Teva Pharma AG

Bevacizumab-Teva 100 mg/4 ml and 400 mg/16 ml concentrate for solution for infusion

Swiss Summary of the Risk Management Plan

Version 1.0 of 12 May 2021

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 Bevacizumab-Teva 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 publishedin 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 effectiveand safe use of Bevacizumab-Teva in Switzerland is the "Arzneimittelinformation/ Information sur le médicament" (see www.swissmedic.ch) approved and authorizedby Swissmedic. Teva Pharma AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Bevacizumab-Teva.

Swiss Summary of the Risk Management Plan (RMP)

Bevacizumab-Teva
100 mg/ 4 ml and 400 mg/16 ml concentrate for solution for infusion
Marketing Authorisation Number 67886

Active substance(s) (INN orcommon name):	Bevacizumab
Pharmacotherapeutic group(ATC Code):	Other antineopolastic agents – monoclonal antibodies L01XC07 Bevacizumab
Name of Marketing Authorisation Holder orApplicant:	Teva Pharma AG Kirschgartenstrasse 14 4051 Basel
Number of medicinal productsto which this RMP refers:	1 product
Product(s) concerned (brandname(s)):	Bevacizumab-Teva, concentrate for solution for infusion 100 mg/4 ml and 400 mg/16 ml
Date of updated RMP Summary:	12 May 2021

Change Log

12 May 2021	Initial version 1.0: Swiss RMP Summary created

SUMMARY OF THE RISK MANAGEMENT PLAN FOR BEVACIZUMAB-TEVA

This is a summary of the risk management plan (RMP) for Bevacizumab-Teva. The RMP details important risks of Bevacizumab-Teva, how these risks can be minimised, and how more information will be obtained about Bevacizumab-Teva's risks and uncertainties (missing information).
Bevacizumab-Teva's Product Information ("Arzneimittelinformation/ Information sur le médicament") give essential information to healthcare professionals and patients on how Bevacizumab-Teva should be used.
This summary of the RMP for Bevacizumab-Teva should be read in the context of all this information.
Important new concerns or changes to the current ones will be included in updates of Bevacizumab-Teva's RMP.

I The medicine and what it is used for

Bevacizumab-Teva is authorised for the treatment of metastatic colorectal cancer, metastatic breast cancer, advanced, metastatic or recurrent non-small cell lung cancer, advanced and/or metastatic renal cell cancer, glioblastoma, and cervical cancer (see Product Information for the full indication). It contains bevacizumab as the active substance and it is administered intravenously

II Risks associated with the medicine and activities to minimise or furthercharacterise the risks.

Important risks of Bevacizumab-Teva, together with measures to minimise such risks and the proposed studies for learning more about Bevacizumab-Teva's risks, are outlined below.
Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and Product Information 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 minimise its risks.

Together, these measures constitute routine risk minimisation measures.

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 Bevacizumab-Teva is not yet available, it is listed under 'missing information' below.

II.A List of Important Risks and Missing Information

Important risks of Bevacizumab-Teva are risks that need special risk management activities to further investigate or minimise 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 Bevacizumab-Teva. 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	
Important identified risks	Thrombotic microangiopathy Pulmonary hypertension Osteonecrosis in children
Important potential risks	None
Missing information	Long-term effects of bevacizumab when used in the paediatric population

II.B Summary of Important Risks

Identified risk 1: Thrombotic Microangiopathy	
Evidence for linking the risk to the medicine	Drug Safety Report "Thrombotic Microangiopathy, including Thrombotic Thrombocytopenic Purpura and Hemolytic-Uremic Syndrome in patients receiving bevacizumab", 20 February 2008. Drug Safety Report Addendum "Thrombotic microangiopathy, including thrombotic thrombocytopenic purpura and hemolytic-uremic syndrome in patients receiving bevacizumab", 24 April 2008
Risk factors and risk groups	− Renal thrombotic microangiopathy − Renal Cancer − Chronic kidney disease
Risk minimisation measures	<u>Routine risk minimisation measures:</u> Labelled in sections Undesirable Effects and Warnings and Precautions of the Product Information <u>Additional risk minimisation measures:</u> None

Identified risk 2: Pulmonary Hypertension	
Evidence for linking the risk to the medicine	Drug Safety Report: Pulmonary hypertension. Genentech, August 2007e
Risk factors and risk groups	− Obstructive sleep apnea − Female gender − Congenital heart disease − Systemic lupus erythematosus − Sickle cell disease − Gene mutations e.g. bone morphogenetic protein type 2 receptor (BMPR2) gene mutation − Medication e.g. fenfluramine derivatives
Risk minimisation measures	Routine risk minimisation measures: Labelled in sections Undesirable Effects and Warnings and Precautions of the Product Information Additional risk minimisation measures: None
Identified risk 3: Osteonecrosis in Children	
Evidence for linking the risk to the medicine	Drug Safety Report No.1061949 "Bone toxicity and bevacizumab use in children". 20 October 2014.
Risk factors and risk groups	Major risk factors for the development of osteonecrosis in children include cancer, use of corticosteroids, major trauma leading to bone fractures and osteomyelitis.
Risk minimisation measures	Routine risk minimisation measures: Labelled in sections Dosage/Use and Undesirable Effects of the Product Information Product is not indicated for paediatric patients. Additional risk minimisation measures: None
Missing information: Long-term effects of bevacizumab when used in the paediatric population	
Risk minimisation measures	Routine risk minimisation measures: Product is not indicated for paediatric patients Additional risk minimisation measures None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: None

II.C Post-Authorisation Development Plan

II.C.1 Studies Which Are Conditions of the Marketing Authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Bevacizumab-Teva.

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

There are no studies required for Bevacizumab-Teva.