outcome.
‡ Includes 4 events with fatal outcome.

Other clinically relevant adverse reactions (<20% any grade) included:

- **General disorders:** infusion-related reaction (7%)
- **Infection:** upper respiratory tract infection (16%), lower respiratory tract infection (10%), herpesvirus infection (12%), cytomegalovirus infection (1.2%)
- **Respiratory:** dyspnea (19%), pneumonitis (1.7%)
- **Nervous system disorders:** dizziness (10%)
- **Investigations:** weight decrease (10%), transaminase elevation (8%), lipase increase (3.5%)
- **Musculoskeletal disorders:** arthralgia (7%)
- **Eye disorders:** blurred vision (1.2%)

6.2 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to polatuzumab vedotin-piiq in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

Across all arms of Study GO29365, 8/134 (6%) patients tested positive for antibodies against polatuzumab vedotin-piiq at one or more post-baseline time points. Across clinical trials, 14/536 (2.6%) evaluable POLIVY-treated patients tested positive for such antibodies at one or more post-baseline time points. Due to the limited number of patients with antibodies against polatuzumab vedotin-piiq, no conclusions can be drawn concerning a potential effect of immunogenicity on efficacy or safety.

7 DRUG INTERACTIONS

7.1 Effects of Other Drugs on POLIVY

Strong CYP3A Inhibitors

Concomitant use with a strong CYP3A4 inhibitor may increase unconjugated MMAE AUC *[see Clinical Pharmacology (12.3)]*, which may increase POLIVY toxicities. Monitor patients for signs of toxicity.

Strong CYP3A Inducers

Concomitant use with a strong CYP3A4 inducer may decrease unconjugated MMAE AUC *[see Clinical Pharmacology (12.3)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on findings from animal studies and its mechanism of action *[see Clinical Pharmacology (12.1)]*, POLIVY can cause fetal harm. There are no available data in pregnant women to inform the drug-associated risk. In animal reproduction studies, administration of the small molecule component of POLIVY, MMAE, to pregnant rats during organogenesis at exposures below the clinical exposure at the recommended dose of 1.8 mg/kg POLIVY every 21 days resulted in embryo-fetal mortality and structural abnormalities *(see Data)*. Advise a pregnant woman of the potential risks to a fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2–4% and 15–20%, respectively.

Data

Animal Data

No embryo-fetal development studies in animals have been performed with polatuzumab vedotin-piiq. In an embryo-fetal developmental study in pregnant rats, administration of two intravenous doses of MMAE, the small molecule component of POLIVY, on gestational days 6 and 13 caused embryo-fetal mortality and structural abnormalities, including protruding tongue, malrotated limbs, gastroschisis, and agnathia compared to controls at a dose of 0.2 mg/kg (approximately 0.5-fold the human area under the curve [AUC] at the recommended dose).

8.2 Lactation

Risk Summary

There is no information regarding the presence of polatuzumab vedotin-piiq in human milk, the effects on the breastfed child, or milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with POLIVY and for at least 2 months after the last dose.

8.3 Females and Males of Reproductive Potential

Pregnancy Testing

Verify pregnancy status in females of reproductive potential prior to initiating POLIVY *[see Use in Specific Populations (8.1)]*.

Contraception

Females

POLIVY can cause embryo-fetal harm when administered to pregnant women *[see Use in Specific Populations (8.1)]*. Advise females of reproductive potential to use effective

contraception during treatment with POLIVY and for 3 months after the final dose *[see Nonclinical Toxicology (13.1)]*.

Males

Based on genotoxicity findings, advise males with female partners of reproductive potential to use effective contraception during treatment with POLIVY and for at least 5 months after the final dose *[see Nonclinical Toxicity (13.1)]*.

Infertility

Based on findings from animal studies, POLIVY may impair male fertility. The reversibility of this effect is unknown *[see Nonclinical Toxicology (13.1)]*.

8.4 Pediatric Use

Safety and effectiveness of POLIVY have not been established in pediatric patients.

8.5 Geriatric Use

Among 173 patients treated with POLIVY in Study GO29365, 95 (55%) were ≥65 years of age. Patients aged ≥65 had a numerically higher incidence of serious adverse reactions (64%) than patients aged <65 (53%). Clinical studies of POLIVY did not include sufficient numbers of patients aged ≥65 to determine whether they respond differently from younger patients.

