SANDOZ A Novartis Division

Chief Medical Office & Patient Safety

# Rituximab (GP2013)
# 100 mg and 500 mg
# Concentrate for solution for infusion

GP2013

## Summary of the EU Safety Risk Management Plan
## Sandoz Pharmaceuticals AG, Rotkreuz, CH

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| Active substance(s) (INN or common name): | Rituximab |
| Product(s) concerned (brand name(s)): | Rixathon,<br>Riximyo |
| Document status: | Final |
| Version number of the RMP Public Summary: | 6.0 |
| Date of final sign off of the RMP Public Summary | 07-Dec-2022 |
| Number of pages | 8 |



*Sandoz template version 1.0, dated 20-May-2019 (based on Novartis template v4.0)*

## Disclaimer:

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 Rixathon / Riximyo 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 Rixathon in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. Sandoz Pharmaceuticals AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Rixathon / Riximyo.

# Summary of the risk management plan Rixathon / Riximyo (rituximab)

This is a summary of the risk management plan (RMP) for Rixathon / Riximyo, a biosimilar to MabThera. The RMP details important risks of Rixathon / Riximyo, how these risks can be minimized, and how more information will be obtained about Rixathon's / Riximyo's risks and uncertainties (missing information).

Rixathon's / Riximyo's summaries of product characteristics (SmPC) and their package leaflets give essential information to healthcare professionals and patients on how Rixathon / Riximyo should be used.

This summary of the RMP for Rixathon / Riximyo 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 Rixathon's / Riximyo's RMP.

## I. The medicine and what it is used for

Rixathon / Riximyo is authorized for use in adults to treat the following blood cancers and inflammatory conditions (see SmPCs for the full indication):

- follicular lymphoma and diffuse large B cell non-Hodgkin's lymphoma (two types of non-Hodgkin's lymphoma, a blood cancer);
- chronic lymphocytic leukemia (CLL, another blood cancer affecting white blood cells);
- granulomatosis with polyangiitis (GPA or Wegener's granulomatosis) and microscopic polyangiitis (MPA), which are inflammatory conditions of the blood vessels;
- pemphigus vulgaris;
- for Rixathon only: severe rheumatoid arthritis (an inflammatory condition of the joints).

Rixathon / Riximyo is authorized for use in paediatric patients to treat the following:

- in paediatric patients (aged ≥ 6 months to < 18 years old) with previously untreated advanced stage CD20 positive diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma (BL)/Burkitt leukaemia (mature B-cell acute leukaemia) (BAL) or Burkitt-like lymphoma (BLL)
- in paediatric patients (aged ≥ 2 to < 18 years old) with severe, active GPA (Wegener's) and MPA.

It contains rituximab as the active substance, and it is given by intravenous infusion.

Further information about the evaluation of Rixathon's / Riximyo's benefits and risks can be found in Rixathon's / Riximyo's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage:

Rixathon:
http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/003903/WC500232462.pdf

Riximyo:
http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/004729/WC500232539.pdf

## II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of Rixathon / Riximyo, together with measures to minimize such risks and the proposed studies for learning more about Rixathon's / Riximyo'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 package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- 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 Rixathon / Riximyo, these measures are supplemented with *additional risk minimization measures* mentioned under relevant important risks below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of Rixathon / Riximyo is not yet available, it is listed under 'missing information' below.

## II.A: List of important risks and missing information

Important risks of Rixathon / Riximyo are risks that need special risk management activities to further investigate or minimize the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Rixathon / Riximyo. 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. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

### List of important risks and missing information

| List of important risks and missing information | |
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| Important identified risks | Infections (including serious infections) (all indications)<br>Progressive multifocal leukoencephalopathy (PML) (all indications)<br>Hepatitis B reactivation (all indications)<br>Hypogammaglobulinemia (non-oncology indications) |
| Important potential risks | Administration route error (NHL/CLL)<br>Relapses (GPA/MPA) |
| Missing information | Long-term use in GPA/MPA patients |

## II.B: Summary of important risks

### All indications: Important identified risk 'Infections (including serious infections)'

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| Evidence for linking the risk to the medicine | Infections (including serious infections) are listed in section 4.4 Special warnings and precautions for use and section 4.8 Undesirable effects of the SmPC MabThera and are therefore considered as an important identified risk of GP2013. |
| Risk factors and risk groups | Patients are at risk who present with a history of recurring or chronic infections or with underlying conditions which may further predispose patients to serious infection. |
| Risk minimization measures | Routine risk minimization measures:<br>SmPC sections 4.3, 4.4 and 4.8; section 4.4 where recommendation for exercising caution when considering the use of rituximab in patients with a history of recurring or chronic infections or with underlying conditions which may further predispose patients to serious infection is included<br>PL section 2 and in PL section 4 Possible side effects recommendation to reach out to the doctor immediately if there are signs of an infection including fever, cough, sore throat, burning pain when passing urine or feeling weak or generally unwell is included |

