PART VI: SUMMARY OF THE EUROPEAN UNION RISK MANAGEMENT PLAN

This is a summary of the European Union risk management plan (RMP) for Oxbryta. The RMP details important risks of Oxbryta, how these risks can be minimised, and how more information will be obtained about Oxbryta's risks and uncertainties (missing information).

Oxbryta's prescribing information and its package leaflet give essential information to healthcare professionals and patients on how Oxbryta should be used.

I. The medicine and what it is used for

Oxbryta is authorised for treatment of haemolytic anaemia due to sickle cell disease (SCD) in adults and paediatric patients 12 years of age or older (see Summary of Product Characteristics [SmPC] for the full indication). It contains voxelotor as the active substance and it is given by mouth.

Further information about the evaluation of Oxbryta's benefits can be found in Oxbryta's European public assessment report (EPAR), including in its plain-language summary, available on the European Medicines Agency (EMA) website, under the medicine's webpage https://www.ema.europa.eu/en/medicines/human/EPAR/oxbryta

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

Important risks of Oxbryta, together with measures to minimise such risks and the proposed studies for learning more about Oxbryta'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 (eg, 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 Periodic Benefit-Risk Evaluation Report (PBRER) 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 Oxbryta is not yet available, it is listed under "missing information" below.

II.A List of important risks and missing information

Important risks of Oxbryta 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 Oxbryta. 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 (eg, on the long-term use of the medicine).

List of Important Identified and Important Potential Risks and Missing Information	
Important identified risks	Not applicable
Important potential risks	Not applicable
Missing information	Safety in pregnancy and lactation Safety in patients with SCD with ESRD requiring dialysis Long-term safety Drug-drug interaction potential with voxelotor and OATP1B1, OAT3 and MATE1 substrates, and the drug-drug interaction potential with voxelotor and CYP2B6, CYP2C8, CYP2C9, CYP2C19, and CYP3A4 substrates Safety in immunocompromised patients (including patients with HIV)

CYP, cytochrome P450; ESRD, end-stage renal disease; HIV, human immunodeficiency virus; MATE, multidrug and toxin extrusion; OAT, organic anion transporter; OATP, organic anion transporting polypeptide; SCD, sickle cell disease.

II.B Summary of Important Risks

There are no important risks associated with Oxbryta.

Missing Information: Safety in Pregnancy and Lactation	
Risk minimisation measures	Routine risk minimisation measures SmPC, Section 4.6, Section 5.3 PL Section 2 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Missing Information: Safety in Patients With SCD with ESRD Requiring Dialysis	
Risk minimisation measures	Routine risk minimisation measures SmPC, Section 4.2, Section 4.4, Section 5.2 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Missing Information: Long-Term Safety	
Risk minimisation measures	Routine risk minimisation measures None Additional risk minimisation measures None
Additional pharmacovigilance activities	GBT440-034 - An Open Label Extension Study of Voxelotor (GBT440) Administered Orally to Participants with Sickle Cell Disease Who Have Participated in Voxelotor Clinical Trials

Missing Information: Drug-drug Interaction Potential With Voxelotor and OATP1B1, OAT3 and MATE1, and Effect of Voxelotor on CYP2B6, CYP2C8, CYP2C9, CYP2C19, and CYP3A4 Substrates	
Risk minimisation measures	Routine risk minimisation measures SmPC, Section 4.5, Section 5.2 Additional risk minimisation measures None
Additional pharmacovigilance activities	Study GBT440-0120: A Phase 1, Open-Label, Fixed-Sequence, Two-Period, Drug-Drug Interaction Study to Evaluate Effect of Voxelotor on the Pharmacokinetics of Probe Substrates for CYP2B6, CYP2C8, CYP2C9, CYP2C19, and CYP3A4 in Healthy Subjects Study GBT440-0121: A Phase 1, Open-Label Study to Evaluate the Effect of Multiple Doses of Voxelotor on the Pharmacokinetics of Probe Substrates for MATE1, OAT3, and OATP1B1 in Healthy Subjects

Missing Information: Safety in Immunocompromised Patients (Including Patients with HIV)	
Risk minimisation measures	Routine risk minimisation measures SmPC, Section 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

II.C Postauthorisation development plan

II.C.1 Studies that are conditions of the marketing authorisation

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

II.C.2 Other studies in postauthorisation development plan

There are no studies planned.