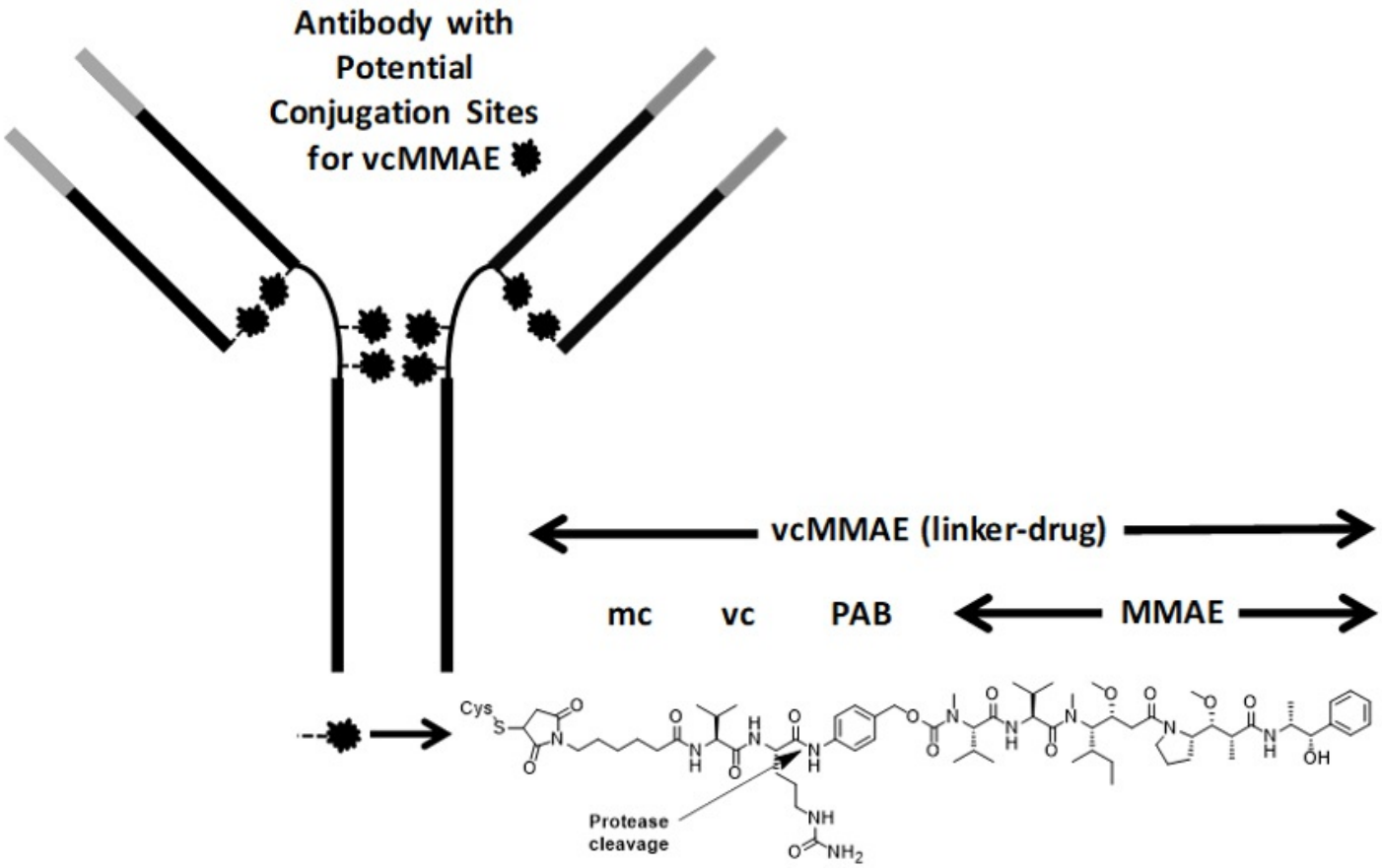
8.6 Hepatic Impairment

Avoid the administration of POLIVY in patients with moderate or severe hepatic impairment (bilirubin greater than 1.5 × ULN). Patients with moderate or severe hepatic impairment are likely to have increased exposure to MMAE, which may increase the risk of adverse reactions. POLIVY has not been studied in patients with moderate or severe hepatic impairment *[see Clinical Pharmacology (12.3) and Warnings and Precautions (5.7)].*

No adjustment in the starting dose is required when administering POLIVY to patients with mild hepatic impairment (bilirubin greater than ULN to less than or equal to 1.5 × ULN or AST greater than ULN).

