EU RISK MANAGEMENT PLAN

for Eribulin Baxter 0.44 mg/ml solution for injection (eribulin)

Version 1.0

Issued 30 APR 2024

Details of current RMP submission

RMP version to be assessed as part of this application	1.0
Data lock point for this RMP	29 APR 2024
Date of final sign-off	30 APR 2024
Rationale for submitting initial RMP	New marketing authorization application

Other RMP versions under evaluation

Not applicable; there are currently no other Risk Management Plan (RMP) versions for Eribulin Baxter 0.44 mg/ml solution for injection (hereafter Eribulin Baxter) under evaluation in the European Union (EU).

Details of the currently approved RMP

Not applicable; this is the first RMP for Eribulin Baxter in the EU.

EU QPPV oversight

EU Qualified person responsible for pharmacovigilance (QPPV)/ QPPV Deputy name	Örjan Mortimer, MD/ Iva Slavcevova, MD
EU QPPV/ QPPV Deputy oversight declaration	The content of this RMP has been reviewed and approved by Baxter's QPPV or QPPV Deputy (by delegation). The electronic signature is available on file.

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ABBREVIATIONS

Abbreviation	Definition
EEA	European Economic Area
EMA	European Medicines Agency
EPAR	European Public Assessment Report
EU	European Union
GVP	Good Pharmacovigilance Practices
mg	Milligram(s)
ml	Milliliter(s)
PL	Package Leaflet
QPPV	Qualified person responsible for pharmacovigilance
RMP	Risk Management Plan
SmPC	Summary of Product Characteristics

PART I: PRODUCT(S) OVERVIEW

Active substance(s) (INN or common name)	Eribulin mesilate
Pharmacotherapeutic group(s) (ATC Code)	Other antineoplastic agents (L01XX41)
Marketing Authorization Applicant	Baxter Holding B.V.
Number of medicinal products to which this RMP refers	1
Invented name(s) in the European Economic Area (EEA)	Eribulin Baxter 0.44 mg/ml solution for injection
Marketing authorization procedure	Centralized procedure
Brief description of the product	**Chemical class:** Eribulin mesilate is a microtubule dynamics inhibitor belonging to the halichondrin class of antineoplastic agents.
	Summary of mode of action: Eribulin inhibits the growth phase of microtubules without affecting the shortening phase and sequesters tubulin into non-productive aggregates. Eribulin exerts its effects via a tubulin-based antimitotic mechanism leading to G2/M cell-cycle block, disruption of mitotic spindles, and, ultimately, apoptotic cell death after prolonged and irreversible mitotic blockage.
	Important information about its composition: Eribulin is a structurally simplified synthetic analogue of halichondrin B, a natural product isolated from the marine sponge *Halichondria okadai*. Each 2 milliliters (ml) vial of Eribulin Baxter contains: • less than 1 millimole sodium (23 milligrams (mg)) per vial; it is essentially 'sodium-free'. • 78.9 mg (0.1 ml) of alcohol. The amount in 2 ml of this medicine is equivalent to 2 ml beer or less than 1 ml wine. The small amount of alcohol will not have any noticeable effects.
Hyperlink to the product information	Proposed Summary of Product Characteristics (SmPC): Eribulin Baxter 0.44 mg/ml solution for injection Proposed Package Leaflet (PL): Eribulin Baxter 0.44 mg/ml solution for injection
Indication(s) in the EEA	**Current:** Eribulin Baxter is indicated for: • The treatment of adult patients with locally advanced or metastatic breast cancer who have progressed after at least

	one chemotherapeutic regimen for advanced disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting unless patients were not suitable for these treatments. • The treatment of adult patients with unresectable liposarcoma who have received prior anthracycline containing therapy (unless unsuitable) for advanced or metastatic disease.
	Proposed: Not applicable.
Dosage(s) in the EEA	**Current:** The recommended dose of Eribulin Baxter as the ready to use solution is 1.23 mg/square meter which should be administered intravenously over 2 to 5 minutes on days 1 and 8 of every 21-day cycle. For additional posology information, refer to the SmPC.
	Proposed: Not applicable.
Pharmaceutical form(s) and strength(s)	**Current:** Pharmaceutical form: Clear, colourless aqueous solution for injection essentially free from visible particles (pH: 6.5 – 8.5; osmolality: 750-950 milliosmole/kilogram). Strength: One ml contains 0.5 mg eribulin mesilate equivalent to 0.44 mg eribulin. Each 2 ml vial contains 1 mg eribulin mesilate equivalent to 0.88 mg eribulin.
	Proposed: Not applicable.
Is/will the product be subject to additional monitoring in the EU?	No

PART II: SAFETY SPECIFICATION

Per European Medicines Agency (EMA) Good Pharmacovigilance Practices (GVP) Module V Revision 2, Part II Modules SI – SVI are not required for generic applications.

PART II: MODULE SI – EPIDEMIOLOGY OF THE INDICATION(S) AND TARGET POPULATION(S)

Not applicable.

PART II: MODULE SII – NON-CLINICAL PART OF THE SAFETY SPECIFICATION

Not applicable.

