Roche	**SIX-MONTHLY SUSAR REPORT** **No. 1065053**
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Name	**Reason for Signing**	**Date and Time** (UTC)
Banzet,Sophie	Safety Science Cluster Head	09-Jun-2015 08:13:06

During the current review period, 18 November 2014 to 17 May 2015 (inclusive), the Sponsor submitted 31 Suspected Unexpected Serious Adverse Reactions (SUSARs) for rituximab. In addition, there were three non–company Investigational Medicinal Product (IMP) SUSARs in trials where rituximab is the primary IMP.

The reported SUSARs did not necessitate changes to the rituximab study documentation during the current reporting interval.

After review of the clinical details of the reported SUSARs, the Sponsor concludes that no changes to the conduct of the ongoing clinical trials with rituximab are warranted. Based on the information presented in this report, the benefit-risk assessment of the use of rituximab in the indications under investigation remains favorable.

1. INTRODUCTION

This is a Six-Monthly Suspected Unexpected Serious Adverse Reaction (SUSAR) Report (SSR 1065053) prepared for rituximab in accordance with the European Union (EU) Clinical Trials Directive [1] and 'CT-3' guidance [2]. This SSR covers the reporting interval from 18 November 2014 to 17 May 2015, inclusive.

Methodology used to prepare this report is described in Section 4.

2. ACTIONS TAKEN IN THE REPORTING INTERVAL RELATED TO REPORTED SUSARS

2.1 CHANGES TO REFERENCE SAFETY INFORMATION

The reference safety information (RSI) in effect at the start of the reporting interval for autoimmune indications was the Investigator's Brochure (IB) version 13.0 dated May 2014 which incorporates the Developmental Core Safety Information (DCSI) version 5.0 dated June 2014.

The IB for rituximab oncology subcutaneous formulation, version 5.0 dated February 2014 which incorporated DCSI version 7.0 dated February 2014 was used as the safety reference document till February 2015. In February 2015, IB version 6.0 (containing Section 6 "Guidance for the Investigator (RSI)") became available and was used as the safety reference document for the remaining review period.

The IB format has recently undergone a change in order to clarify which serious adverse drug reactions (ADRs) are considered "expected" for regulatory reporting purposes by the Sponsor. The prior DCSI has been removed and the new IB format now consolidates information from the prior DCSI into Section 6 Guidance for the Investigator. The new Section 6 now contains the list of ADRs. However, changes to these documents were not necessitated by the reported SUSARs.

The IB for rituximab oncology intravenous formulation, version 19.0 dated July 2014 (containing Section 6 "Guidance for the Investigator (RSI)"), was used as the safety reference document for the review period.

The Sponsor used the rituximab EU Summary of Product Characteristics (SPC) as the RSI in trials where the Investigators use local label as the safety reference document.

The following documents were used as the RSI for non-company Investigational Medicinal Product (IMP) SUSARs during the review interval:

- Cladribine, cyclophosphamide, fludarabine EU SPCs were used to determine SUSARs to cladribine, cyclophosphamide, fludarabine respectively

2.2 CHANGES TO OTHER STUDY DOCUMENTATION

The reported SUSARs did not necessitate changes to other study documentation for rituximab during the current reporting period.

3. CONCLUSION

After review of the clinical details of the reported SUSARs, the Sponsor concludes that no changes to the conduct of the ongoing clinical trials with rituximab are warranted. Based on the information presented in this report, the benefit-risk assessment of the use of rituximab in the indications under investigation remains favorable.

4. METHODOLOGY

4.1 CASE INCLUSION

This report includes a line listing of all SUSAR cases submitted to the Investigators in the six-monthly reporting period outlined in Section 1, for a given Roche IMP (hereinafter referred to as the SSR drug), and/or any non-Roche IMPs used in clinical trials where the SSR drug is the primary IMP.

Roche expedites all initial SUSAR cases to the Investigators. In addition, follow-up SUSAR cases are submitted to the Investigators if a change in event seriousness, causality, preferred term, or expectedness for safety reference document occurs, or an additional (existing or new) event in the case qualifies for a SUSAR.