11 DESCRIPTION

Polatuzumab vedotin-piiq is a CD79b-directed antibody-drug conjugate (ADC) consisting of three components: 1) the humanized immunoglobulin G1 (IgG1) monoclonal antibody specific for human CD79b; 2) the small molecule anti-mitotic agent MMAE; and 3) a protease-cleavable linker maleimidocaproyl-valine-citrulline-p-aminobenzyloxycarbonyl (mc-vc-PAB) that covalently attaches MMAE to the polatuzumab antibody.



Polatuzumab vedotin-piiq has an approximate molecular weight of 150 kDa. An average of 3.5 molecules of MMAE are attached to each antibody molecule. Polatuzumab vedotin-piiq is produced by chemical conjugation of the antibody and small molecule components. The antibody is produced by mammalian (Chinese hamster ovary) cells, and the small molecule components are produced by chemical synthesis.

POLIVY (polatuzumab vedotin-piiq) for injection is supplied as a sterile, white to grayish-white, preservative-free, lyophilized powder, which has a cake-like appearance, for intravenous infusion after reconstitution and dilution.

Each single-dose 30 mg POLIVY vial delivers 30 mg of polatuzumab vedotin-piiq, polysorbate-20 (1.8 mg), sodium hydroxide (0.82 mg), succinic acid (1.77 mg), and sucrose (62 mg). After reconstitution with 1.8 mL of Sterile Water for Injection, USP, the final concentration is 20 mg/mL with a pH of approximately 5.3.

Each single-dose 140 mg POLIVY vial delivers 140 mg of polatuzumab vedotin-piiq, polysorbate-20 (8.4 mg), sodium hydroxide (3.80 mg), succinic acid (8.27 mg), and sucrose (288 mg). After reconstitution with 7.2 mL of Sterile Water for Injection, USP, the final concentration is 20 mg/mL with a pH of approximately 5.3.

The POLIVY vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Polatuzumab vedotin-piiq is a CD79b-directed antibody-drug conjugate with activity against dividing B cells. The small molecule, MMAE, is an anti-mitotic agent covalently

attached to the antibody via a cleavable linker. The monoclonal antibody binds to CD79b, a B-cell specific surface protein, which is a component of the B-cell receptor. Upon binding CD79b, polatuzumab vedotin-piiq is 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.

12.2 Pharmacodynamics

Over polatuzumab vedotin-piiq dosages of 0.1 to 2.4 mg/kg (0.06 to 1.33 times the approved recommended dosage), a higher exposure was associated with higher incidence of some adverse reactions (e.g., ≥Grade 2 peripheral neuropathy, ≥Grade 3 anemia) and a lower exposure was associated with lower efficacy.

Cardiac Electrophysiology

Polatuzumab vedotin-piiq did not prolong the mean QTc interval to any clinically relevant extent based on ECG data from two open-label studies in patients with previously treated B-cell malignancies at the recommended dosage.

12.3 Pharmacokinetics

The exposure parameters of antibody-conjugated MMAE (acMMAE) and unconjugated MMAE (the cytotoxic component of polatuzumab vedotin-piiq) are summarized in Table 7. The plasma exposure of acMMAE and unconjugated MMAE increased proportionally over a polatuzumab vedotin-piiq dose range from 0.1 to 2.4 mg/kg (0.06 to 1.33 times the approved recommended dosage). Cycle 3 acMMAE AUC were predicted to increase by approximately 30% over Cycle 1 AUC, and achieved more than 90% of the Cycle 6 AUC. Unconjugated MMAE plasma exposures were <3% of acMMAE exposures, and the AUC and C_{max} were predicted to decrease after repeated every-3-week dosing.

Table 7 Exposure Parameters of acMMAE and Unconjugated MMAE*

	acMMAE Mean (± SD)	**Unconjugated MMAE Mean (± SD)**
C_{max} (ng/mL)	803 (± 233)	6.82 (± 4.73)
AUC_{inf} (day*ng/mL)	1860 (± 966)	52.3 (± 18.0)

C_{max} = maximum concentration, AUC_{inf} = area under the concentration-time curve from time zero to infinity.

* After the first polatuzumab vedotin-piiq dose of 1.8 mg/kg.

Distribution

The acMMAE central volume of distribution estimated based on population PK analysis is 3.15 L. For humans, MMAE plasma protein binding is 71% to 77% and the blood-to-plasma ratio is 0.79 to 0.98, in vitro.

