A resource for the transplant care team

REZUROCK®
(belumosudil) tablets

An innovative way to treat cGVHD[1-3]

REZUROCK can help patients

ROCK ON

For patients with cGVHD aged ≥12 years after failure of any 2 prior lines of systemic therapy[1]

cGVHD, chronic graft-versus-host disease.

INDICATION

REZUROCK® (belumosudil) is indicated for the treatment of adult and pediatric patients 12 years and older with chronic graft-versus-host disease (chronic GVHD) after failure of at least two prior lines of systemic therapy.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- **Embryo-Fetal Toxicity:** Based on findings in animals and its mechanism of action, REZUROCK can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with REZUROCK and for at least one week after the last dose

Please see additional Important Safety Information throughout.

Please see full Prescribing Information.

Chronic GVHD presents **multiple challenges** for patients, who have already suffered so much[1,4,5]

Chronic GVHD is a common and serious complication that affects about half of alloHCT recipients[6]

- Chronic GVHD is a widespread immune reaction involving donor B and T cells and is characterized by the presence of inflammatory and fibrotic manifestations[7]
- Acute GVHD is characterized by inflammation and primarily involves the skin, GI tract and liver. Unlike aGVHD, cGVHD involves fibrosis across multiple organ systems[7]
- The burden of cGVHD is multifaceted, with patients experiencing poor QOL and progressive disability[4,8]
- Immunosuppressive therapy plays an important role in cGVHD; however, it is not always effective and may be associated with a high AE burden[9-11]

Chronic GVHD affects immune homeostasis, throwing the immune system out of balance.[7]

Patients with cGVHD can develop multiorgan manifestations in the[12]

AE, adverse event; aGVHD, acute graft-versus-host disease; alloHCT, allogeneic hematopoietic cell transplant; GI, gastrointestinal; GVHD, graft-versus-host disease; QOL, quality of life.

Chronic GVHD affects each patient differently[6]; however, it typically presents as[6,11]

- Skin rashes and lesions
- Skin thickening or tightening
- Joint stiffness and loss of mobility and dexterity
- Impaired lung function
- Nausea, vomiting, diarrhea or loss of appetite
- General decline in health, including fatigue
- Ocular dysfunction
- Abnormal liver function, measured by various tests

HEAR FROM PATIENTS WITH cGVHD

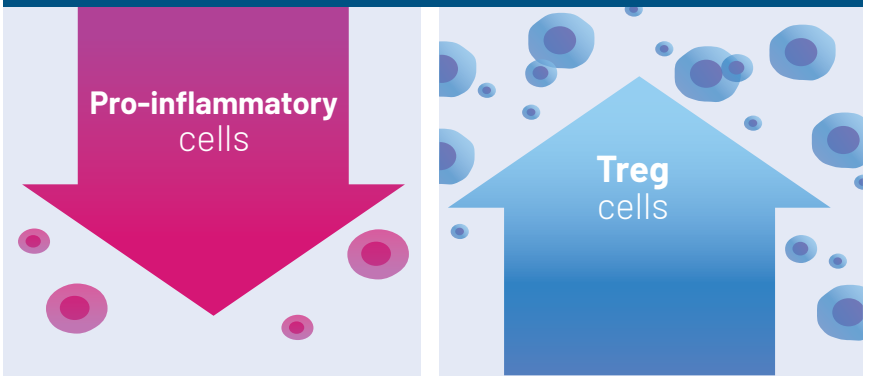
CLICK or TAP to access videos of patients with cGVHD talking about their condition.

REZUROCK works differently by targeting both the inflammatory and the fibrotic processes of cGVHD[1-3]

REZUROCK® (belumosudil) tablets

As an oral selective ROCK2 inhibitor, REZUROCK is an innovative treatment designed to **restore immune homeostasis** and to **downregulate the fibrotic processes** of cGVHD.[1-3]

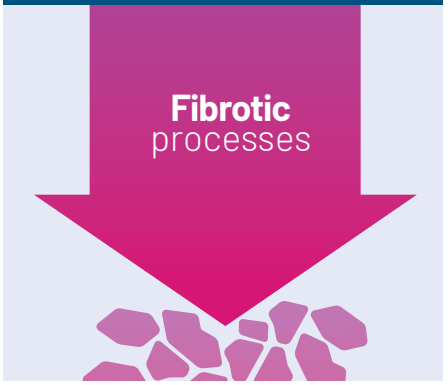
Reduces inflammation via its immunomodulatory effect[2,13]



Downregulates pro-inflammatory Tfh and Th17 cells[2,13]

Upregulates Treg cells, restoring immune homeostasis[14]

Downregulates fibrosis[3,15]



Prevents upregulation of profibrotic genes and processes[15]

To learn more about the MOA of REZUROCK, visit **REZUROCKhcp.com**.
The MOA video for patients and caregivers is available at **REZUROCK.com**.

