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Prescribing information can be found on the last 2 pages.

REZUROCK® ▼
(belumosudil) tablets

PATIENT PROFILES

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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Patient profiles

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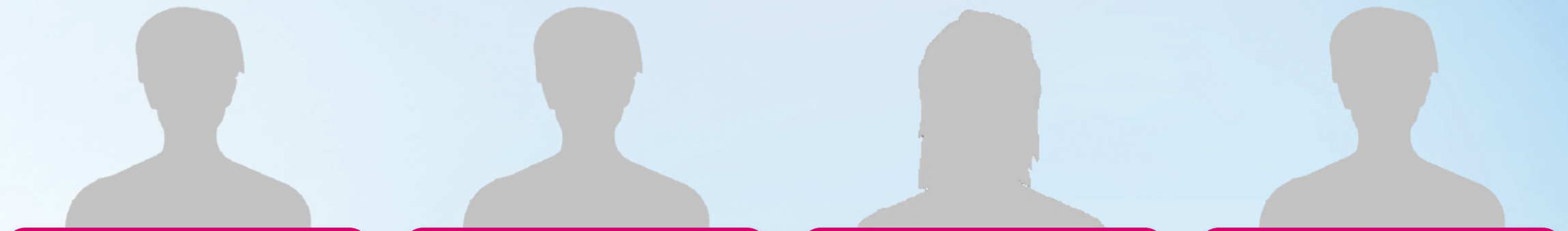

Early in the disease course	Later treatment of cGVHD	Lung-associated cGVHD	After failure of 4 to 5 lines of prior systemic therapy
After CS, CNI, and Sirolimus	Post-ECP		
View profile	View profile	View profile	View profile

cGVHD, chronic graft-versus-host disease; ECP, extracorporeal photopheresis; CS; corticosteroids; CNI, calcineurin inhibitors.

Treatment of cGVHD

Early in the disease course. After CS, CNI, and Sirolimus

Baseline characteristics	
Age, sex	55 years, male
Weight	60kg

Transplant	
Type/malignancy	Allo HCT (MUD peripheral blood) for Acute Myeloid Leukaemia
Date of transplant	October 2022

This is a fictional patient.

Signs, symptoms, and diagnosis

Signs and symptoms

- 4 months post-transplant, patient develops maculopapular erythema, diarrhoea and moderate mouth symptoms with lichenoid features
- 15% of body surface area affected
- Partial limitation of oral intake
- NIH grade 2

Diagnosis

- cGVHD diagnosis February 2023

History of present illness

Multi-organ involvement

- Mouth, skin and GI

Base line NIH cGVHD severity score

- 2 for mouth, skin and GI

QOL impact

- Financial issues due to travel costs
- Fatigued

AlloHCT, allogeneic hematopoietic cell transplant; cGVHD, chronic graft-versus-host disease; NIH, National Institutes of Health; QOL, quality of life; MUD, Matched unrelated donor; GI, gastrointestinal

Treatment history of cGVHD

Early in the disease course. After CS, CNI, and Sirolimus (Cont)

Treatment history

AlloHCT
October 2022

Chronic GVHD diagnosis
February 2023

2023											
JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC

Prednisone (PO)	50mg once daily cGVHD progresses		
Cyclosporin (PO)	75 mg BD progression of cGVHD		
Sirolimus (PO)	**Loading dose:** 6 mg - 1st day	**Maintenance dose:** 2 mg once daily	

Progressive cGVHD was noted after 4 weeks of steroid treatment and no change after the addition of CNI and sirolimus.

Consider REZUROCK for patients with cGVHD after failure of any 2 prior lines of systemic therapy

This is a fictional patient.
Some treatments are not indicated for cGVHD in Great Britain. Please refer to individual Summary of Product Characteristics for more information.

AlloHCT, allogeneic hematopoietic cell transplant; cGVHD, chronic graft-versus-host disease; PO, by mouth; CNI, calcineurin inhibitors

Treatment of cGVHD

Later treatment of cGVHD. Post-ECP

Baseline characteristics	
Age, sex	33 years, male
Weight	63.4 kg

Transplant	
Type/malignancy	AlloHCT for AML
Date of transplant	April 2022

This is a fictional patient.