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| | Legal status: Prescription only<br>Additional risk minimization measures (for non oncology indication):<br>Health care professional (HCP) educational leaflet<br>Patient educational leaflet<br>Patient alert card |

## All indications: Important identified risk 'Progressive multifocal leukoencephalopathy (PML)'

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| Evidence for linking the risk to the medicine | PML is listed in section 4.4 Special warnings and precautions for use and section 4.8 Undesirable effects of the SmPC MabThera and is therefore considered as an important identified risk of GP2013. |
| Risk factors and risk groups | There are currently no known risk groups or risk factors for the development of PML associated with rituximab.<br>PML general occurs in patients with suppressed cellular immunity. |
| Risk minimization measures | Routine risk minimization measures:<br>SmPC sections 4.3, 4.4 and 4.8; section 4.4 where recommendation for monitoring of patients at regular intervals and suspension of further dosing if PML is suspected, in case of doubt considering further evaluation including MRI scan preferably with contrast, cerebrospinal fluid (CSF) testing for JC Viral DNA and repeat neurological assessments and permanently discontinuing dosing of Rixathon / Riximyo if a patient develops PML is included<br>PL section 4 Possible side effects recommendation to reach out to the doctor immediately if there are signs of an infection including memory loss, trouble thinking, difficulty walking or sight loss – these may be due to a very rare, serious brain infection, which has been fatal (Progressive Multifocal Leukoencephalopathy or PML) have been included.<br>Legal status: Prescription only<br>Additional risk minimization measures: (for non oncology indication):<br>Health care professional (HCP) educational leaflet<br>Patient educational leaflet<br>Patient alert card |

## All indications: Important identified risk 'Hepatitis B virus (HBV) reactivation'

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| Evidence for linking the risk to the medicine | HBV reactivation is listed in section 4.4 Special warnings and precautions for use and section 4.8 Undesirable effects of the SmPC<br>MabThera and is therefore considered as an important identified risk<br>of GP2013. |

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| Risk factors and risk groups | The majority of patients developing a HBV reactivation during treatment with rituximab were also exposed to chemotherapy.<br>Pre-chemotherapy HBV DNA level and the use of steroids were also<br>considered as risk factors. |
| Risk minimization measures | Routine risk minimization measures:<br>SmPC section 4.4 and 4.8; section 4.4 where recommendation for<br>HBV screening before initiation of treatment with Rixathon / Riximyo is<br>included;<br>PL sections 2 and 4<br>Legal status: Prescription only |

## Non-oncology indications: Important identified risk 'Hypogammaglobulinemia'

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| Evidence for linking the risk to the medicine | Hypogammaglobulinemia is listed in section 4.4 Special warnings and<br>precautions for use and section 4.8 Undesirable effects of the SmPC<br>MabThera and is therefore considered as an important identified risk<br>of GP2013. |
| Risk factors and risk groups | **RA:**<br>Patients with low immunoglobulin level at baseline had an increased<br>tendency to hypogammaglobulinemia.<br>**Pemphigus vulgaris, GPA and MPA:**<br>No specific risk factor could be identified |
| Risk minimization measures | Routine risk minimization measures:<br>SmPC sections 4.4 and 4.8<br>PL section 4<br>Legal status:<br>Prescription only |

## NHL/CLL: Important potential risk 'Administration route error'

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| Evidence for linking the risk to the medicine | As per SmPC MabThera, it is important to check the medicinal product<br>labels to ensure that the appropriate formulation (intravenous or<br>subcutaneous formulation) is being given to the patient, as prescribed.<br>Administration route error is therefore considered as potential risk of<br>GP2013. |
| Risk factors and risk groups | Patients treated for NHL or CLL |

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| Risk minimization measures | Routine risk minimization measures:<br>SmPC section 4.2<br>PL section 3<br>The outer carton as well as the vial label of the product states: For<br>intravenous use after dilution.<br>Legal status: Prescription only<br>Additional risk minimization measure:<br>HCP alert card |

**GPA and MPA: Important potential risk 'Relapses'**

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| Evidence for linking the risk to the medicine | Relapses have been observed in patients with GPA or MPA (SmPC MabThera) and are therefore considered as potential risk of GP2013. |
| Risk factors and risk groups | No specific risk factor could be identified predisposing patients to relapse following treatment with a rituximab-containing regimen. |
| Risk minimization measures | Routine risk minimization measures:<br>Legal status: Prescription only |

**GPA and MPA: Missing information 'Long-term use in GPA/MPA patients'**

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| Risk minimization measures | Routine risk minimization measures:<br>Legal status: Prescription only |

## II.C: Post-authorization development plan

## II.C.1 Studies which are conditions of the marketing authorization

There are no studies which are conditions of the marketing authorization or specific obligation of Rixathon / Riximyo.

## II.C.2. Other studies in post-authorization development plan

**Other studies in the post-authorization development plan**

None.