The mechanism of action of belumosudil in cGVHD is not fully understood.

MOA, mechanism of action; ROCK2, rho-associated coiled-coil–containing protein kinase-2; Tfh, follicular helper T [cells]; Th17, type 17 helper T [cells]; Treg, regulatory T [cells].

IMPORTANT SAFETY INFORMATION (cont)

Adverse Reactions

- The most common (≥ 20%) adverse reactions, including laboratory abnormalities, were infections, asthenia, nausea, diarrhea, dyspnea, cough, edema, hemorrhage, abdominal pain, musculoskeletal pain, headache, phosphate decreased, gamma glutamyl transferase increased, lymphocytes decreased, and hypertension

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What your patients **should know** about REZUROCK study results

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Your patients and their caregivers may have questions about REZUROCK. This information may be helpful for establishing treatment expectations.

Clinically meaningful responses were seen in the ROCKstar pivotal study (n=66).[1,12,a,b]

- Statistically significant ORR[c,d] of 75% (primary end point; 95% CI, 63-85; *P*<.0001) with the 200-mg once-daily dose in a real-world demographic of patients[1,16]
- 63% of responses were observed between weeks 4 and 8[17]
- 94% of responses were seen by week 24[17]
- Some patients may take longer to respond, especially those with more severe disease and organ involvement with fibrotic manifestations[11]

Patients saw improvement across multiple organs, including the[12]

- Skin
- Eyes
- Mouth
- Upper and lower GI tract
- Esophagus
- Joints/fascia
- Liver
- Lungs

52% of patients[d] in the mITT population reported clinically meaningful improvements in QOL[e] (≥7-point reduction in LSS[f] summary score) with REZUROCK 200 mg once daily in an exploratory analysis.[1,g]

- Both responders (61%) and nonresponders (25%) had improved QOL scores[18]

Some patients had a reduced need for corticosteroids and other immunosuppressants.[12]

REZUROCK can be used in patients after failure of any 2 prior lines of systemic therapy.[1]

Visit **REZUROCKhcp.com** to learn more.

CR, complete response; FDA, US Food and Drug Administration; LSS, Lee Symptom Scale; mITT, modified intent-to-treat; NIH, National Institutes of Health; ORR, overall response rate; PR, partial response.

[a]The final FDA interpretation of the ROCKstar study omitted 1 patient from the REZUROCK 200-mg once-daily arm. As a result, there are minor differences between the ROCKstar publication, where n=66, and the Prescribing Information, where n=65.

[b]The ROCKstar study was an open-label phase 2 study comparing REZUROCK 200 mg once daily (n=66) with REZUROCK 200 mg twice daily (n=66) in patients with cGVHD aged ≥12 years who received 2 to 5 prior lines of systemic therapy.[12] Prespecified key secondary end points not powered to show statistical significance.

[c]Proportion of patients who achieved CR or PR according to the 2014 NIH cGVHD Consensus Criteria.[1]

[d]Based on a final analysis by the FDA (n=65).

[e]Through cycle 7 day 1.[1]

[f]The LSS is a 30-item, 7-subscale symptom scale and QOL measurement tool that evaluates the AEs of cGVHD in the categories of skin, vitality, lung, nutritional status, psychological functioning, eye and mouth.[19]

[g]An exploratory analysis provides a better understanding of a problem but is not proof. It is difficult to measure QOL because every person is different and will have a unique experience with treatment.