Elimination

The acMMAE terminal half-life is approximately 12 days (95% CI: 8.1 to 19.5 days) at Cycle 6 with predicted clearance of 0.9 L/day. The unconjugated MMAE terminal half-life is approximately 4 days after the first polatuzumab vedotin-piiq dose.

Metabolism

Polatuzumab vedotin-piiq catabolism has not been studied in humans; however, it is expected to undergo catabolism to small peptides, amino acids, unconjugated MMAE, and unconjugated MMAE-related catabolites. MMAE is a substrate for CYP3A4.

Specific Populations

No clinically significant differences in the pharmacokinetics of polatuzumab vedotin-piiq were observed based on age (20 to 89 years), sex, or race/ethnicity (Asian and non-Asian). No clinically significant differences in the pharmacokinetics of acMMAE or unconjugated MMAE were observed based on mild to moderate renal impairment (CLcr 30 to 89 mL/min). In mild hepatic impairment (AST or ALT >1.0 to 2.5 × ULN or total bilirubin >1.0 to 1.5 × ULN), there was a 40% increase in MMAE exposure, which was not deemed clinically significant.

The effect of severe renal impairment (CLcr 15 to 29 mL/min), end-stage renal disease with or without dialysis, moderate to severe hepatic impairment (AST or ALT >2.5 × ULN or total bilirubin >1.5 × ULN), or liver transplantation on the pharmacokinetics of acMMAE or unconjugated MMAE is unknown.

Drug Interaction Studies

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

Physiologically-Based Pharmacokinetic (PBPK) Modeling Predictions:

Strong CYP3A Inhibitor: Concomitant use of polatuzumab vedotin-piiq with ketoconazole (strong CYP3A inhibitor) is predicted to increase unconjugated MMAE AUC by 45%.

Strong CYP3A Inducer: Concomitant use of polatuzumab vedotin-piiq with rifampin (strong CYP3A inducer) is predicted to decrease unconjugated MMAE AUC by 63%.

Sensitive CYP3A Substrate: Concomitant use of polatuzumab vedotin-piiq is predicted not to affect exposure to midazolam (sensitive CYP3A substrate).

Population Pharmacokinetic (popPK) Modeling Predictions:

Bendamustine or Rituximab: No clinically significant differences in the pharmacokinetics of acMMAE or unconjugated MMAE when polatuzumab vedotin-piiq is used concomitantly with bendamustine or rituximab.

In Vitro Studies Where Drug Interaction Potential Was Not Further Evaluated Clinically:

Cytochrome P450 (CYP) Enzymes: MMAE does not inhibit CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, or CYP2D6. MMAE does not induce major CYP enzymes.

Transporter Systems: MMAE does not inhibit P-gp. MMAE is a P-gp substrate.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies in animals have not been performed with polatuzumab vedotin-piiq or MMAE.

MMAE was positive for genotoxicity in the in vivo rat bone marrow micronucleus study through an aneugenic mechanism. MMAE was not mutagenic in the bacterial reverse mutation (Ames) assay or the L5178Y mouse lymphoma forward mutation assay.

Fertility studies in animals have not been performed with polatuzumab vedotin-piiq or MMAE. However, results of repeat-dose toxicity in rats indicate the potential for polatuzumab vedotin-piiq to impair male fertility. In the 4-week repeat-dose toxicity study in rats with weekly dosing of 2, 6, and 10 mg/kg, 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 at the recommended dose based on unconjugated MMAE AUC).

14 CLINICAL STUDIES

14.1 Relapsed or Refractory Diffuse Large B-cell Lymphoma

The efficacy of POLIVY was evaluated in Study GO29365 (NCT02257567), an open-label, multicenter clinical trial that included a cohort of 80 patients with relapsed or refractory DLBCL after at least one prior regimen. Patients were randomized 1:1 to receive either POLIVY in combination with bendamustine and a rituximab product (BR) or BR alone for six 21-day cycles. Randomization was stratified by duration of response (DOR) to last therapy. Eligible patients were not candidates for autologous HSCT at study entry. The study excluded patients with Grade 2 or higher peripheral neuropathy, prior allogeneic HSCT, active central nervous system lymphoma, or transformed lymphoma.

Following premedication with an antihistamine and antipyretic, POLIVY was given by intravenous infusion at 1.8 mg/kg on Day 2 of Cycle 1 and on Day 1 of Cycles 2–6. Bendamustine was administered at 90 mg/m^2 intravenously daily on Days 2 and 3 of Cycle 1 and on Days 1 and 2 of Cycles 2–6. A rituximab product was administered at a dose of 375 mg/m^2 intravenously on Day 1 of Cycles 1–6. The cycle length was 21 days.

