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Prescribing information can be found on the last 2 pages.

REZUROCK® ▼
(belumosudil) tablets

SAFETY PROFILE

Explore when considering REZUROCK in the treatment of cGVHD for patients aged 12 years and older who have received at least two prior lines of systemic therapy.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to the Sanofi drug safety department on Tel: 0800 0902 314. Alternatively, send via email to UK-drugsafety@sanofi.com.

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REZUROCK was **generally well tolerated** in patients with cGVHD[1]

Safety was evaluated across 2 clinical studies (n=186)[2,3]

The most common adverse reactions leading to discontinuation were nausea (2.4%) and headache (2.4%). Adverse reactions leading to dose interruption occurred in 9.6% of patients and were mainly investigations (3.6%), including ALT increased, GGT increased and blood creatine phosphokinase increased (1.2% each), and infections (2.4%)[1]

From Rezurock Summary of Product Characteristics, dated December 2023.[1]

The most common adverse reactions (≥5%) were asthenia (21.0%), nausea (12.4%), liver function test abnormalities of elevation of AST (7.5%), elevation of ALT (7.0%) and elevation of GGT (4.8%), headache (8.6%), diarrhoea (7.0%) and musculoskeletal pain (5.9%)[1]

From Rezurock Summary of Product Characteristics, dated December 2023.[1]

Serious adverse reactions were pneumonia (1.1%), cellulitis, infectious colitis, staphylococcal bacteraemia, diarrhoea, nausea, vomiting, microangiopathic haemolytic anaemia, multiple organ dysfunction syndrome and cGVHD (0.5% each)[1]

From Rezurock Summary of Product Characteristics, dated December 2023.[1]

There were **no reports of CMV infection** in both the ROCKstar and the foundational, dose-finding KD025-208 studies, and only **1 report of CMV reactivation** in total[2,3]

ROCKstar data up to 19 August 2020 included.[1]

In the ROCKstar and KD025-208 clinical studies of REZUROCK, **grade ≥3 cytopenias** were reported in **<4%** and **4%** of patients, respectively[2,3]

ROCKstar data up to 19 August 2020 included.[1]

In the 3-year follow-up to the 2021 ROCKstar study, no new safety signals were observed.[4]

Please refer to the full Summary of Product Characteristics before prescribing.

cGVHD, chronic graft-versus-host disease; CMV, cytomegalovirus.

References: 1. REZUROCK. Summary of Product Characteristics. **2.** Jagasia M, Lazaryan A, Bachier CR, *et al*. ROCK2 inhibition with belumosudil (KD025) for the treatment of chronic graft-versus-host disease. *J Clin Oncol*. 2021;39 (17):1888-1898. doi:10.1200/JCO.20.02754. **3.** Cutler C, Lee SJ, Arai S, *et al*; on behalf of the ROCKstar Study Investigators. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. *Blood*.2021;138 (22):2278-2289. doi:10.1182/blood.2021012021. **4.** Lee SJ, Cutler C, Pavletic S, *et al*. Belumosudil for chronic graft-versus-host disease after 2 or more lines of systemic therapy: 3-year follow-up to the ROCKstar study. Poster presented at: Tandem Meetings; February 21, 2024; San Antonio, TX.

Safety results across 2 clinical studies pooled for analysis[1]

Adverse reactions (≥2%) in patients with chronic GVHD who received belumosudil[1]

Table adapted from Rezurock Summary of Product Characteristics, dated December 2023.[1]