Signs, symptoms, and diagnosis

Signs and symptoms

- Patient developed several post-transplant complications, including pancytopenia, dry eye, eye sensitivity and itchy skin rashes

Diagnosis

- Patient was diagnosed with aGVHD in June 2022
- Patient was diagnosed with cGVHD in October 2022

History of present illness

Multi-organ involvement

- Eyes, liver, skin and mouth

Base line NIH cGVHD severity score

- 2 for liver, eyes, skin and mouth

QOL impact

- Patient lost his job due to demands of his work
- Wife works two jobs to help financially support the family
- Fatigued

AML, acute myeloid leukemia; aGVHD, acute graft-versus-host disease; alloHCT, allogeneic hematopoietic cell; cGVHD, chronic graft-versus-host disease; NIH, National Institutes of Health; QOL, quality of life

cGVHD Treatment history

Later treatment of cGVHD. Post-ECP (Cont)

Treatment history

AlloHCT
April 2022

Acute GVHD diagnosis

Chronic GVHD diagnosis
October 2022

		2022							2023			
		JUN	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR
Acute GVHD treatment	**Tacrolimus** (PO)	3 mg twice daily	3 mg once daily	1 mg once daily	0.5 mg once daily ↓ Discontinued due to aGVHD resolution							
Chronic GVHD treatments	**Prednisone** (PO)					60 mg once daily	40 mg once daily	20 mg once daily	40 mg once daily			
	ECP								2 consecutive days every week			**Discontinued due to disease progression**

After receiving ECP for 3 months, an assessment was performed, which revealed that despite previously achieving PR and failing to achieve sustained remission with a CS taper, the patient experienced progressive cGVHD.

Consider REZUROCK for patients with cGVHD after failure of any 2 prior lines of systemic therapy

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ECP, extracorporeal photopheresis; aGVHD, acute graft-versus-host disease; alloHCT, allogeneic hematopoietic cell transplant; cGVHD, chronic graft-versus-host disease; PO, by mouth; CS, corticosteroids; PR, partial response

Treatment of cGVHD

Lung-associated cGVHD

Baseline characteristics	
Age, sex	26 years, female
Weight	50.4 kg

Transplant	
Type/malignancy	AlloHCT for ALL
Date of transplant	June 2020

This is a fictional patient.

Signs, symptoms and diagnosis

Signs and symptoms

- Patient developed various posttransplant complications, including fasciitis, BOS, dysphagia and painful ulcers

Diagnosis

- Patient was diagnosed with cGVHD in April 2021

History of present illness

Multi-organ involvement

- GI and lungs

Base line NIH cGVHD severity score

- 2 for GI tract and lungs

QOL impact

- Patient's significant other ended their relationship
- Patient had to move in with parents for financial and caregiver support

ALL, acute lymphoblastic leukemia; alloHCT, allogeneic hematopoietic cell transplant; BOS, bronchiolitis obliterans syndrome; cGVHD, chronic graft-versus-host disease; GI, gastrointestinal; NIH, National Institutes of Health; QOL, quality of life.

Lung assessments

Lung-associated cGVHD (Cont)

Lung assessments

At time of transplant (June 2020)	**FEV_1** 78%	**FEV_1/FVC** 0.83	**RV** 85%	**FEF_{25-75}** 99%	**DLCO** 75%		
3 months post-transplant (September 2020)	**FEV_1** 70%	**FEV_1/FVC** 0.75	**RV** 111%	**FEF_{25-75}** 85%	**DLCO** 51%		
10 months post-transplant (April 2021)	**FEV_1** 52%	**FEV_1/FVC** 0.67	**RV** 125%	**FEF_{25-75}** 71%	**DLCO** 41%	**Expiratory CT scan** air trapping	**BOS grade** 2

Consider REZUROCK for patients with cGVHD after failure of any 2 prior lines of systemic therapy

This is a fictional patient.

BOS, bronchiolitis obliterans syndrome; CT, computed tomography; DLCO, diffusing capacity of the lungs for carbon monoxide; FEF25-75, forced expiratory flow between 25% to 75% maximum; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; RV, residual volume.