If two or more SUSAR case versions are submitted during the reporting period, only the version most recently submitted during the reporting period is presented in the report. SUSAR cases submitted during the reporting period that no longer qualify for a SUSAR in the most recently submitted version, or were logically deleted subsequent to submission, are not presented in the report.

4.2 LISTING PRESENTATION

The version of Medical Dictionary for Regulatory Activities used to generate the line listing is printed in the listing is printed in the footnote of the listing.

The line listing is sorted by indication coded by Medical Dictionary for Regulatory Activities preferred term. Under each indication, the reports are shown under two

different sub-sections: “SUSARs” and “SUSARs to Other IMPs and Comparators”. Separate tables are produced for each indication.

If more than one indication is investigated in a study (e.g., refractory solid tumors or lymphoma) and the indication is not provided by the reporter, the company initially codes all study indications in the case. As a result, such a case appears in more than one indication table. This is taken into consideration when counting SUSARs to prevent over count.

All IMPs for which the event is a SUSAR are shown in bold – for the SSR drug and other Roche IMPs in the “SUSARs” table, and for non-Roche IMPs, in trials where the SSR drug is the primary IMP, in the “SUSARs to Other IMPs and Comparators” table. If the suspect medication column contains more than one SUSAR drug, then each SUSAR event is marked with the list of drug sequence numbers to which it is related.

Only SUSARs to the SSR drug and non-Roche IMPs in trials where the SSR drug is the primary IMP are counted in this report, because SUSARs to other Roche IMPs are counted in their respective SSRs.

Events in a SUSAR case that do not qualify for a SUSAR are not presented in the report.

4.3 CAUSALITY ASSESSMENT

Both the reporter and the company causality assessments are shown for each SUSAR. Roche’s medical assessment of causality is based on the information provided in the individual case safety report. This assessment does not represent a full evaluation of all similar cases and epidemiological data of the therapeutic population. The company assessment of causal relationship at the event level, within the safety database, is not intended to suggest, imply, or confirm the event in question is a reaction to the medicinal product. Rather this assessment fulfills a regulatory requirement to indicate a potential association between product and event.

Adverse events where the causal relationship to the IMP is assessed by the reporter, or the company, as unknown will be considered by Roche to be suspected adverse reactions for reporting purposes, and thus submitted to Investigators if meeting other SUSAR criteria. Submission of adverse events where the causal relationship to the IMP is not provided by the reporter is driven by the company causality assessment.

4.4 REFERENCE SAFETY INFORMATION

The RSI for Roche IMPs is primarily the IB, which incorporates the DCSI. The DCSI details which events are to be considered expected, and will be updated

with only those events evaluated by the Sponsor and preliminarily identified as suspected ADRs.

From 1 April 2014, the company uses EU SPC to assess event listedness in trials where the Investigators use local label as the reference safety document. Prior to this date, Core Data Sheet was used for this assessment.

The reference safety document for non-Roche IMPs is the EU SPC (or United Kingdom SPC if an EU SPC is not available), or the IB, as defined in the respective study protocols.

Expectedness (or listedness) for each SUSAR is determined based on reference safety document version in effect at the time of case entry.

5. REFERENCES

1. Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use
2. Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use ('CT-3') (2011/C 172/01)

RITUXIMAB

Indication: B-CELL LYMPHOMA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
BO21223 1092263(2.0) 2010-024132-41 209368 56656 GERMANY 60 Years Female	**1 # RITUXIMAB**	Intravenous (not otherwise specified) 1x---- / 4 Weeks	-- --	Hypertension Depression	HYPERLEUKOCYTOSIS Leukocytosis (24JUL2012) SYNKOPE Syncope (24JUL2012)	Related Related EU-SPC Recovering/resolving Related Related EU-SPC Recovering/resolving
	2 BENDAMUSTINE	Intravenous (not otherwise specified) 1x---- / 4 Weeks	-- --			
BO22334 1300857(2.0) 2010-021377-36 206042 2399 FRANCE 63 Years Female	**1 # RITUXIMAB**	Intravenous (not otherwise specified) --	13DEC2012/ --	Asthma Mitral valve incompetence Phlebitis Hypertension Hypercholesterolaemia Depression Insomnia Tendon rupture Back pain	TRANSIENT ISCHEMIC ATTACK Transient ischaemic attack (13MAR2015)	Related Related IB Recovered/resolved (16MAR2015)

