POLIVY® (Polatuzumab vedotin) Treatment Guide

Indication[1]:

- POLIVY® in combination with bendamustine and rituximab is indicated for the treatment of adult patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) who are not candidates for haematopoietic stem cell transplant

Dosing and Adminstration[1]:

- POLIVY® + Bendamustine + Rituximab is a fixed-duration treatment administered every 21 days over 6 cycles[1]
- Administer an antihistamine and an antipyretic prior to POLIVY®

Recommended dosing schedule for POLIVY®[1]

Day 1

POLIVY®
1.8 mg/kg IV

Bendamustine
90 mg/m^2 IV

Rituximab
375 mg/m^2 IV

Day 2

Bendamustine
90 mg/m^2 IV

Day 3 - 21

Wait 3 weeks
Between infusions

Repeat
For a total of
6 cycles

Administration of POLIVY®[1]

90-MINUTE INITIAL IV INFUSION
Monitor patients for infusion-related reactions during the infusion and for a minimum of 90 minutes following completion of the dose.

30-MINUTE SUBSEQUENT INFUSIONS may be administered if the initial infusion was well tolerated. Patients should be monitored during subsequent infusions and for at least 30 minutes after completion of these infusions.

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Dose Modifications[1]:

Peripheral Neuropathy[1]

Severity on Day 1 of Any Cycle	Dose Modification
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®.

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Dose Modifications[1]:

Myelosuppression[1]

Severity on Day 1 of Any Cycle	Dose Modification*
Grade 3-4 neutropenia	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 reductions. If ANC recovers to >1000/µL after Day 7: • Restart all treatment, with a dose reduction of bendamustine from 90 mg/m^2 to 70 mg/m^2 or from 70 mg/m^2 to 50 mg/m^2 • If a bendamustine dose reduction to 50 mg/m^2 has already occurred, discontinue all treatment
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/m^2 to 70 mg/m^2 or from 70 mg/m^2 to 50 mg/m^2 • If a bendamustine dose reduction to 50 mg/m^2 has already occurred, discontinue all treatment

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*If primary cause is due to lymphoma, the dose of bendamustine may not need to be reduced.
ANC=absolute neutrophil count.

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Dose Modifications[1]:

Severity of Infusion-Related Reactions (IRRs)[1]

Severity on Day 1 of Any Cycle	Dose Modification
Grade 1-3 IRR	Interrupt POLIVY® infusion and give supportive treatment. For the first instance of Grade 3 wheezing, bronchospasm, or generalized urticarial, permanently discontinue POLIVY®. For recurrent Grade 2 wheezing or urticarial, 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 IRR	Stop POLIVY® infusion immediately. Give supportive treatment. Permanently discontinue POLIVY®.

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Pharmaceutical Particulars[1]:

Reconstituted Solution[1]:

- This should be used immediately
- If not used immediately, it should not be refrigerated for longer than 24 hours (between 2 − 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 refrigerated (2 −8°C) and up to 24 hours at room temperature (9 − 25°C).

Diluted Solution[1]:

- The prepared solution for infusion should be used immediately
- If not used immediately, it should not be refrigerated for longer than 24 hours (between 2 − 8°C), unless dilution has taken place in controlled and validated aseptic conditions
- The diluted solution must be discarded if storage time exceeds the limits specified (See Table).

Diluent used to prepare solution for infusion	Solution for infusion storage conditions
Sodium chloride 9 mg/mL (0.9%)	Up to 24 hours refrigerated (2 − 8°C) or up to 4 hours at room temperature (9 − 25°C)
Sodium chloride 4.5 mg/mL (0.45%)	Up to 72 hours refrigerated (2 − 8°C) or up to 8 hours at room temperature (9 − 25°C)
5% Glucose	Up to 72 hours refrigerated (2 − 8°C) or up to 8 hours at room temperature (9 − 25°C)

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Storage and Transportation[1]:

Special Precautions for Storage:

- Store in a refrigerator (2 – 8ºC)
- Do not freeze
- Keep the vial in the outer carton to protect it from light

Transportation:

- Avoid transportation of the prepared solution for infusion as agitation stress can result in aggregation
- If the prepared infusion will be transported, remove air from the infusion bag and limit transportation to 30 minutes at room temperature (9 − 25ºC) or 24 hours refrigerated (2 − 8ºC)
- If air is removed, an infusion set with a vented spike is required to ensure accurate dosing during the infusion
- The total storage plus transportation times of the diluted product should not exceed the storage duration which specified in previous slide

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Abbreviated Product Information:

Polivy 140 mg powder for concentrate for solution for infusion (Polatuzumab vedotin)

Indications:
Polivy in combination with bendamustine and rituximab is indicated for the treatment of adult patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) who are not candidates for haematopoietic stem cell transplant.
Dosage and Administration:
Administer Polivy as IV infusion at 1.8 mg/kg every 21 days in combination with bendamustine and rituximab for 6 cycles. Administered Polivy, bendamustine and rituximab in any order on Day 1 of each cycle. Recommended dose of bendamustine is 90 mg/m^2/day on Day 1 & 2 of each cycle; recommended dose of rituximab is 375 mg/m^2 on Day 1 of each cycle. Administration of Polivy >240mg/cycle not recommended. Premedication with antihistamine and anti-pyretic should be administered prior to Polivy.
Dose modifications for peripheral neuropathy, myelosuppresion and infusion-related reactions applied. Please refer to the full prescribing information for details.
Warnings and Precautions:
Serious and severe neutropenia and febrile neutropenia have been reported for some first cycle treatment. Grade 3 or 4 thrombocytopenia or anaemia can occur. Complete blood counts should be monitored prior each dose and freq. Monitoring and/or treatment interruptions should considered. Peripheral neuropathy has been reported in patient as in the first cycle of treatment, risk increases with subsequent doses. Patients should be monitored for symptoms of PN. Delay, dose reduction or discontinuation of Polivy should considered. Serious, life threatening or fatal infections have been reported. Closely monitor for signs of bacterial, fungal or viral infections during treatment. Consider anti-infective prophylaxis. Polivy should not administered in the presence of active severe infection. Discontinue treatment if serious infections developed. Live or live-attenuated vaccines should not be given concurrently. Progressive multifocal leukoencephalopathy (PML) has been reported. Withhold treatment if PML is suspected and discontinued if confirmed. Refer to local guidelines for appropriate measures/prophylaxis prior treatment. Closely monitor for Tumour lysis syndrome (TLS). Interrupt infusion is infusion-related reactions occur. Administer antihistamine and antipyretic prior treatment and closely monitor throughout infusion. Pregnant women should be advised regarding potential harmful risk to the foetus. Male patients with female partners of childbearing potential and women of childbearing potential should advise to use effective contraception during treatment and for certain period after the last dose. Advised make patients to preserve sperm sample before treatment for male. Risk of hepatic toxicity. Monitor liver enzymes and bilirubin level.
Contraindications:
Hypersensitivity to the active substance or to any of the excipients. Polivy should not be administered in the presence of active severe infection.
Interactions: No dedicated clinical drug-drug interaction studies with polatuzumab vedotin in humans have been conducted. Cautions is advised in case of concomitant treatment with CYP3A4 inhibitor. Closely monitoring for signs of toxicities for patient receiving concomitant strong CYP3Ar inhibitors.
Adverse Effects: Please refer to the full prescribing information for detailed information. Adverse reaction: *Very common*: pneumonia, herpes virus infection, upper respiratory tract infection, febrile neutropenia, neutropenia, thrombocytopenia, anaemia, leukopenia, lymphopenia, hypokalaemia, hypocalcaemia, hypoalbuminemia, decreased appetite, neuropathy peripheral, peripheral sensory neuropathy, dizziness, cough, diarrhoea, nausea, constipation, vomiting, abdominal pain, upper abdominal pain, pruritis, fatigue, pyrexia, asthenia, chills, weight decreased, infusion-related reactions. Common: sepsis, cytomegalovirus infection, pancytopenia, gait disturbance, paraesthesia, hypoaesthesia, vision blurred, pneumonitis, arthralgia, transaminase elevation, lipase increase, hypophosphataemia
Full prescribing information should be viewed prior to prescribing.
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Roche Hong Kong Limited
22/F, FTLife Tower, 18 Sheung Yuet Road, Kowloon Bay
Tel: +852 2723 2832
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