Of the 80 patients randomized to receive POLIVY plus BR (n = 40) or BR alone (n = 40), the median age was 69 years (range: 30–86 years), 66% were male, and 71% were white. Most patients (98%) had DLBCL not otherwise specified. The 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% receiving one prior therapy, 25% receiving 2 prior therapies, and 46% receiving 3 or more prior therapies. Eighty percent of patients had refractory disease to last therapy.

In the POLIVY plus BR arm, patients received a median of 5 cycles, with 49% receiving 6 cycles. In the BR arm, patients received a median of 3 cycles, with 23% receiving 6 cycles.

Efficacy was based on complete response (CR) rate at the end of treatment and DOR, as determined by an independent review committee (IRC). Other efficacy measures included IRC-assessed best overall response.

Response rates are summarized in Table 8.

Table 8 Response Rates in Patients with Relapsed or Refractory DLBCL

Response per IRC, n (%)*	POLIVY + BR n = 40	BR n = 40
Objective Response at End of Treatment† (95% CI)	18 (45) (29, 62)	7 (18) (7, 33)
CR (95% CI)	16 (40) (25, 57)	7 (18) (7, 33)
Difference in CR rates, % (95% CI)‡	22 (3, 41)	
Best Overall Response of CR or PR§ (95% CI)	25 (63) (46, 77)	10 (25) (13, 41)
Best Response of CR (95% CI)	20 (50) (34, 66)	9 (23) (11, 38)

PR = partial remission.

* PET-CT based response per modified Lugano 2014 criteria. Bone marrow confirmation of PET-CT CR was required. PET-CT PR required meeting both PET criteria and CT criteria for PR.
† End of treatment was defined as 6–8 weeks after Day 1 of Cycle 6 or last study treatment.
‡ Miettinen-Nurminen method.
§ PET-CT results were prioritized over CT results.

In the POLIVY plus BR arm, of the 25 patients who achieved a partial or complete response, 16 (64%) had a DOR of at least 6 months, and 12 (48%) had a DOR of at least 12 months. In the BR arm, of the 10 patients who achieved a partial or complete response, 3 (30%) had a DOR lasting at least 6 months, and 2 (20%) had a DOR lasting at least 12 months.

15 REFERENCES

1. "OSHA Hazardous Drugs." *OSHA*. http://www.osha.gov/SLTC/hazardousdrugs/index.html

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

POLIVY (polatuzumab vedotin-piiq) for injection is a preservative-free, white to grayish-white lyophilized powder, which has a cake-like appearance. POLIVY is supplied as:

Carton Contents	NDC
One 30 mg single-dose vial	NDC 50242-103-01
One 140 mg single-dose vial	NDC 50242-105-01

16.2 Storage and Handling

Store refrigerated at 2°C to 8°C (36°F to 46°F) in original carton to protect from light. Do not use beyond the expiration date shown on the carton. Do not freeze. Do not shake.

POLIVY is a cytotoxic drug. Follow applicable special handling and disposal procedures.[1]

17 PATIENT COUNSELING INFORMATION

Peripheral Neuropathy

Advise patients that POLIVY can cause peripheral neuropathy. Advise patients to report to their healthcare provider any numbness or tingling of the hands or feet or any muscle weakness *[see Warnings and Precautions (5.1)]*.

Infusion-Related Reactions

Advise patients to contact their healthcare provider if they experience signs and symptoms of infusion reactions, including fever, chills, rash, or breathing problems, within 24 hours of infusion *[see Warnings and Precautions (5.2)]*.

Myelosuppression

Advise patients to report signs or symptoms of bleeding or infection immediately. Advise patients of the need for periodic monitoring of blood counts *[see Warnings and Precautions (5.3)]*.

Infections

Advise patients to contact their healthcare provider if a fever of 38°C (100.4°F) or greater or other evidence of potential infection such as chills, cough, or pain on urination develops. Advise patients of the need for periodic monitoring of blood counts *[see Warnings and Precautions (5.4)]*.

Progressive Multifocal Leukoencephalopathy

Advise patients to seek immediate medical attention for new or changes in neurological symptoms such as confusion, dizziness, or loss of balance; difficulty talking or walking; or changes in vision *[see Warnings and Precautions (5.5)]*.