RITUXIMAB

Indication: B-CELL LYMPHOMA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
BO22334 1397248(4.0) 2010-021377-36 204270 2036 UNITED KINGDOM 86 Years Male	**1 # RITUXIMAB**	Intravenous (not otherwise specified) 1x---- / 3 Weeks Intravenous (not otherwise specified) 1x---- / 8 Weeks	20MAR2013/ -- -- --	Chronic obstructive pulmonary disease Hypertension Prostate cancer Muscle spasms Restless legs syndrome Dry skin Upper-airway cough syndrome Joint swelling Actinic keratosis Rash Constipation Dry skin Rash Back pain Oedema peripheral Atrial fibrillation Dyspepsia	COMMUNITY ACQUIRED PNEUMONIA Pneumonia (07DEC2014)	Related Related IB Fatal
	2 CYCLOPHOSPHAMIDE	Intravenous (not otherwise specified) --x1500mg / -- --	22MAY2013/ --			
	3 VINCRISTINE	Intravenous (not otherwise specified) --x2mg / -- --	22MAY2013/ --			
	4 PREDNISONE	Oral --x50Unit Not Reported / -- -- Oral --	22MAY2013/ -- -- --			

RITUXIMAB

Indication: B-CELL LYMPHOMA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
ML21685 1521397(1.0) 2008-005859-16 126 71557 GERMANY 69 Years Male	**1 # RITUXIMAB** 2 BENDAMUSTINE	Intravenous (not otherwise specified) 1x700mg / 2 Months Intravenous (not otherwise specified) --x700mg / -- -- Intravenous (not otherwise specified) --x170mg / -- --	19NOV2012/ -- 26JUL2012/ -- 26JUL2012/ --	Diabetes mellitus	SYNCOPE Syncope (29DEC2012)	Related Related EU-SPC Recovered/resolved (19JAN2015)
MO25455 1533845(0.0) 2010-023407-95 262974 262974002 TURKEY 78 Years Female	**1 # RITUXIMAB** **2 # RITUXIMAB**	Intravenous (not otherwise specified) -- Subcutaneous 1x1400mg / 28 Days	19JUN2014/ -- -- --	Hypertension Hyperlipidaemia Hypothyroidism Arthralgia Dyspepsia Constipation	VERTIGO Vertigo [SUSAR Drugs 1, 2] (26JAN2015)	Related Related IB Not recovered/not resolved

RITUXIMAB

Indication: B-CELL LYMPHOMA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
MO25455 1544361(0.0) 2010-023407-95 237871 237871001 NORWAY 66 Years Female	**1 # RITUXIMAB**	Subcutaneous 1x1400mg / 8 Weeks	10OCT2012/ --	Chronic obstructive pulmonary disease Sinus tachycardia Nausea Mucosal infection Upper respiratory tract infection Dyspnoea Lacrimation increased Musculoskeletal pain	COPD EXACERBATION Chronic obstructive pulmonary disease [SUSAR Drugs 1, 2] (20FEB2015)	Related Related IB Recovered/resolved (24FEB2015)
	2 # RITUXIMAB	Intravenous (not otherwise specified) --x700mg / -- --	10SEP2012/ 10SEP2012			
MO25455 1571149(0.0) 2010-023407-95 236217 236217007 NORWAY 75 Years Male	**1 # RITUXIMAB**	Intravenous (not otherwise specified) --x611mg / -- --	06MAR2013/ --	Osteoporosis Hypertension Myocardial infarction	DUODENAL ULCER Duodenal ulcer [SUSAR Drugs 1, 2] (30MAR2015)	Related Related IB Recovering/resolving
	2 # RITUXIMAB	Subcutaneous 1x1400mg / 8 Weeks	03APR2013/ --			