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REZUROCK was **well tolerated** in patients with cGVHD[1,9]

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Safety was evaluated across 2 clinical studies[1,a]

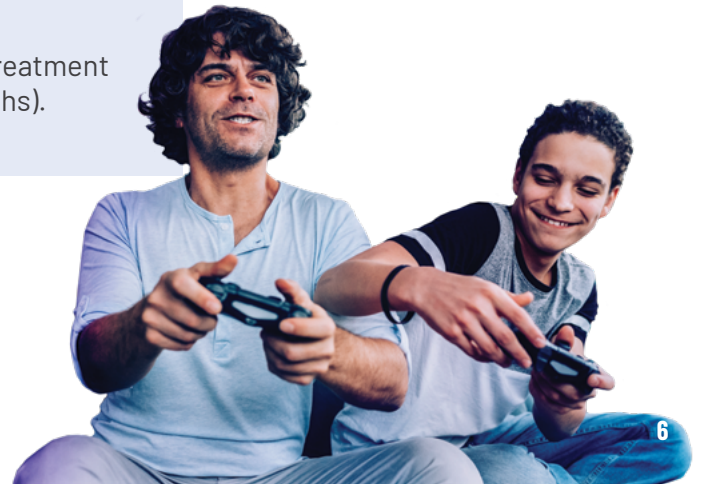
Consider the safety profile of REZUROCK in patients with cGVHD who often receive immunosuppressive therapy.

- Fatal adverse reaction was reported in 1 patient with severe nausea, vomiting, diarrhea and multiorgan failure[1]
- Permanent discontinuation of REZUROCK due to adverse reactions occurred in 18% of patients. The adverse reactions which resulted in permanent discontinuation of REZUROCK in >3% of patients included nausea (4%)[1]
- The most common (≥20%) adverse reactions, including laboratory abnormalities, were infections, asthenia, nausea, diarrhea, dyspnea, cough, edema, hemorrhage, abdominal pain, musculoskeletal pain, headache, phosphate decreased, gamma glutamyl transferase increased, lymphocytes decreased and hypertension[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[12,20]
- In the ROCKstar and KD025-208 clinical studies of REZUROCK, grade ≥3 cytopenias were reported in <4% and 4% of patients, respectively[12,20]

MOST PATIENTS WERE ABLE TO MAINTAIN TREATMENT WITH REZUROCK 200 mg ONCE DAILY (n=83)[1,a]

9.2 MONTHS

Patients had a median duration of treatment of 9.2 months (range, 0.5-44.7 months).



CMV, cytomegalovirus.

[a]Data included results from a dose-finding multicenter study of REZUROCK for the treatment of patients with cGVHD (N=54) who had received 1 to 3 prior lines of systemic therapy and required additional treatment. REZUROCK was administered by mouth at 200 mg once daily, 200 mg twice daily or 400 mg once daily.[20]

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

REZUROCK® (belumosudil) tablets

NONLABORATORY ADVERSE REACTIONS IN ≥10% OF PATIENTS WITH cGVHD TREATED WITH REZUROCK 200 mg ONCE DAILY (n=83)[1,a,b]

		All grades, %	Grades 3-4, %
Infections and infestations	Infection (pathogen not specified)	53	16
	Viral infection	19	4
	Bacterial infection	16	4
General disorders and administration site conditions	Asthenia	46	4
	Edema	27	1
	Pyrexia	18	1
Gastrointestinal	Nausea	42	4
	Diarrhea	35	5
	Abdominal pain	22	1
	Dysphagia	16	0
Respiratory, thoracic and mediastinal	Dyspnea	33	5
	Cough	30	0
	Nasal congestion	12	0
Vascular	Hemorrhage	23	5
	Hypertension	21	7
Musculoskeletal and connective tissue	Musculoskeletal pain	22	4
	Muscle spasm	17	0
	Arthralgia	15	2
Nervous system	Headache	21	0
Metabolism and nutrition	Decreased appetite	17	1
Skin and subcutaneous	Rash	12	0
	Pruritus	11	0

[a]Data included results from a dose-finding multicenter study of REZUROCK for the treatment of patients with cGVHD (N=54) who had received 1 to 3 prior lines of systemic therapy and required additional treatment. REZUROCK was administered by mouth at 200 mg once daily, 200 mg twice daily or 400 mg once daily.[20]

[b]Please see Table 2 of the REZUROCK Prescribing Information for complete details on nonlaboratory adverse reactions.

Please see Important Safety Information throughout.

Please see full Prescribing Information.