Tumor Lysis Syndrome

Advise patients to seek immediate medical attention for symptoms of tumor lysis syndrome such as nausea, vomiting, diarrhea, and lethargy *[see Warnings and Precautions (5.6)]*.

Hepatotoxicity

Advise patients to report symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine, or jaundice *[see Warnings and Precautions (5.7)]*.

Embryo-Fetal Toxicity

Advise females of reproductive potential of the potential risk to a fetus. Advise females to contact their healthcare provider if they become pregnant, or if pregnancy is suspected, during treatment with POLIVY *[see Warnings and Precautions (5.8)* and *Use in Specific Populations (8.1)]*.

Females and Males of Reproductive Potential

Advise females of reproductive potential, and males with female partners of reproductive potential, to use effective contraception during treatment with POLIVY and for at least 3 months and 5 months after the last dose, respectively *[see Use in Specific Populations (8.3)]*.

Lactation

Advise women not to breastfeed while receiving POLIVY and for at least 2 months after the last dose *[see Use in Specific Populations (8.2)]*.

POLIVY® [polatuzumab vedotin-piiq]

Manufactured by:
Genentech, Inc.
A Member of the Roche Group
1 DNA Way
South San Francisco, CA 94080-4990

POLIVY is a registered trademark of Genentech, Inc.

U.S. License No. 1048

Representative sample of labeling (see the HOW SUPPLIED section for complete listing):

PRINCIPAL DISPLAY PANEL - 140 mg Vial Carton

NDC 50242-105-01
Polivy™
(polatuzumab vedotin-piiq)
For Injection

140 mg per vial

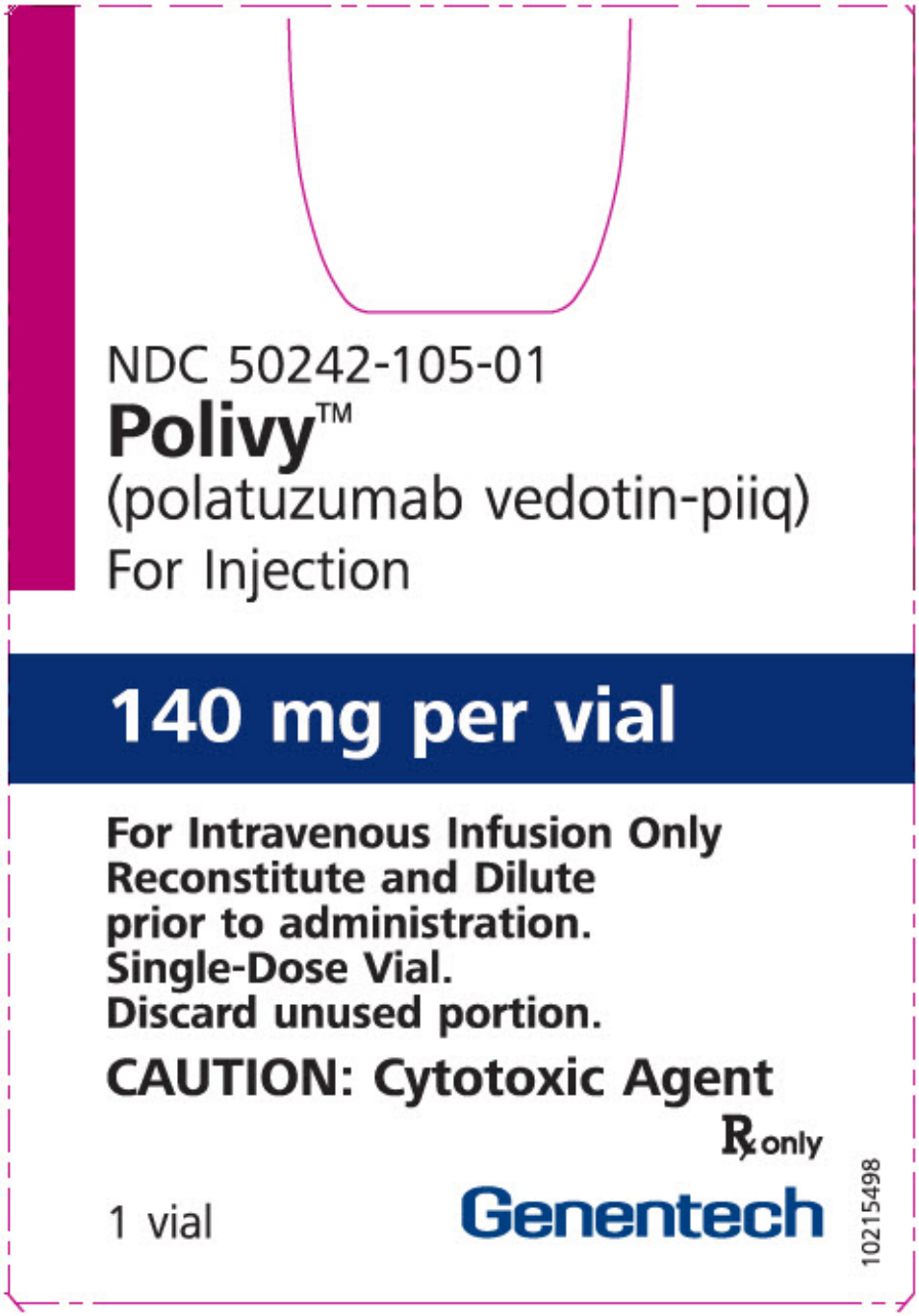
For Intravenous Infusion Only
Reconstitute and Dilute
prior to administration.
Single-Dose Vial.
Discard unused portion.