Pooled chronic GVHD (N=186)	All severity grades Frequency category	All grades[a] (%)	Grade 3-4[a] (%)
Infections and infestations			
Upper respiratory tract infections[b]	**Common**	7 (3.8%)	0
Lower respiratory tract infections[c]	**Common**	5 (2.7%)	2 (1.1%)
Blood and lymphatic system disorders			
Anaemia*	**Common**	6 (3.2%)	1 (0.5%)
Leukopenia[d]*	**Common**	9 (4.8%)	3 (1.6%)
Platelet count decreased	**Common**	5 (2.7%)	0
Metabolism and nutrition disorders			
Decreased appetite	**Common**	7 (3.8%)	1 (0.5%)
Hyperglycaemia	**Common**	7 (3.8%)	0
Nervous system disorders			
Headache	**Common**	16 (8.6%)	1 (0.5%)
Neuropathy peripheral	**Common**	6 (3.2%)	0
Dizziness	**Common**	4 (2.2%)	0
Vascular disorders			
Hypertension	**Common**	6 (3.2%)	3 (1.6%)
Respiratory, thoracic and mediastinal disorders			
Dyspnea[e]	**Common**	7 (3.8%)	0
Cough[f]	**Common**	7 (3.8%)	0
Gastrointestinal disorders			
Nausea	**Very Common**	23 (12.4%)	2 (1.1%)
Diarrhoea	**Common**	13 (7.0%)	2 (1.1%)
Vomiting	**Common**	9 (4.8%)	1 (0.5%)
Abdominal pain[g]	**Common**	5 (2.7%)	0
Constipation	**Common**	5 (2.7%)	1 (0.5%)
Hepatobiliary disorders			
Aspartate aminotransferase increased	**Common**	14 (7.5%)	3 (1.6%)
Alanine aminotransferase increased	**Common**	13 (7.0%)	2 (1.1%)
Gamma-glutamyltransferase increased	**Common**	9 (4.8%)	2 (1.1%)
Skin and subcutaneous tissue disorders			
Pruritus	**Common**	5 (2.7%)	0
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain[h]	**Common**	11 (5.9%)	0
Muscle spasms	**Common**	8 (4.3%)	0
Blood alkaline phosphatase increased	**Common**	7 (3.8%)	0
Blood creatine phosphokinase increased	**Common**	4 (2.2%)	1 (0.5%)
Renal and urinary disorders			
Blood creatinine increased	**Common**	4 (2.2%)	0
General disorders and administration site conditions			
Asthenia[i]	**Very Common**	39 (21.0%)	5 (2.7%)
Oedema[j]	**Common**	9 (4.8%)	0
Pyrexia	**Common**	3 (1.6%)	0
Investigations			
Weight decreased	**Common**	6 (3.2%)	0

Please refer to the full Summary of Product Characteristics before prescribing.

[a]National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 5.0 and version 4.03 for studies KD025-208 and KD025-213, respectively.

[b]includes upper respiratory tract infection, sinusitis.

[c]includes pneumonia, bronchitis, bronchitis viral.

[d]includes leukopenia, neutropenia, neutrophil count decreased, white blood cell count decreased, lymphocyte count decreased.

[e]includes dyspnea, dyspnea exertional.

[f]includes cough, productive cough.

[g]includes abdominal pain, abdominal pain upper.

[h]includes arthralgia, pain in extremity, back pain, neck pain.

[i]includes fatigue, asthenia, malaise.

[j]includes oedema peripheral, face oedema, localized oedema, swelling.

*See description of selected adverse reactions in full SmPC.

GVHD, graft-versus-host disease.

Reference: 1. REZUROCK. Summary of Product Characteristics.

Prescribing Information: REZUROCK (belumosudil) ▼ 200mg film coated tablets (Licence valid in GB only)

