Oxbryta™ 500 mg tablets Abbreviated Prescribing Information

Presentation: Film-coated tablet (tablet)Light yellow to yellow, oval shaped, biconvex, film-coated tablet, debossed with "GBT 500" on one side. **Therapeutic indications:** *OXBRYTA is indicated for the treatment of sickle cell disease (SCD) in adults and pediatric patients 12 years of age and older. OXBRYTA can be administered alone or in combination with hydroxyurea (HU).* **Posology and method of administration:** *The recommended dosage of OXBRYTA is 1500 mg taken orally once daily with or without food. If a dose is missed, dosing should be continued on the day following the missed dose. OXBRYTA may be given with or without hydroxyurea (HU).* **Pediatric use:** The safety and effectiveness of voxelotor for sickle cell disease have been established in pediatric patients aged 12 years and older in Study GBT440-031 (HOPE). Pharmacokinetics, safety, and efficacy in pediatric patients 12 years to < 18 years were similar to that observed in adults. **Geriatric use:** Clinical studies of voxelotor did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Renal impairment. No clinically significant differences in the pharmacokinetics of voxelotor were observed in patients with mild to severe **renal impairment**. OXBRYTA has not been evaluated in patients with end stage renal disease requiring dialysis. No dose modification is recommended. **Hepatic impairment:** Severe hepatic impairment increases voxelotor exposures. The recommended dosage of OXBRYTA in patients with severe hepatic impairment (Child Pugh C) is 1000 mg taken once daily with or without food. No dosage adjustment of OXBRYTA is required for patients with mild or moderate hepatic impairment. Concomitant moderate or strong inducers, strong inhibitors of CYP3A4, or Fluconazole. Avoid concomitant use of strong or moderate CYP3A4 inducers, strong CYP3A4 inhibitors, or fluconazole with OXBRYTA. If concomitant use of strong or moderate CYP3A4 inducers, strong CYP3A4 inhibitors, or fluconazole is unavoidable, adjust the OXBRYTA dosage as recommended below. OXBRYTA recommended dosage for concomitant medications. Concomitant medication Recommended OXBRYTA dosage: Strong CYP3A4 inhibitors or fluconazole 1000 mg once daily. Strong or moderate CYP3A4 inducers 2500 mg once daily **Method of administration** OXBRYTA is for oral use. OXBRYTA tablets should be swallowed whole. The film-coated tablets should not be cut, crushed, or chewed. **Contraindications:** Voxelotor is contraindicated in patients with a history of serious drug hypersensitivity reaction to voxelotor or excipients **Special warnings and precautions for use: Hypersensitivity reactions:** Serious hypersensitivity reactions have been observed in < 1% of patients treated with voxelotor in clinical trials. Clinical manifestations may include generalized rash, urticaria, mild shortness of breath, mild facial swelling, and eosinophilia. If hypersensitivity reactions occur, discontinue voxelotor and administer appropriate medical therapy Do not reinitiate voxelotor in patients who experience these symptoms with previous use. **Interactions:** Effect of other drugs on voxelotor. Strong CYP3A4 inhibitors or Fluconazole Co-administration of strong CYP3A4 inhibitors or fluconazole may increase voxelotor plasma concentrations and may lead to increased toxicity. Avoid co-administration of voxelotor with strong CYP3A4 inhibitors or fluconazole and replace these drugs with alternative drugs when possible. Decrease the voxelotor dosage when co-administration with a strong CYP3A4 inhibitor or

fluconazole is unavoidable. Strong or moderate CYP3A4 inducers Co-administration of strong or moderate CYP3A4 inducers may decrease voxelotor plasma concentrations and may lead to reduced efficacy. Effect of voxelotor on other drugs. Voxelotor increased the systemic exposure of midazolam (a sensitive CYP3A4 substrate). Avoid co-administration of voxelotor with sensitive CYP3A4 substrates with a narrow therapeutic index. If concomitant use is unavoidable, consider dose reduction of the sensitive CYP3A4 substrate(s). Laboratory test interference OXBRYTA administration may interfere with measurement of Hb subtypes (HbA, HbS, and HbF) by HPLC (see Section 4.4). If precise quantitation of Hb species is required, chromatography should be performed when the patient is not receiving OXBRYTA therapy. **Fertility:** No human data are available on the effect of voxelotor on fertility. **Pregnancy**: There are no available data on voxelotor use in pregnant women to evaluate the drug associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. In animal reproduction studies, oral administration of voxelotor to pregnant rats and rabbits during organogenesis at exposures up to 2.8-times (rats) and 0.3-times (rabbits) the exposure at the maximum recommended human dose resulted in no adverse developmental effects. **Lactation:** There are no data on the presence of voxelotor in human milk, the effects on the breastfed child, or the effects on milk production. Voxelotor was detected in milk in lactating rats. Plasma concentrations of voxelotor in pregnant rats were higher than the concentration in milk. When a drug is present in animal milk, it is likely that the drug will be present in human milk. The concentration of voxelotor in animal milk does not necessarily predict the concentration of drug in human milk. Because of the potential for serious adverse reactions in the breastfed child, including changes in the hematopoietic system, advise patients that breastfeeding is not recommended during treatment with voxelotor, and for at least 2 weeks after the last dose. **Undesirable effects: System organ class Adverse reactions**[a]: **Gastrointestinal disorders**: Very common: Diarrhea, Abdominal pain (grouped PTs)[b], Nausea. **General disorders and administration site conditions**: Very common: Fatigue, Pyrexia

Immune system disorders: Common Drug hypersensitivity**. Nervous system disorders:** Very common: Headache**. Skin and subcutaneous tissue disorders:** Very common: Rash[c, a] Adverse reactions were Grades 1 or 2 except for Grade 3 diarrhea (1), nausea (1), rash (1), and rash generalized (3). [b] Abdominal pain (grouped PTs) included the following PTs: abdominal pain and upper abdominal pain. [c] Rash (grouped PTs) includes the following PTs: rash, urticaria, generalized rash, maculo-papular rash, pruritic rash, popular rash, erythematous rash, and vesicular rash.

Reference: Oxbryta™ SUMMARY OF PRODUCT CHARACTERISTICS, March 2021. Date of this document: May 2023.

Full prescribing information is available upon request.