CAUTION: Cytotoxic Agent

Rx only

1 vial
Genentech

10215498



PRINCIPAL DISPLAY PANEL - 30 mg Vial Carton

NDC 50242-103-01
Polivy®
(polatuzumab vedotin-piiq)
For Injection

30 mg per vial

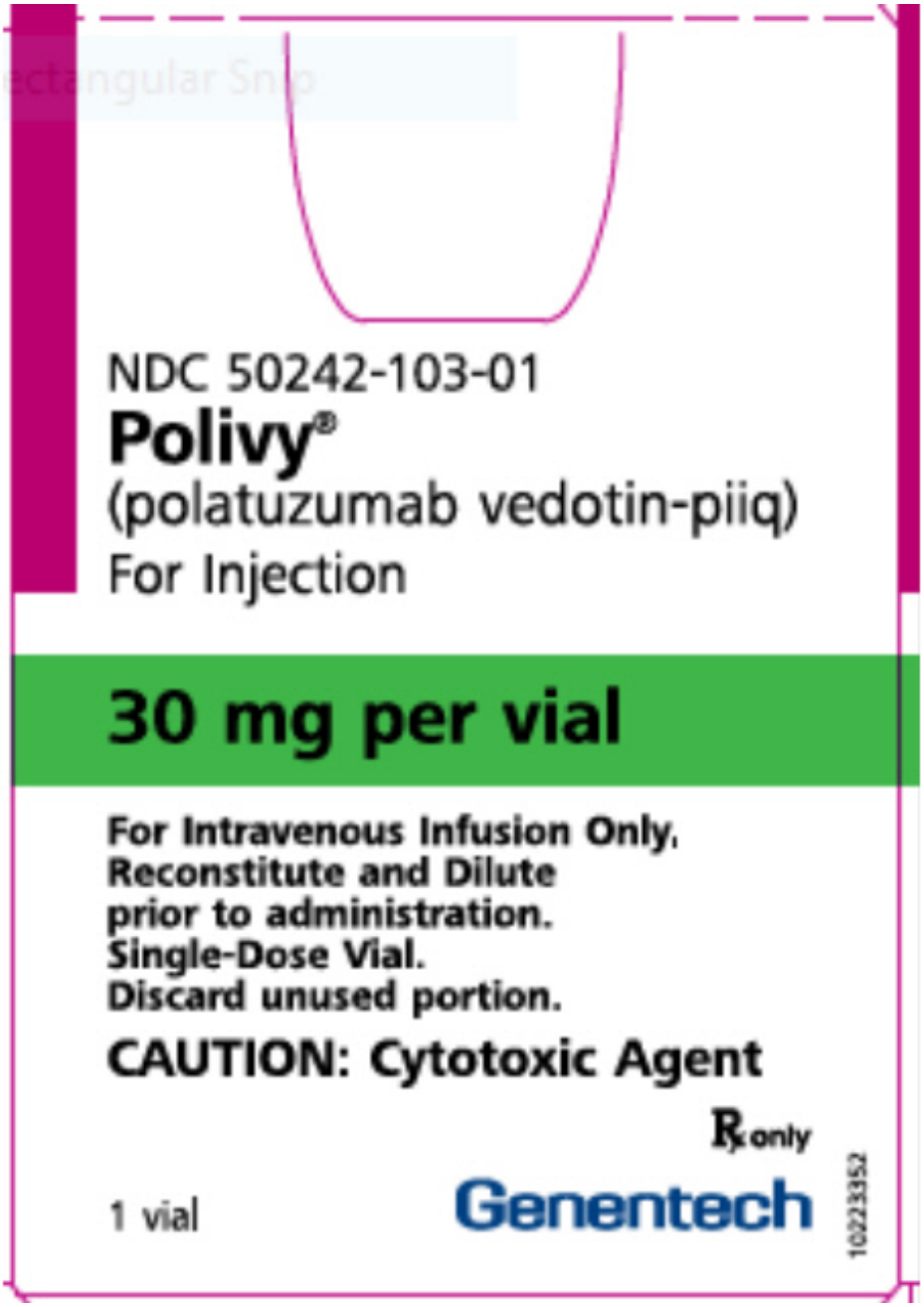
For Intravenous Infusion Only.
Reconstitute and Dilute
prior to administration.
Single-Dose Vial.
Discard unused portion.