REZUROCK: A once-daily oral tablet for patients with cGVHD[1]

REZUROCK® (belumosudil) tablets

The recommended dose of REZUROCK is 200 mg once daily administered orally[1]

Inform patients that the REZUROCK tablets should be swallowed whole with a glass of water **without cutting, crushing or chewing the tablets**.

Advise patients to take REZUROCK at approximately the **same time each day** with a meal. It is important for patients to understand that **a meal is not a snack**, and that it is about the same amount of calories as they might have for lunch or dinner.

If the patient misses a dose of REZUROCK, instruct the patient **not to take extra doses** to make up for the missed dose.

Monitor total bilirubin, AST and ALT at least monthly (see full Prescribing Information for more details on when to hold or discontinue REZUROCK due to hepatotoxicity or other adverse reactions).

If patients are **taking strong CYP3A inducers or proton pump inhibitors**, increase the dosage of REZUROCK to 200 mg twice daily.

ALT, alanine aminotransferase; AST, aspartate aminotransferase.

IMPORTANT SAFETY INFORMATION (cont)

Adverse Reactions (cont)

- Permanent discontinuation of REZUROCK due to adverse reactions occurred in 18% of patients. The adverse reactions which resulted in permanent discontinuation of REZUROCK in > 3% of patients included nausea (4%). Adverse reactions leading to dose interruption occurred in 29% of patients. The adverse reactions leading to dose interruption in ≥ 2% were infections (11%), diarrhea (4%), and asthenia, dyspnea, hemorrhage, hypotension, liver function test abnormal, nausea, pyrexia, edema, and renal failure with (2% each)

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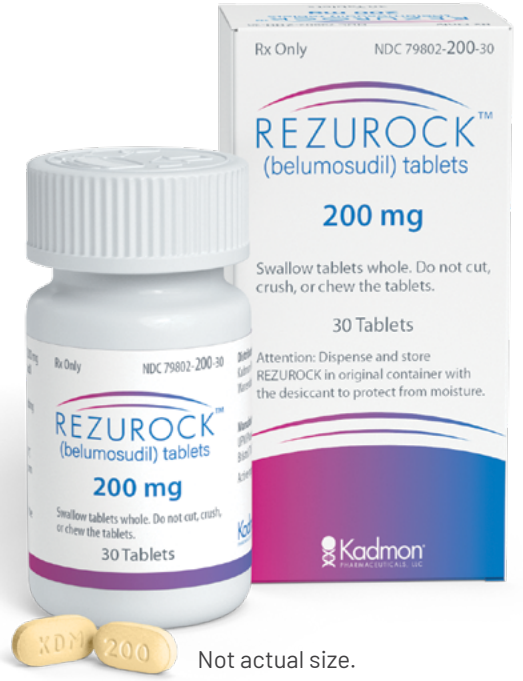

Not actual size.

Store REZUROCK tablets at room temperature (68 °F-77 °F [20 °C-25 °C]) in the original container.[1]

REZUROCK should be dispensed to the patient in the original container only. Store in original container to protect from moisture. Replace cap securely each time after opening. Do not discard desiccant.[1]

Each pale-yellow, oblong, 200-mg tablet is debossed with "KDM" on one side and "200" on the other side.[1]

