# PRADAXA (Dabigatranetexilat)
# Kapseln
# ZL-Nr.: 61385

*Public Risk Management Plan (RMP) Summary*

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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 Pradaxa 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 Pradaxa in Switzerland is the “Arzneimittelinformation/ Information sur le médicament” (see www.swissmedic.ch) approved and authorized by Swissmedic.

Boehringer Ingelheim (Schweiz) GmbH is fully responsible for the accuracy and correctness of the content of the published summary RMP of Pradaxa.

**SUMMARY OF RISK MANAGEMENT PLAN FOR PRADAXA (dabigatran etexilate)**

This is a summary of the Risk Management Plan (RMP) for Pradaxa. The RMP details important risks of Pradaxa, how these risks can be minimised, and how more information will be obtained about Pradaxa's risks and uncertainties (missing information).

Pradaxa's Summary of Product Characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Pradaxa should be used.

This summary of the RMP for Pradaxa 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 Pradaxa's RMP.

## I. THE MEDICINE AND WHAT IT IS USED FOR

Pradaxa contains the active substance dabigatran and belongs to a group of medicines called anticoagulants. It works by blocking the activity of a substance in the body which is involved in blood clot formation.

Pradaxa is used in adults to (see SmPC for the full indications):

- Prevent the formation of blood clots in the veins after knee or hip replacement surgery
- Prevent blood clots in the brain (stroke) and other blood vessels in the body if you have a form of irregular heart rhythm called nonvalvular atrial fibrillation and at least one additional risk factor
- Treat blood clots in the veins of your legs and lungs and to prevent blood clots from re-occurring in the vein of your legs and lungs

Pradaxa is used in children to (see SmPC for the full indication):

- Treat blood clots and prevent blood clots from reoccurring

Further information about the evaluation of Pradaxa's benefits can be found in Pradaxa's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage.

## II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Pradaxa, together with measures to minimise such risks and the proposed studies for learning more about Pradaxa'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 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 minimise its risks.

Together, these measures constitute routine risk minimisation measures.

In the case of Pradaxa, these measures are supplemented with additional risk minimisation 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 Pradaxa is not yet available, it is listed under 'missing information' below.

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

Important risks of Pradaxa are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. 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 Pradaxa. 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 | Haemorrhage |
| Important potential risks | Medication error due to complexity of reconstitution of and dosing with the oral solution (paediatric population below 1 year of age)[1] |
| Important missing information | Patients aged 0 to 2 years who were born prematurely[1] |
| | Paediatric patients with renal dysfunction (eGFR <50ml/min)[1] |

[1]These safety concerns are only valid in countries where the paediatric indication is approved.

## II.B Summary of important risks

| **Important identified risk Haemorrhage** | |
|---|---|
| Evidence for linking the risk to the medicine | Anticoagulation bears an inherent risk of haemorrhage. Based on clinical and post-marketing data, haemorrhage was defined as an important identified risk for Pradaxa. Dabigatran (the active substance of Pradaxa) is eliminated through the kidneys, and kidney function diminishes with increasing age. Therefore, the rates of haemorrhages depend on the dose and are related to renal (kidney) failure and age. |
| Risk factors and risk groups | The risk of haemorrhages with Pradaxa increases with declining kidney function. Kidney function diminishes with age. Therefore, the elimination of dabigatran may be reduced, and dabigatran blood levels may be increased, in elderly patients and in patient with reduced kidney function. As a consequence, the risk of bleeding is increased in these patients. The highest rates occur in the very elderly (age >75 years) with poor kidney function. |
| Risk minimisation measures | Routine risk minimisation measures:<br>• SmPC Sections 4.2, 4.3, 4.4, 4.5, 4.8, and 4.9<br>• PL Sections 2, 3, and 4<br>Other risk minimisation measures:<br>• Praxbind (idarucizumab) has been approved in adult patients as a specific reversal agent for rapid reversal of the anticoagulation effect of dabigatran case of emergency surgery or urgent procedures for situations of life-threatening or uncontrolled bleeding. A paediatric investigation plan for idarucizumab has been completed. In paediatric patients for whom the specific reversal agent cannot be used, haemodialysis can remove dabigatran.<br>Additional risk minimisation measures:<br>• Prescriber guide and patient alert card |
| Additional pharmacovigilance activities | Additional pharmacovigilance activities:<br>• Study 1160.307<br>See Section II.C of this summary for an overview of the post-authorisation development plan. |