Therapy should be initiated and supervised by physicians experienced in the management of chronic GVHD. Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Presentation: Each film-coated tablet contains belumosudil mesilate, equivalent to 200mg belumosudil.
Indication: Rezurock is indicated for the treatment of patients aged 12 years and older with chronic graft-versus- host disease (chronic GVHD) who have received at least two prior lines of systemic therapy.
Dosage and Administration: The recommended dose of Rezurock is 200mg administered orally once daily at approximately the same time with a meal. The film-coated tablet should not be broken, crushed or chewed. Treatment should continue until disease progression or unacceptable toxicity. A complete blood cell count and liver function test must be performed before initiating therapy with Rezurock. Perform liver function tests at least monthly throughout treatment. Dose modification due to hepatotoxicity and other adverse reactions: For Grade 3 alanine aminotransferase (ALT) or aspartate aminotransferase (AST) (>5 – 20 × upper limit of normal (ULN)) or Grade 2 bilirubin (>1.5 – 3 × ULN) or other Grade 3 adverse reactions, hold Rezurock until recovery to ≤Grade 1, then resume Rezurock at the recommended dose at physician's discretion. For Grade 4 ALT or AST (>20 × ULN) or Grade ≥3 bilirubin (>3 × ULN) or other Grade 4 adverse reactions, permanently discontinue Rezurock. Dose modification due to drug interactions: *Strong CYP3A Inducers:* Increase the dosage of Rezurock to 200mg twice daily when co-administered with strong CYP3A inducers. *Proton Pump Inhibitors:* Increase the dosage of Rezurock to 200mg twice daily when co- administered with proton pump inhibitors. Delayed or missed dose: If a dose is missed or delayed for <12 hours after the scheduled dose, the dose should be taken as soon as possible on the same day with a return to the normal schedule the following day. If a dose is missed or delayed for >12 hours after the scheduled dose, the dose should be taken at the usual time the following day. If a patient vomits following the intake of a dose, the next dose should be taken at the usual time the following day. Patients should not take extra doses to make up the missed dose.
Special Populations: Hepatic impairment: Dose modification is not recommended when administering belumosudil to patients with mild or moderate hepatic impairment (Child-Pugh A and B). Belumosudil is not recommended in patients with severe hepatic impairment. The safety and efficacy of belumosudil in severe (Child-Pugh C) hepatic impairment has not been evaluated. For patients with pre-existing severe hepatic impairment (Child-Pugh C), consider the risks and potential benefits before initiating treatment with belumosudil. Monitor patients frequently for adverse reactions.
Renal impairment: No dose modification of Rezurock is required in patients with mild or moderate renal impairment (creatine clearance ≥30 mL/min). No data are available for patients with severe renal impairment (creatine clearance<30 mL/min) or for patients with end-stage renal disease on dialysis. Use with caution. Elderly patients (≥65 years): No additional dose adjustments are recommended for elderly patients. Paediatric population: The posology is the same in adults and adolescents aged 12 – 18 years. The safety and efficacy of Rezurock in children and adolescents aged below 12 years of age have not been established. No data are available.
Contraindications: Pregnancy. Hypersensitivity to the active substance or to any of the excipients.
Precautions and Warnings: Female patients of childbearing potential and male patients with female partners of childbearing potential: Women of childbearing potential (WOCBP) should be advised to avoid becoming pregnant while they or their male partner are taking belumosudil and of the potential risk to a fetus. WOCBP should be advised to have a pregnancy test prior to starting treatment with belumosudil. WOCBP and male patients with female partners of childbearing potential must use a highly effective method of contraception during treatment with belumosudil and for at least one week after the last dose of belumosudil. Hepatotoxicity: Increases in liver function tests were observed in clinical studies with belumosudil and generally occurred early during treatment with the incidence decreasing thereafter. Liver function tests should be performed prior to the initiation of treatment with belumosudil and monitored at least monthly during treatment with belumosudil and the dose should be adjusted for ≥Grade 2 toxicities. Sodium: This product is essentially sodium free. **Interactions:** Effect of CYP3A inhibitors on belumosudil: The co-administration of multiple doses of itraconazole did not alter exposure to belumosudil to any clinically relevant extent. Effect of CYP3A inducers on belumosudil: The co- administration of multiple doses of rifampin decreased belumosudil Cmax by 59% and AUC by 72%. The co- administration of strong CYP3A4 inducers with belumosudil may decrease belumosudil exposure. Increase the dose of belumosudil to 200mg twice daily. The co-administration of moderate CYP3A4 inducers e.g., efavirenz is predicted to have a reduced effect on belumosudil as compared to strong CYP3A4 inducers. The co-administration of moderate CYP3A4 inducers with belumosudil may decrease belumosudil exposure. No dose adjustment is recommended. Effect of proton pump inhibitors on belumosudil: The co-administration of multiple doses of rabeprazole decreased belumosudil Cmax by 87% and AUC by 80%. The co-administration of multiple doses of omeprazole decreased belumosudil Cmax by 68% and AUC by 47%. The co-administration of proton pump inhibitors with belumosudil may decrease belumosudil exposure. Increase the dose of belumosudil to 200mg twice daily. Effect of other gastric acid reducing agents on belumosudil: The co-administration of belumosudil with gastric acid reducing agents other than proton pump inhibitors may decrease belumosudil exposure. No dose adjustment is recommended, however belumosudil and the gastric acid reducing agent should be taken 12 hours apart. In vitro studies: *Effect of belumosudil on CYP3A substrates:* The co- administration of belumosudil is predicted to increase midazolam Cmax and AUC approximately 1.3- and 1.5-fold, respectively. No dose adjustment is recommended.