References: 1. REZUROCK. Package insert. Kadmon Pharmaceuticals, LLC; 2021. **2.** Zanin-Zhorov A, Weiss JM, Nyuydzefe MS, et al. Selective oral ROCK2 inhibitor down-regulates IL-21 and IL-17 secretion in human T cells via STAT3-dependent mechanism. *Proc Natl Acad Sci USA*. 2014;111(47):16814-16819. doi:10.1073/pnas.1414189111 **3.** Flynn R, Paz K, Du J, et al. Targeted Rho-associated kinase 2 inhibition suppresses murine and human chronic GVHD through a Stat3-dependent mechanism. *Blood*. 2016;127(17):2144-2154. doi:10.1182/blood-2015-10-678706 **4.** Kurosawa S, Oshima K, Yamaguchi T, et al. Quality of life after allogeneic hematopoietic cell transplantation according to affected organ and severity of chronic graft-versus-host disease. *Biol Blood Marrow Transplant*. 2017;23(10):1749-1758. doi:10.1016/j.bbmt.2017.06.011 **5.** Riding the emotional roller coaster of chronic graft-versus-host disease (cGVHD). BMT InfoNet. Accessed May 19, 2022. https://www.bmtinfonet.org/video/riding-emotional-roller-coaster-graft-versus-host-disease **6.** Chronic graft-versus-host disease (cGVHD). BMT InfoNet. Accessed May 19, 2022. https://www.bmtinfonet.org/transplant-article/chronic-graft-versus-host-disease-cgvhd **7.** Zeiser R, Blazar BR. Pathophysiology of chronic graft-versus-host disease and therapeutic targets. *N Engl J Med*. 2017;377(26):2565-2579. doi:10.1056/NEJMra1703472 **8.** Hamilton BK, Storer BE, Wood WA, et al. Disability related to chronic graft-versus-host disease. *Biol Blood Marrow Transplant*. 2020;26(4):772-777. doi:10.1016/j.bbmt.2019.10.019 **9.** Yalniz FF, Murad MH, Lee SJ, et al. Steroid refractory chronic graft-versus-host disease: cost-effectiveness analysis. *Biol Blood Marrow Transplant*. 2018;24(9):1920-1927. doi:10.1016/j.bbmt.2018.03.00810 **10.** Lee SJ, Nguyen TD, Onstad L, et al. Success of immunosuppressive treatments in patients with chronic graft-versus-host disease. *Biol Blood Marrow Transplant*. 2018;24(3):555-562. doi:10.1016/j.bbmt.2017.10/042 **11.** Flowers MED, Martin PJ. How we treat chronic graft-versus-host disease. *Blood*. 2015;125(4):606-615. doi:10.1182/blood-2014-08-551994 **12.** 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 **13.** Weiss JM, Chen W, Nyuydzefe MS, et al. ROCK2 signaling is required to induce a subset of T follicular helper cells through opposing effects on STATs in autoimmune settings. *Sci Signal*. 2016;9(437):ra73. doi:10.1126/scisignal.aad8953 **14.** Chen W, Nyuydzefe MS, Weiss JM, Zhang J, Waksal SD, Zanin-Zhorov A. ROCK2, but not ROCK1 interacts with phosphorylated STAT3 and co-occupies TH17/TFH gene promoters in TH17-activated human T cells. *Sci Rep*. 2018;8(1):16636. doi:10.1038/s41598-018-35109-9 **15.** Riches DWH, Backos DS, Redente EF. ROCK and Rho: promising therapeutic targets to ameliorate pulmonary fibrosis. *Am J Pathol*. 2015;185(4):909-912. doi:10.1016/j.ajpath.2015.01.005 **16.** Data on file 1. Kadmon Pharmaceuticals, LLC; 2021. **17.** Data on file 2. Kadmon Pharmaceuticals, LLC; 2021. **18.** Data on file 3. Kadmon Pharmaceuticals, LLC; 2022. **19.** Lee SJ, Cook EF, Soiffer R, Antin JH. Development and validation of a scale to measure symptoms of chronic graft-versus-host disease. *Biol Blood Marrow Transplant*. 2002;8(8):444-452. doi:10.1053/bbmt.2002.v8.pm12234170 **20.** 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

Please see Important Safety Information throughout.
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Important Safety Information

REZUROCK® (belumosudil) tablets

INDICATION

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IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- **Embryo-Fetal Toxicity:** Based on findings in animals and its mechanism of action, REZUROCK can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with REZUROCK and for at least one week after the last dose

Adverse Reactions

- The most common (≥ 20%) adverse reactions, including laboratory abnormalities, were infections, asthenia, nausea, diarrhea, dyspnea, cough, edema, hemorrhage, abdominal pain, musculoskeletal pain, headache, phosphate decreased, gamma glutamyl transferase increased, lymphocytes decreased, and hypertension
- Permanent discontinuation of REZUROCK due to adverse reactions occurred in 18% of patients. The adverse reactions which resulted in permanent discontinuation of REZUROCK in > 3% of patients included nausea (4%). Adverse reactions leading to dose interruption occurred in 29% of patients. The adverse reactions leading to dose interruption in ≥ 2% were infections (11%), diarrhea (4%), and asthenia, dyspnea, hemorrhage, hypotension, liver function test abnormal, nausea, pyrexia, edema, and renal failure with (2% each)
- Monitor total bilirubin, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) at least monthly

Drug Interactions

- **Strong CYP3A Inducers:** Coadministration of REZUROCK with strong CYP3A inducers decreases belumosudil exposure, which may reduce the efficacy of REZUROCK. Increase the dosage of REZUROCK to 200 mg twice daily when coadministered with strong CYP3A inducers

Please see full Prescribing Information.