PART II: MODULE SIII – CLINICAL TRIAL EXPOSURE

Not applicable.

PART II: MODULE SIV – POPULATIONS NOT STUDIED IN CLINICAL TRIALS

Not applicable.

PART II: MODULE SV – POST-AUTHORIZATION EXPERIENCE

Not applicable.

PART II: MODULE SVI – ADDITIONAL EU REQUIREMENTS FOR THE SAFETY SPECIFICATION

Not applicable.

PART II: MODULE SVII – IDENTIFIED AND POTENTIAL RISKS

Per EMA GVP Module V Revision 2, Part II: Module SVII is not required as the safety concerns are aligned to the current RMP of the reference product (v8.0 issued 02Jun2023) for Halaven (Eisai GmbH, EU Centralized procedure - EMEA/H/C/002084; Halaven EPAR RMP 2023).

PART II: MODULE SVIII – SUMMARY OF THE SAFETY CONCERNS

Important identified risks	Tachycardia
	Disseminated intravascular coagulation
Important potential risks	Adverse pregnancy outcomes
	Male infertility
	Gastrointestinal perforation
Missing information	None

PART III: PHARMACOVIGILANCE PLAN (INCLUDING POST-AUTHORIZATION STUDIES)

III.1 Routine pharmacovigilance activities

All safety concerns are subject to routine pharmacovigilance monitoring through standard adverse reaction reporting and routine signal detection activities. These activities are considered sufficient for all safety concerns discussed in this RMP.

Adverse reaction follow-up questionnaires

None proposed.

Other forms of routine pharmacovigilance, beyond adverse reaction reporting and routine signal detection

None proposed.

III.2 Additional pharmacovigilance activities

None proposed.

III.3 Summary table of additional pharmacovigilance activities

None proposed.

PART IV: PLANS FOR POST-AUTHORIZATION EFFICACY STUDIES

There are no ongoing or planned post-authorization efficacy studies which have been imposed as a condition of the marketing authorization or as a specific obligation.

PART V: RISK MINIMIZATION MEASURES

Per EMA GVP Module V Revision 2 guidelines, Part V is not applicable, as the safety information in the proposed product information is aligned to the reference medicinal product.

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of Risk Management Plan for Eribulin Baxter 0.44 mg/ml solution for injection (eribulin)

This is a summary of the Risk Management Plan (RMP) for Eribulin Baxter 0.44 mg/ml solution for injection (hereafter Eribulin Baxter). The RMP provides details on the important risks of Eribulin Baxter, how these risks can be minimized, and how more information will be obtained about the important risks for Eribulin Baxter.

The Summary of Product Characteristics (SmPC) and Package Leaflet (PL) for Eribulin Baxter provide essential information to healthcare professionals and patients on how Eribulin Baxter should be used.

This summary of the RMP for Eribulin Baxter should be read in the context of all other related information, including the assessment report of the evaluation and its plain-language summary, all of which are part of the European Public Assessment Report (EPAR).

New safety concerns and/or changes to the current safety concerns will be included in future updates of the RMP.

I. The medicine and what it is used for

Eribulin Baxter is authorized for:

- The treatment of adult patients with locally advanced or metastatic breast cancer who have progressed after at least one chemotherapeutic regimen for advanced disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting unless patients were not suitable for these treatments.
- The treatment of adult patients with unresectable liposarcoma who have received prior anthracycline containing therapy (unless unsuitable) for advanced or metastatic disease.

It contains eribulin mesilate as the active substance, and it is given intravenously on Days 1 and 8 of every 21-day cycle.

Further information about the evaluation of Eribulin Baxter's benefits can be found in the EPAR, including in its plain-language summary, available on the EMA website under the medicine's webpage: https://www.ema.europa.eu/en/medicines/human/EPAR/eribulin-baxter

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

The important risks of Eribulin Baxter, together with measures to minimize such 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 PL 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;
- The medicine's legal status – the way a medicine is supplied to the patient (e.g., with or without prescription).

Together, these measures constitute *routine risk minimization measures*.

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

II.A List of important risks and missing information

Important risks of medicinal products 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 medicinal products. Potential risks are concerns for which an association with the use of the medicinal product is possible based on available data, but this association has not been established yet and needs to be further monitored. Missing information refers to information on the safety of the medicinal product that is currently missing and further information may need to be collected (e.g., on the long-term use of the medicine).

The table below presents the list of important risks and missing information included in the RMP for Eribulin Baxter.

List of important risks and missing information	
Important identified risks	Tachycardia
	Disseminated intravascular coagulation

Important potential risks	Adverse pregnancy outcomes
	Male infertility
	Gastrointestinal perforation
Missing information	None

II.B Summary of important risks and missing information

The safety information in the proposed product information is aligned to the reference medicinal product.

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 obligations of Eribulin Baxter.

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

There are no studies required for Eribulin Baxter.

Annex 4: Specific adverse drug reaction follow-up forms

Not applicable.

Annex 6: Details of proposed additional risk minimization measures

None proposed.