Indication: B-CELL LYMPHOMA - SUSARs to non-company IMPs

NO SUSARS WERE IDENTIFIED

RITUXIMAB

Indication: CHRONIC GRAFT VERSUS HOST DISEASE - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
ML19922 1489255(0.0) 2008-004125-42 -- 32 NETHERLANDS 57 Years Male	**1 # RITUXIMAB** 2 NILOTINIB	Intravenous (not otherwise specified) --x375mg/m2 / -- -- Unknown --x375mg/m2 / -- -- Unknown --x375mg/m2 / -- -- Unknown --x375mg/m2 / -- -- Unknown --x300mg / -- --	10DEC2013/ -- 17DEC2013/ -- 27DEC2013/ -- 03JAN2014/ -- 13JAN2014/ 13JUL2014	Plasma cell myeloma Pruritus Deep vein thrombosis Fluid retention Stem cell transplant Chronic graft versus host disease Spinal cord injury Stem cell transplant	BILATERAL PLEURAL EFFUSIONS Pleural effusion (04NOV2014)	Related Not Related IB Not Reported

Indication: CHRONIC GRAFT VERSUS HOST DISEASE - SUSARs to non-company IMPs

NO SUSARS WERE IDENTIFIED

RITUXIMAB

Indication: CHRONIC LYMPHOCYTIC LEUKAEMIA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
BO25341 1500800(3.0) 2010-021380-32 205437 2422 BRAZIL 61 Years Female	**1 # RITUXIMAB**	Intravenous (not otherwise specified) --x---- / 28 Days	23APR2013/ --	Hypertension Osteoarthritis Dyslipidaemia Nausea	SEPTIC SHOCK Septic shock (12JAN2015)	Related Related IB Fatal
BO21004 1560312(0.0) 2009-012476-28 166938 2561 FRANCE 69 Years Male	**1 # RITUXIMAB** 2 CHLORAMBUCIL	Intravenous (not otherwise specified) --x375mg/m2 / -- -- Oral --x28mg / -- --	05OCT2010/ 28FEB2011 05OCT2010/ 28FEB2011		SQAMOUS CELL CARCINOMA Squamous cell carcinoma (07OCT2014)	Related Related EU-SPC Recovered/resolved (28OCT2014)

RITUXIMAB

Indication: CHRONIC LYMPHOCYTIC LEUKAEMIA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
ML21283 755693(4.0) 2008-001140-39 117920 IM11 POLAND 68 Years Male	**1 # RITUXIMAB**	Intravenous (not otherwise specified) 1x1065mg / 1 Months	03DEC2010/ --	Chronic lymphocytic leukaemia	BRONCHOPNEUMONIA Bronchopneumonia (28FEB2011)	Related Related IB Fatal
	2 CLADRIBINE	Intravenous (not otherwise specified) 3x10mg / 1 Months	04DEC2010/ --			
	3 CYCLOPHOSPHAMIDE	Intravenous (not otherwise specified) 3x530mg / 1 Months	04DEC2010/ --			

Indication: CHRONIC LYMPHOCYTIC LEUKAEMIA - SUSARs to non-company IMPs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**

Indication: CHRONIC LYMPHOCYTIC LEUKAEMIA - SUSARs to non-company IMPs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
ML21283 755693(4.0) 2008-001140-39 117920 IM11 POLAND 68 Years Male	1 RITUXIMAB	Intravenous (not otherwise specified) 1x1065mg / 1 Months	03DEC2010/ --	Chronic lymphocytic leukaemia	BRONCHOPNEUMONIA Bronchopneumonia [SUSAR Drugs 2] (28FEB2011) NEUTROPENIC FEVER Febrile neutropenia [SUSAR Drugs 3] (13JAN2011)	Related Related EU-SPC Fatal Related Related EU-SPC Not recovered/not resolved
	2 # CLADRIBINE	Intravenous (not otherwise specified) 3x10mg / 1 Months	04DEC2010/ --			
	3 # CYCLOPHOSPHAMIDE	Intravenous (not otherwise specified) 3x530mg / 1 Months	04DEC2010/ --			