| **Important potential risk Medication error due to complexity of reconstitution of and dosing with the oral solution (paediatric population below than 1 year of age)** | |
|---|---|
| Evidence for linking the risk to the medicine | Administration of Pradaxa oral solution requires several complex steps of preparation and administration. The instructions for use reflect the complexity of reconstitution and dosing for the dabigatran etexilate oral solution |
| Risk factors and risk groups | Infants at the age of less than 1 year will be impacted. Risk factors are poor training of those who reconstitute/dose the oral solution and distractions while performing these tasks |
| Risk minimisation measures | Routine risk minimisation measures:<br>• SmPC Section 4.2<br>• PL Sections 3 and 7<br>Other risk minimisation measures:<br>• Reconstitution by HCPs with caregiver reconstitution if the treating physician deems it is appropriate<br>• Instructions for use and administration in each medication kit<br>• Medication errors reported with the use of the oral solution will be summarised in Pradaxa PBRERs<br>Additional risk minimisation activities:<br>• Prescriber Guide for the paediatric indication with special section for the oral solution<br>• Training video for healthcare professionals and caregivers for reconstitution and use of the oral solution with mandatory training<br>• Technical support via phone |
| Additional pharmacovigilance activities | Additional pharmacovigilance activities:<br>• Human factors study<br>See Section II.C of this summary for an overview of the post-authorisation development plan. |

| Missing information Patients aged 0 to 2 years who were born prematurely | |
|---|---|
| Risk minimisation measures | No risk minimisation measures |

| Missing information Paediatric patients with renal dysfunction (eGFR <50ml/min) | |
|---|---|
| Risk minimisation measures | Routine risk minimisation measures:<br>• SmPC Sections 4.2 and 4.4<br>• PL Section 2 |

## II.C Post-authorisation development plan

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

The following studies are conditions of the marketing authorisation:

There are no studies which are conditions of the marketing authorisation or specific obligation of Pradaxa.

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

- Study 1160.307: Safety of dabigatran etexilate for treatment of VTE and prevention of recurrent VTE in paediatric patients from birth to less than 2 years of age: a European non-interventional cohort study based on new data collection

  Purpose of the study: Conducted clinical trials evaluated limited numbers of young children with VTE. There exists a need for post-authorisation data collection to characterise the safety profile of dabigatran for treatment of VTE in children under 2 years of age.

  The main objective of this non-interventional study is to estimate the incidence of any bleeding events (major bleeding according to ISTH definition and minor bleeding events) among children under 2 years of age treated with dabigatran etexilate.

- Human factors study to assess effectiveness of a training video to mitigate potential medication errors during the reconstitution and dosing of the dabigatran etexilate paediatric oral solution

  Purpose of the study: This human factors study will serve as a surrogate for assessment of effectiveness of the healthcare professional and caregiver training using a video to mitigate potential medication errors during the reconstitution and dosing of the dabigatran etexilate paediatric oral solution.

The main objective is to assess effectiveness of a training video to mitigate potential medication errors during the reconstitution and dosing of the dabigatran etexilate paediatric oral solution.

## ABBREVIATIONS

| | |
|---|---|
| ADR | Adverse drug reaction |
| AF | Atrial fibrillation |
| EEA | European Economic Area |
| EMA | European Medicines Agency |
| EPAR | European Public Asessment Report |
| EU | European Union |
| GLORIA-AF | Global Registry on Long-Term Oral Antithrombotic Treatment In Patients with Atrial Fibrillation |
| PL | Patient leaflet |
| RMP | Risk Management Plan |
| SCAR | Severe cutaneous adverse reaction |
| SmPC | Summary of Product Characteristics |