Polivy (Polatuzumab vedotin)

Public Risk Management Plan (RMP) Summary

Polivy® (Polatuzumab vedotin) 140 mg/vial, 30 mg/vial Pulver für ein Konzentrat zur Herstellung einer Infusionslösung
Zul.-Nr. 67165

Document Version 1.0

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The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them. The RMP summary of "Polivy" is a concise document and does not claim to be exhaustive. As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of "Polivy" in Switzerland is the "Arzneimittelinformation/ Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. "Roche Pharma (Schweiz) AG" is fully responsible for the accuracy and correctness of the content of the published summary RMP of 'Polivy'.

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PART VI: SUMMARY OF THE RISK-MANAGEMENT PLAN

SUMMARY OF RISK MANAGEMENT PLAN FOR POLATUZUMAB VEDOTIN

This is a summary of the risk-management plan (RMP) for polatuzumab vedotin. The RMP details important risks of polatuzumab vedotin, how these risks can be minimized, and how more information will be obtained about polatuzumab vedotin's risks and uncertainties (missing information).

Polatuzumab vedotin's Summary of Product Characteristics (SmPC) and its Patient Information Leaflet (PIL) give essential information to healthcare professionals and patients on how polatuzumab vedotin should be used.

This summary of the RMP for polatuzumab vedotin should be read in the context of all this information, including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of polatuzumab vedotin's RMP.

I. THE MEDICINE AND WHAT IT IS USED FOR

Polatuzumab vedotin in combination with bendamustine and rituximab is authorized for the treatment of adult patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) who are not candidates for hematopoietic stem cell transplant (see SmPC for the full indication). It contains polatuzumab vedotin as the active substance, and it is given as an intravenous infusion.

Further information about the evaluation of polatuzumab vedotin's benefits can be found in polatuzumab vedotin's EPAR, including in its plain-language summary, available on the EMA Web site, under the medicine's Web page.

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMIZE OR FURTHER CHARACTERIZE THE RISKS

Important risks of polatuzumab vedotin, together with measures to minimize such risks and the proposed studies for learning more about polatuzumab vedotin's risks, are outlined below.

Measures to minimize the risks identified for medicinal products can be:

- Specific Information, such as warnings, precautions, and advice on correct use, in the PIL and SmPC addressed to patients and healthcare professionals
- Important advice on the medicine's packaging
- The authorized pack size—The amount of medicine in a pack is chosen so as to ensure that the medicine is used correctly.

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- The medicine's legal status—The way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimize its risks.

Together, these measures constitute routine risk minimization measures.

In the case of polatuzumab vedotin, these measures are not supplemented with additional risk-minimization measures.

In addition to these measures, information about adverse events is collected continuously and regularly analyzed, including PSUR assessment, so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities. There will be additional collection and analysis of the specific information from the ongoing pivotal clinical study GO29365 with the aim to further characterize the important potential risk of carcinogenicity and from the ongoing clinical study GO39942 with the scope of characterizing long-term safety that is listed under safety concerns as missing information.

If important information that may affect the safe use of polatuzumab vedotin is not yet available, it is listed under "missing Information" below.

II.A List of Important Risks and Missing Information

Important risks of polatuzumab vedotin can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of polatuzumab vedotin. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation.

List of Important Risks and Missing Information	
Important identified risks	Not applicable
Important potential risks	Carcinogenicity
Missing information	Long-Term Safety Use in Severe Hepatic Impairment Use in Severe Renal Impairment Use in Pregnancy and Lactation

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II.B Summary of Important Risks

Important Potential Risk: Carcinogenicity	
Evidence for linking the risk to the medicine	Clinical trial data from studies GO29365, GO27834, GO29044, and DCS4968g of polatuzumab vedotin. Second primary malignancies were reported with a frequency of 0%–7.9% across the four studies. No increase over the control arms in the randomized cohorts was noticed, and the majority of cases included myelodysplastic syndrome and non-melanoma skin cancers.
Risk factors and risk groups	Patients with R/R DLBCL are at increased risk of developing second malignancies due to multiple factors including immune dysfunction associated with DLBCL as well as prior and concomitant exposures to chemotherapy, anti-CD20, and radiation therapy.
Risk-minimization measures	**Routine risk-minimization measures:** *Proposed risk communication is described in* *SmPC:* • Section 5.3 Preclinical safety data **Additional risk-minimization measures**: None
Additional pharmacovigilance activities	**Additional pharmacovigilance activities** GO29365

ADC=antibody-drug conjugate; DLBCL=diffuse large B-cell lymphoma; R/R=relapsed/refractory; SmPC=summary of product characteristics.

Missing Information: Long-Term Safety	
Risk-minimization measures	**Routine risk-minimization measures:** *Proposed risk communication is described in* *SmPC:* • None **Additional risk-minimization measures**: None
Additional pharmacovigilance activities	**Additional pharmacovigilance activities**: GO39942

SmPC=summary of product characteristics.

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Missing Information: Use in Severe Hepatic Impairment	
Risk-minimization measures	**Routine risk-minimization measures:** *Proposed risk communication is described in* *SmPC:* • Section 4.2 Posology and method of administration • Section 5.2 Pharmacokinetic properties **Additional risk-minimization measures**: None
Additional pharmacovigilance activities	**Additional pharmacovigilance activities:** None

SmPC=summary of product characteristics.

Missing Information: Use in Severe Renal Impairment	
Risk-minimization measures	**Routine risk-minimization measures:** *Proposed risk communication is described in* *SmPC:* • Section 4.2 Posology and method of administration • Section 5.2 Pharmacokinetic properties **Additional risk-minimization measures**: None
Additional pharmacovigilance activities	**Additional pharmacovigilance activities**: None

SmPC=summary of product characteristics.

Missing Information: Use in Pregnancy and Lactation	
Risk-minimization measures	**Routine risk-minimization measures:** *Proposed risk communication is described in* *SmPC:* • Section 4.6 Fertility, pregnancy and lactation *PIL:* • Section 2 What you need to know before you use Polivy **Additional risk-minimization measures**: None
Additional pharmacovigilance activities	**Additional pharmacovigilance activities**: None

PIL=patient information leaflet; SmPC=summary of product characteristics.

II.C Post-Authorization Development Plan

II.C.1 Studies That Are Conditions of the Marketing Authorization

Study GO29365: A Phase Ib/II, multicenter, open-label study evaluating the safety, tolerability, and anti-tumor activity of polatuzumab vedotin (DCDS4501A) in combination with rituximab or

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obinutuzumab plus bendamustine in patients with R/R follicular lymphoma or R/R diffuse large B-cell lymphoma.

Study GO39942: A Phase III, multicenter, randomized, double-blind, placebo-controlled trial comparing the efficacy and safety of polatuzumab vedotin in combination with rituximab and CHP (R-CHP) versus rituximab and CHOP (R-CHOP) in previously untreated patients with diffuse large b-cell lymphoma.

II.C.2 Other Studies in Post-Authorization Development Plan

None.

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