Treatment history

Lung-associated cGVHD (Cont)

Treatment history

AlloHCT
June 2020

Chronic GVHD diagnosis
April 2021

	2021									2022					
	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN
Budesonide/ formoterol (inhaled)	160 mg/4.5 mg twice daily														
Montelukast (PO)	10 mg once daily														
Omeprazole (PO)	40 mg once daily														
Prednisone (PO)	50 mg once daily			30 mg once daily						25 mg once daily			30 mg once daily		
Rituximab (IV)								567 mg weekly		**Discontinued due to intolerability**					
Ruxolitinib (PO)						5 mg twice daily							**Continued treatment with PR**		

After previously achieving PR, lung progression remains a concern

Consider REZUROCK for patients with cGVHD after failure of any 2 prior lines of systemic therapy

This is a fictional patient.
Some treatments are not indicated for cGVHD in Great Britain. Please refer to individual Summary of Product Characteristics for more information.

PR, partial response; alloHCT, allogeneic hematopoietic cell transplant; cGVHD, chronic graft-versus-host disease; IV, intravenous; PO, by mouth

Treatment of cGVHD

After failure of 4 to 5 lines of prior systemic therapy

Baseline characteristics	
Age, sex	57 years, male
Weight	86.4 kg

Transplant	
Type/malignancy	AlloHCT for ALL
Date of transplant	June 2020

This is a fictional patient.

Signs, symptoms and diagnosis

Signs and symptoms

- Posttransplant complications, including dry mouth; dry, tight and itchy skin; photosensitivity of the eyes; and muscle cramps

Diagnosis

- Patient was diagnosed with cGVHD in October 2020

History of present illness

Multi-organ involvement

- Eyes, skin, mouth and joints/fascia

Base line NIH cGVHD severity score

- 3 for eyes; 2 for skin, mouth and joints/fascia

QOL impact

- Patient was forced to retire early

QOL, quality of life; alloHCT, allogeneic hematopoietic cell transplant; cGVHD, chronic graft-versus-host disease; NIH, National Institutes of Health; ALL, Acute lymphoblastic leukaemia

Treatment history

After failure of 4 to 5 lines of prior systemic therapy (Cont)

Treatment history

AlloHCT
June 2020

Chronic GVHD diagnosis
October 2020

	2020			2021										
	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
Prednisone (PO)	80 mg once daily					65 mg once daily			40 mg once daily						
Sirolimus (PO)		**Loading dose** 6 mg **Maintenance dose** 2 mg once daily		**Discontinued due to progressive disease**											
ECP				2 consecutive days every other week				**Discontinued due to QOL burden and transient availability of ruxolitinib**					**Restart** 2 consecutive days every other week		
Ruxolitinib								10 mg twice daily		5 mg twice daily			**Discontinued due to intolerability**		

After previously achieving PR, progressive cGVHD was noted.

Consider REZUROCK for patients with cGVHD after failure of any 2 prior lines of systemic therapy

This is a fictional patient.
Some treatments are not indicated for cGVHD in Great Britain. Please refer to individual Summary of Product Characteristics for more information.

QOL, quality of life; alloHCT, allogeneic hematopoietic cell transplant; cGVHD, chronic graft-versus-host disease; ECP, extracorporeal photopheresis; PO, by mouth; PR, partial response

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. Co-administration of belumosudil with drugs transported by OATP1B1 and BCRP substrates can lead to an increase in exposure of these concomitant drugs (e.g. rosuvastatin). *Proton Pump Inhibitors:* Increase the dosage of Rezurock to 200mg twice daily when co- administered with proton pump inhibitors. *OATP1B1/BCRP substrates:* Consider switching to a drug less sensitive to OATP1B1 and BCRP inhibition when possible. If used together the dose of rosuvastatin should not exceed 5 mg once daily. Monitor patients closely for signs and symptoms of excessive exposure to the drugs that are substrates of OATP1B1 and BCRP. 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 (creatinine clearance ≥30 mL/min). No data are available for patients with severe renal impairment (creatinine 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). The co-administration of belumosudil with drugs transported by OATP1B1 and BCRP can lead to an increase in exposure of these concomitant drugs (e.g. rosuvastatin) which may increase the risk of these substrate-related toxicities. Co-administration of belumosudil increases rosuvastatin C_{max} and AUC by 3.6 and 4.6-fold, respectively.

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

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