Indication: CHRONIC LYMPHOCYTIC LEUKAEMIA - SUSARs to non-company IMPs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
ML25464 795374(4.0) EVCT-999999-25 207931 1 ISRAEL 79 Years Male	1 RITUXIMAB	Intravenous (not otherwise specified) 1x700mg / 28 Days	25JUL2011/ --	Chronic lymphocytic leukaemia	NEUTROPENIC FEVER Febrile neutropenia (01AUG2011)	Related Related EU-SPC Not recovered/not resolved
	2 # FLUDARABINE	Intravenous (not otherwise specified) 3x23.25mg / 28 Days	18JUL2011/ --			
	3 CYCLOPHOSPHAMIDE	Intravenous (not otherwise specified) 3x280mg / 28 Days	18JUL2011/ --			

RITUXIMAB

Indication: DIFFUSE LARGE B-CELL LYMPHOMA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
MO28107 1258559(3.0) 2012-000669-19 250139 250139003 THAILAND 64 Years Male	**1 # RITUXIMAB**	Intravenous (not otherwise specified) --x375mg/m2 / -- --	01MAY2013/ --		SEPTIC SHOCK Septic shock [SUSAR Drugs 1, 2] (03AUG2013)	Related Related IB Fatal
	2 # RITUXIMAB	Subcutaneous 1x1400mg / 3 Weeks	-- --			
	3 CYCLOPHOSPHAMIDE	Unknown --	-- --			
	4 DOXORUBICIN	Unknown --	-- --			
	5 VINCRISTINE	Unknown --	-- --			
	6 PREDNISOLONE	Unknown --	-- --			

RITUXIMAB

Indication: DIFFUSE LARGE B-CELL LYMPHOMA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
BO21005 1275586(10.0) 2010-024194-39 210624 11607 ITALY 59 Years Female	**1 # RITUXIMAB**	Intravenous (not otherwise specified) 1x---- / 3 Weeks	16MAY2013/ --	Chronic obstructive pulmonary disease Aortic valve sclerosis	COPD WORSENING Chronic obstructive pulmonary disease (27OCT2013)	Related Related EU-SPC Recovered/resolved (02NOV2013)
	2 CYCLOPHOSPHAMIDE	Intravenous (not otherwise specified) 1x---- / 3 Weeks	17MAY2013/ --			
	3 DOXORUBICIN	Intravenous (not otherwise specified) 1x---- / 3 Weeks	17MAY2013/ --			
	4 VINCRISTINE	-- 1x---- / 3 Weeks	17MAY2013/ --			
	5 PREDNISONE	Oral 1x---- / 3 Weeks	16MAY2013/ --			

RITUXIMAB

Indication: DIFFUSE LARGE B-CELL LYMPHOMA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
MO28457 1312423(13.0) 2012-003230-17 252540 252540001 MALAYSIA 49 Years Male	**1 # RITUXIMAB**	Intravenous (not otherwise specified) 1x611mg / 21 Days Intravenous (not otherwise specified) 1x375mg/m2 / 21 Days	28SEP2013/ -- -- --	Autoimmune haemolytic anaemia Neutropenia Anaemia	LUNG INFECTION Lung infection (29NOV2013) LONG SEGMENT THROMBOSIS AT LEFT BRACHIAL VEIN Venous thrombosis limb (09OCT2013)	Related Related IB Fatal Related Related IB Not recovered/not resolved
	2 CYCLOPHOSPHAMIDE	Unknown --	-- --			
	3 DOXORUBICIN	Unknown --	-- --			
	4 VINCRISTINE	Unknown --	-- --			
	5 PREDNISONE	Unknown --	-- --			
MO28457 1396108(3.0) 2012-003230-17 257287 257287011 INDONESIA 72 Years Male	**1 # RITUXIMAB**	Intravenous (not otherwise specified) 1x540mg / 21 Days	25APR2014/ --	Hypertension	LOWER GASTROINTESTINAL OBSTRUCTION Gastrointestinal obstruction (28APR2014)	Related Related IB Recovered/resolved (07MAY2014)