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The co- administration of belumosudil may increase exposure of sensitive CYP3A4 substrates with a narrow therapeutic index such as ciclosporin and tacrolimus. No dose adjustment is recommended. *Effect of belumosudil on CYP2C9 substrates*: The co-administration of belumosudil is not expected to have clinically meaningful effect on the exposure of CYP2C9 substrates (such as warfarin). *Effect of belumosudil on CYP2C8 substrates*: The co-administration of belumosudil is not expected to have clinically meaningful effect on the exposure of CYP2C8 substrates that are not an OATP1B1 substrate. *Effect of belumosudil on UGT1A1 substrates*: Belumosudil is a weak inhibitor of UGT1A1, the clinical consequences are not known. *Transporters*: Belumosudil is a substrate of P-gp. Belumosudil inhibits BCRP, P-gp, and OATP1B1. The co-administration of oral BCRP, P-gp and OATP1B1 substrates with belumosudil may increase the concentrations of the substrate drugs (such as digoxin and docetaxel).

Pregnancy: There are no data on the use of belumosudil in pregnant women. Belumosudil can cause fetal harm based on findings from animal studies and its mechanism of action. As a precautionary measure, belumosudil is contraindicated in pregnancy. **Breast-feeding:** It is unknown whether belumosudil or its metabolites are excreted in human milk. No data are available regarding the presence of belumosudil or its metabolites in animal or human milk or its effects on the breast-fed child, or on milk production. A risk to the infant cannot be excluded. Because of the potential for serious adverse reactions in a breast-fed child, breast-feeding should be discontinued during treatment with belumosudil and for at least one week after the last dose. **Fertility:** There are no human data on the effect of belumosudil on fertility. Based on findings from animal studies, belumosudil may impair male and female fertility at dose levels above the recommended clinical dose. The effects on fertility are reversible.

Adverse Reactions: Very common: Nausea, asthenia. Common: upper and lower respiratory tract infections, anaemia, leukopenia, platelet count decreased, decreased appetite, hyperglycaemia, headache, neuropathy peripheral, dizziness, hypertension, dyspnoea, cough, diarrhoea, vomiting, abdominal pain, constipation, AST and ALT increased, gamma-glutamyltransferase increased, pruritus, musculoskeletal pain, muscle spasms, blood alkaline phosphatase increased, blood creatine phosphokinase increased, blood creatinine increased, oedema, pyrexia, weight decreased. *Prescribers should consult the SmPC in relation to other adverse reactions.*

Legal Category: POM

GB List Price and Marketing Authorisation Number:
200mg x 30 tablets (PLGB 04425/0902): £6708.

Marketing Authorisation Holder: Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK.

Further information is available from: Medical Information, Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK.
uk-medicalinformation@sanofi.com

Date of preparation: January 2024

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