IMPORTANT SAFETY INFORMATION (cont)

Drug Interactions (cont)

- **Proton Pump Inhibitors:** Coadministration of REZUROCK with proton pump inhibitors decreases belumosudil exposure, which may reduce the efficacy of REZUROCK. Increase the dosage of REZUROCK to 200 mg twice daily when coadministered with proton pump inhibitors

Use in Specific Populations

- **Pregnancy:** Based on findings from animal studies and the mechanism of action, REZUROCK can cause fetal harm when administered to pregnant women. There are no available human data on REZUROCK use in pregnant women to evaluate for a drug-associated risk. Advise pregnant women and females of reproductive potential of the potential risk to the fetus
- **Lactation:** There are no data available on the presence of belumosudil or its metabolites in human milk or the effects on the breastfed child, or milk production. Because of the potential for serious adverse reactions from belumosudil in the breastfed child, advise lactating women not to breastfeed during treatment with REZUROCK and for at least one week after the last dose
- **Pediatric Use:** The safety and effectiveness of REZUROCK have been established in pediatric patients 12 years and older. The safety and effectiveness of REZUROCK in pediatric patients less than 12 years old have not been established
- **Geriatric Use:** Of the 186 patients with chronic GVHD in clinical studies of REZUROCK, 26% were 65 years and older. No clinically meaningful differences in safety or effectiveness of REZUROCK were observed in comparison to younger patients
- **Renal and Hepatic Impairment:** Treatment with REZUROCK has not been studied in patients with pre-existing severe renal or hepatic impairment. For patients with pre-existing severe renal or hepatic impairment, consider the risks and potential benefits before initiating treatment with REZUROCK

You are encouraged to report side effects of prescription drugs to the FDA. Visit **www.FDA.gov/medwatch** or call **1-800-FDA-1088**. You may also contact Kadmon Pharmaceuticals, LLC, at **1-877-377-7862** to report side effects.

Please see full Prescribing Information.

Kadmon ASSIST™

Kadmon ASSIST is committed to helping support patients, and their caregivers, throughout their treatment journey with REZUROCK

Enroll patients into Kadmon ASSIST so our specialists can determine which programs are available to patients.

Services include

INSURANCE

Navigating coverage and providing insurance assistance

ACCESS

Providing a free 30-day supply of REZUROCK to eligible patients who experience delays or gaps in their insurance coverage

CO-PAY SAVINGS

Co-pay savings program[a] for commercially or privately insured patients

EDUCATION

Connecting with nurses regarding disease management and treatment with REZUROCK

For full Terms and Conditions, and to enroll patients in Kadmon ASSIST, please visit KadmonASSIST.com or call 1-844-KADMON1 (523-6661), Monday through Friday, 8 AM–8 PM ET.

[a]Patient Terms and Conditions: The Kadmon ASSIST Commercial Co-pay Savings Program provides co-pay/coinsurance support for out-of-pocket costs on REZUROCK® (belumosudil) tablets prescriptions, up to $25,000 per calendar year, limit one 30-day supply per 30 days. This program is not health insurance. This program is for commercially or privately insured patients only; uninsured or cash-paying patients are not eligible. Patients are not eligible if prescriptions are paid, in whole or in part, by any state- or federally funded programs, including, but not limited to, Medicare (including Part D, even in the coverage gap) or Medicaid, Medigap, VA, DOD, TriCare, private indemnity or HMO insurance plans that reimburse you for the entire cost of your prescription drugs, or where prohibited by law. The co-pay program may not be combined with any other rebate, coupon or offer. Kadmon Pharmaceuticals, LLC, reserves the right to rescind, revoke or amend this offer without further notice. Any savings provided by the co-pay program may vary depending on patients' out-of-pocket costs. Card is valid through December 31 of the year of activation. On January 1 of the following year, the card automatically resets and is subject to annual limits if the prescription benefit remains the same. Upon registration, patients receive all program details.

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Please see full Prescribing Information.

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