RITUXIMAB

Indication: DIFFUSE LARGE B-CELL LYMPHOMA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
MO28457 1423467(13.0) 2012-003230-17 256788 256788007 GERMANY 80 Years Female	**1 # RITUXIMAB**	Intravenous (not otherwise specified) --x630mg / -- -- Intravenous (not otherwise specified) --x630mg / -- -- Intravenous (not otherwise specified) --x630mg / -- -- Intravenous (not otherwise specified) --x630mg / -- --	13MAY2014/ -- 27MAY2014/ -- 10JUN2014/ -- 01JUL2014/ --	Diabetes mellitus Atrial fibrillation Hypertension Guillain-Barre syndrome Leukopenia Hypovitaminosis	HYPERTHYREOSIS Hyperthyroidism (18JUN2014)	Related Related IB Recovered/resolved (29SEP2014)
	2 CYCLOPHOSPHAMIDE	Unknown --	-- --			
	3 DOXORUBICIN	Unknown --	-- --			
	4 VINCRISTINE	Unknown --	-- --			
	5 PREDNISONE	Unknown --	-- --			

RITUXIMAB

Indication: DIFFUSE LARGE B-CELL LYMPHOMA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
MO28457 1436376(4.0) 2012-003230-17 257287 257287011 INDONESIA 70 Years Male	**1 # RITUXIMAB**	Intravenous (not otherwise specified) 1x540mg / 21 Days	25APR2014/ 14AUG2014	Hypertension	MYOPATHY Myopathy (03JUL2014)	Related Related IB Not recovered/not resolved
	2 VINCRISTINE	Unknown --	--/ 14AUG2014			
GO29044 1502637(0.0) 2013-003541-42 266062 30204 USA 68 Years Male	**1 # POLATUZUMAB VEDOTIN**	Intravenous (not otherwise specified) 1x---- / 21 Days	14NOV2014/ --	Hypertension Hyperlipidaemia Arthritis Vitamin D deficiency Cholecystectomy Appendicectomy	PULMONARY EMBOLISM Pulmonary embolism [SUSAR Drugs 1, 2] (02DEC2014)	Related Related IB/EU-SPC Not recovered/not resolved
	2 # RITUXIMAB	Intravenous (not otherwise specified) 1x---- / 21 Days	13NOV2014/ --			
	3 DOXORUBICIN	Intravenous (not otherwise specified) 1x---- / 21 Days	13NOV2014/ --			
	4 CYCLOPHOSPHAMIDE	Intravenous (not otherwise specified) 1x---- / 21 Days	13NOV2014/ --			
	5 PREDNISONE	Oral --	13NOV2014/ --			

Indication: DIFFUSE LARGE B-CELL LYMPHOMA - SUSARs to non-company IMPs

NO SUSARS WERE IDENTIFIED

RITUXIMAB

Indication: LYMPHOPLASMACYTOID LYMPHOMA/IMMUNOCYTOMA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
ML21685 1547648(2.0) 2008-005859-16 212 72236 GERMANY 75 Years Female	**1 # RITUXIMAB**	Intravenous (not otherwise specified) 1x640mg / 4 Weeks	25FEB2015/ --	Multiple sclerosis Vertigo Asthenia Depression Waldenstrom's macroglobulinaemia Viral infection	SYNCOPE/SUDDEN FAINTING Syncope (01MAR2015) REDUCED GENERAL STATE (GENERAL PHYSICAL HEALTH DETERIORATION) General physical health deterioration (07MAR2015)	Related Related EU-SPC Recovered/resolved (04MAR2015) Related Related EU-SPC Recovered/resolved (10MAR2015)
	2 BENDAMUSTINE	Intravenous (not otherwise specified) 1x150mg / 4 Weeks	25FEB2015/ --			

Indication: LYMPHOPLASMACYTOID LYMPHOMA/IMMUNOCYTOMA - SUSARs to non-company IMPs