CAUTION: Cytotoxic Agent

Rx only

1 vial
Genentech

10223352



POLIVY
polatuzumab vedotin injection, powder, lyophilized, for solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:50242-105

Route of Administration	INTRAVENOUS

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
POLATUZUMAB VEDOTIN (UNII: KG6VO684Z6) (POLATUZUMAB VEDOTIN - UNII:KG6VO684Z6)	POLATUZUMAB VEDOTIN	140 mg in 7.52 mL

Inactive Ingredients

Ingredient Name	Strength
SUCCINIC ACID (UNII: AB6MNQ6J6L)	8.27 mg in 7.52 mL
SODIUM HYDROXIDE (UNII: 55X04QC32I)	3.8 mg in 7.52 mL
SUCROSE (UNII: C151H8M554)	288 mg in 7.52 mL
POLYSORBATE 20 (UNII: 7T1F30V5YH)	8.4 mg in 7.52 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:50242-105-01	1 in 1 CARTON	06/10/2019	
1		20 mL in 1 VIAL, SINGLE-DOSE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA761121	06/10/2019	

POLIVY

polatuzumab vedotin injection, powder, lyophilized, for solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:50242-103
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
POLATUZUMAB VEDOTIN (UNII: KG6VO684Z6) (POLATUZUMAB VEDOTIN - UNII:KG6VO684Z6)	POLATUZUMAB VEDOTIN	30 mg in 1.88 mL

Inactive Ingredients

Ingredient Name	Strength
SUCCINIC ACID (UNII: AB6MNQ6J6L)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
SUCROSE (UNII: C151H8M554)	
POLYSORBATE 20 (UNII: 7T1F30V5YH)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:50242-103-01	1 in 1 CARTON	09/18/2020	
1		6 mL in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA761121	06/10/2019	

Labeler - Genentech, Inc. (080129000)

Establishment

Name	Address	ID/FEI	Business Operations
Genentech, Inc.		080129000	ANALYSIS(50242-103, 50242-105) , MANUFACTURE(50242-103, 50242-105) , API MANUFACTURE(50242-103, 50242-105)

Establishment

Name	Address	ID/FEI	Business Operations
Genentech, Inc.		146373191	ANALYSIS(50242-103, 50242-105)

Establishment

Name	Address	ID/FEI	Business Operations
Roche Singapore Technical Operations Pte. Ltd.		937189173	ANALYSIS(50242-103, 50242-105)

Establishment

Name	Address	ID/FEI	Business Operations
F. Hoffmann-La Roche Ltd		485244961	MANUFACTURE(50242-103, 50242-105) , ANALYSIS(50242-103, 50242-105) , LABEL(50242-103, 50242-105) , PACK(50242-103, 50242-105)

Establishment

Name	Address	ID/FEI	Business Operations
Genentech, Inc.		833220176	PACK(50242-105) , LABEL(50242-105)

Establishment

Name	Address	ID/FEI	Business Operations
Roche Diagnostics GmbH		315028860	ANALYSIS(50242-103, 50242-105) , PACK(50242-103, 50242-105) , LABEL(50242-103, 50242-105)

Establishment

Name	Address	ID/FEI	Business Operations
Roche Diagnostics GmbH		323105205	ANALYSIS(50242-103, 50242-105)

Revised: 5/2020

Genentech, Inc.