NO SUSARS WERE IDENTIFIED

RITUXIMAB

Indication: MANTLE CELL LYMPHOMA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
MO17244 1572438(0.0) EVCT-000000-16 21 207 GERMANY 71 Years Male	**1 # RITUXIMAB**	Intravenous (not otherwise specified) --	--/ 30OCT2007	Cardiovascular disorder	ACUTE TRANSFUSION REACTION Transfusion reaction (31OCT2007)	Related Related IB Recovered/resolved (01NOV2007)
	2 FLUDARABINE	Unknown --	--/ 02NOV2007			
	3 CYCLOPHOSPHAMIDE	Intravenous (not otherwise specified) --	--/ 02NOV2007			
MO17244 1572444(0.0) EVCT-000000-16 23 316 GERMANY 76 Years Male	**1 # RITUXIMAB**	Intravenous (not otherwise specified) --x375mg/m2 / -- --	JAN2007/ AUG2007		SECONDARY ACUTE MYELOID LEUKEMIA Acute myeloid leukaemia (MAR2009)	Related Related IB Not recovered/not resolved
	2 FLUDARABINE	Intravenous (not otherwise specified) --	JAN2007/ AUG2007			
	3 CYCLOPHOSPHAMIDE	Intravenous (not otherwise specified) --	JAN2007/ AUG2007			
	4 PEGINTERFERON ALFA-2B	Subcutaneous --	31AUG2007/ --			

RITUXIMAB

Indication: MANTLE CELL LYMPHOMA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
MO17244 1572685(0.0) EVCT-999999-25 36 266 GERMANY 67 Years Male	**1 # RITUXIMAB**	Unknown --	-- --	Hypertension	EXSICCOSIS Dehydration (01JAN2010)	Related Related IB Recovered/resolved (05JAN2010)
MO17244 1573136(0.0) EVCT-999999-25 245 211 GERMANY 81 Years Female	**1 # RITUXIMAB**	Intravenous (not otherwise specified) --x375mg/m2 / -- --	FEB2009/ --	Osteoporosis Obesity Goitre	MDS Myelodysplastic syndrome (30MAY2012)	Related Related IB Not recovered/not resolved

RITUXIMAB

Indication: MANTLE CELL LYMPHOMA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
MO17244 1573295(0.0) EVCT-999999-25 585 201 GERMANY 81 Years Female	**1 # RITUXIMAB**	Intravenous (not otherwise specified) --x375mg/m2 / -- --	JUN2006/ --	Skin ulcer	MALIGNANT MELANOMA Malignant melanoma (06OCT2011)	Related Related IB Unknown
	2 CYCLOPHOSPHAMIDE	Intravenous (not otherwise specified) --x750mg/m2 / -- --	JUN2006/ DEC2006			
	3 DOXORUBICIN	Intravenous (not otherwise specified) --x50mg/m2 / -- --	JUN2006/ DEC2006			
	4 VINCRISTINE	Intravenous (not otherwise specified) --x1.5mg/m2 / -- --	JUN2006/ DEC2006			
	5 PREDNISONE	Oral --x100mg / -- --	JUN2006/ DEC2006			
MO17244 1573732(0.0) EVCT-999999-25 -- 225 GERMANY 82 Years Male	**1 # RITUXIMAB**	Intravenous (not otherwise specified) --	11FEB2008/ 05OCT2009		SEPSIS Sepsis (29NOV2009)	Related Related IB Fatal

RITUXIMAB

Indication: MANTLE CELL LYMPHOMA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
MO17244 1573957(0.0) EVCT-999999-25 494 201 NETHERLANDS 65 Years Female	**1 # RITUXIMAB**	Intravenous (not otherwise specified) --	16MAR2005/ --		EXACERBATION OF COPD Chronic obstructive pulmonary disease (03APR2005)	Related Related IB Recovered/resolved (09APR2005)

Indication: MANTLE CELL LYMPHOMA - SUSARs to non-company IMPs

NO SUSARS WERE IDENTIFIED

RITUXIMAB

Indication: NON-HODGKIN'S LYMPHOMA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
MO25455 1500004(4.0) 2010-023407-95 208731 208731003 BRAZIL 29 Years Female	**1 # RITUXIMAB**	Intravenous (not otherwise specified) --x675mg / -- --	11JUL2012/ --		IMMUNOSUPPRESSION Immunosuppression [SUSAR Drugs 1, 2] (10NOV2014)	Related Related IB Recovered/resolved (05DEC2014)
	2 # RITUXIMAB	Subcutaneous 1x1400mg / 8 Weeks Subcutaneous 1x1400mg / 8 Weeks Subcutaneous 1x1400mg / 8 Weeks Subcutaneous 1x1400mg / 8 Weeks Subcutaneous 1x1400mg / 8 Weeks Subcutaneous 1x1400mg / 8 Weeks Subcutaneous 1x1400mg / 8 Weeks Subcutaneous 1x1400mg / 8 Weeks Subcutaneous 1x1400mg / 8 Weeks Subcutaneous 1x1400mg / 8 Weeks Subcutaneous	25JUL2012/ -- 08AUG2012/ -- 03SEP2012/ -- 03OCT2012/ -- 17OCT2012/ -- 07NOV2012/ -- 04DEC2012/ -- 03JAN2013/ -- 30JAN2013/ -- 28MAR2013/ -- 23MAY2013/ -- 18JUL2013/			

RITUXIMAB

Indication: NON-HODGKIN'S LYMPHOMA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
		1x1400mg / 8 Weeks Subcutaneous 1x1400mg / 8 Weeks Subcutaneous 1x1400mg / 8 Weeks Subcutaneous 1x1400mg / 8 Weeks Subcutaneous 1x1400mg / 8 Weeks Subcutaneous 1x1400mg / 8 Weeks Subcutaneous 1x1400mg / 8 Weeks Subcutaneous 1x1400mg / 8 Weeks	-- 12SEP2013/ -- 07NOV2013/ -- 03JAN2014/ -- 05MAR2014/ -- 06MAY2014/ -- 03JUL2014/ -- 04SEP2014/ -- 30OCT2014/ --			

RITUXIMAB

Indication: NON-HODGKIN'S LYMPHOMA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
ML21685 716011(3.0) 2008-005859-16 119 74012 GERMANY 68 Years Male	**1 # RITUXIMAB**	Intravenous (not otherwise specified) 1x773mg / 4 Weeks Intravenous (not otherwise specified) -- Intravenous (not otherwise specified) -- Intravenous (not otherwise specified) -- Intravenous (not otherwise specified) -- Intravenous (not otherwise specified) -- Intravenous (not otherwise specified) -- Intravenous (not otherwise specified) --	13AUG2009/ -- SEP2009/ -- 12OCT2009/ 14OCT2009 11NOV2009/ -- 09DEC2009/ -- 12JAN2010/ -- 12FEB2010/ -- 12MAR2010/ --	Hypertension Chronic kidney disease Chronic obstructive pulmonary disease Intervertebral disc protrusion Hypertension Sacroiliitis Atrial fibrillation Thyroidectomy Laryngeal cancer Rib fracture Peripheral nerve destruction	DEATH Death (--)	Unknown Not Related EU-SPC Fatal

RITUXIMAB

Indication: NON-HODGKIN'S LYMPHOMA - SUSARs

Protocol No. **AER No. (Ver. No.)** **EudraCT No.** **Site No.** **Patient No.** **Country** **Age** **Sex**	**Suspect Medication** **# = SUSAR Drug**	**Route** **Regimen**	**Treatment** **Start/Stop** **or Duration**	**Medical** **History**	**SUSAR** **Reported Term** **Preferred Term** **(Onset Date)**	**Drug-Event** **Relationship:** **Reporter Causality** **Company Causality** **Ref. Doc.** **Event Outcome** **(Resolved Date)**
	2 BENDAMUSTINE	Intravenous (not otherwise specified) 1x185mg / 4 Weeks Intravenous (not otherwise specified) -- Intravenous (not otherwise specified) -- Intravenous (not otherwise specified) -- Intravenous (not otherwise specified) -- Intravenous (not otherwise specified) --	14AUG2009/ -- SEP2009/ -- 12OCT2009/ 14OCT2009 11NOV2009/ -- 09DEC2009/ -- 12JAN2010/ 13JAN2010			

Indication: NON-HODGKIN'S LYMPHOMA - SUSARs to non-company IMPs

NO SUSARS WERE IDENTIFIED

Dataset Parameters	
Dataset Name	17MAY2015_SSR_1065053
Date range (Informed Date)	from 18NOV2014 to 17MAY2015
Report Parameters	
SSR Drug	RITUXIMAB (FORM UNKNOWN);RITUXIMAB (IV);RITUXIMAB (SC)
Unblinded Report?	No

Current MedDRA Version: v.18.0

Report ID: SSR02 v1.1.1.0