WELIREG®
(belzutifan) 40 mg tablets

GETTING YOUR PATIENTS STARTED WITH WELIREG

ONE	TWO	THREE
Consider the recommended dosage and administration 	Send prescription to the pharmacy 	Inform patients about how they will receive WELIREG 

WELIREG is indicated for the treatment of adult patients with von Hippel-Lindau (VHL) disease who require therapy for associated renal cell carcinoma (RCC), central nervous system (CNS) hemangioblastomas, or pancreatic neuroendocrine tumors (pNET), not requiring immediate surgery.

WELIREG is indicated for the treatment of adult patients with advanced renal cell carcinoma (RCC) with a clear cell component following a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and a vascular endothelial growth factor tyrosine kinase inhibitor (VEGF-TKI).

SELECTED SAFETY INFORMATION

WARNING: EMBRYO-FETAL TOXICITY

- **Exposure to WELIREG during pregnancy can cause embryo-fetal harm.**
- **Verify pregnancy status prior to the initiation of WELIREG.**
- **Advise patients of these risks and the need for effective non-hormonal contraception as WELIREG can render some hormonal contraceptives ineffective.**

WELIREG can cause severe anemia that can require blood transfusion. Monitor for anemia before initiation of, and periodically throughout, treatment.

WELIREG can cause severe hypoxia that may require discontinuation, supplemental oxygen, or hospitalization. Monitor oxygen saturation before initiation of, and periodically throughout, treatment.

Before prescribing WELIREG, please read the additional Selected Safety Information on pages 5–6 and the accompanying Prescribing Information, including the Boxed Warning about embryo-fetal toxicity. The Medication Guide also is available.

1 Consider the recommended dosage and administration

For adult patients with previously treated clear cell RCC or certain VHL disease–associated tumors

Start patients on the recommended dose of 120 mg (three 40-mg tablets) once daily

Not actual size.

WELIREG® (belzutifan) should be taken at the same time each day and may be taken with or without food

- **Advise patients to swallow tablets whole. Do not chew, crush, or split WELIREG prior to swallowing.**
- **If a dose of WELIREG is missed, it can be taken as soon as possible on the same day. Resume the regular daily dose schedule for WELIREG the next day. Do not take extra tablets to make up for the missed dose.**
- **If vomiting occurs any time after taking WELIREG, do not retake the dose. Take the next dose on the next day.**

Additional dosing information

For more information regarding dosing, including dosage modifications for WELIREG, visit **welireghcp.com**.

A **Treatment Guide** is also available for your patients on WELIREG. Contact your Merck Representative for more information.

Refill options for WELIREG:

- The number of prescription refills may vary based on your instructions
- Remind your patients that your team is available to assist with any questions or concerns regarding prescription refills
- The pharmacy will fill the prescription as written for dosing and refills. Uninterrupted supply of WELIREG can be ensured by clarifying the number of refills at initiation

Advise your patients to contact you immediately should adverse reactions occur.

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2 Send prescription to the pharmacy

WELIREG® (belzutifan) prescriptions can be filled through EITHER the specialty pharmacy network or certain physician practices with dispensing capabilities and certain hospital pharmacies

Specialty pharmacy network

Biologics Pharmacy
Phone: 800-850-4306
Fax: 800-823-4506
biologics.mckesson.com

Onco360 Oncology Pharmacy
Phone: 877-662-6633
Fax: 877-662-6355
onco360.com

Merck is not affiliated with and does not endorse one specialty pharmacy over another.

When filling a prescription for WELIREG through a specialty pharmacy, the specialty pharmacy may help answer any questions about benefits investigations, prior authorization and appeals, as well as financial assistance options.

OR

Physician practices with dispensing capabilities & hospital pharmacies

Inform your patients about your institution's process for benefits investigations, prior authorization and appeals, as well as financial assistance options.

Merck Access Program

If a physician practice or hospital pharmacy is filling the prescription, the Merck Access Program may be able to answer questions about:

- Benefits investigations
- Potential financial assistance options for eligible patients, including information about co-pay assistance for eligible, privately insured patients
- Prior authorizations and appeals
- Referral to the **Merck Patient Assistance Program** for eligibility determination (provided through the Merck Patient Assistance Program, Inc.)

For resources to help patients get access and support for WELIREG, visit **The Merck Access Program** website.

Did you know?

Your eligible, privately insured patients may save on their out-of-pocket costs for **WELIREG** with the Co-pay Coupon.

Eligible patients may visit **welireg.com** to learn more and view the Terms and Conditions.

Not all patients are eligible. Certain restrictions apply.

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3 Inform patients about how they will receive WELIREG

Receiving WELIREG® (belzutifan) from their pharmacy

Advise patients to be on the lookout for a call from the pharmacy

The pharmacy will coordinate the delivery of WELIREG with patients

- The pharmacy may work closely with your team to obtain the necessary prescriptions and prior authorizations
- They may coordinate with patients on an ongoing basis while patients remain on therapy

Remind patients to save the specialty pharmacy, practice, or hospital pharmacy contact information and to accept all calls from their pharmacy.

Specialty pharmacy, practice, or hospital pharmacy may not ship WELIREG without speaking to patients first.

The pharmacy may call patients in advance to confirm a refill. Advise patients to follow instructions and stay consistent with their WELIREG prescription.

Consider patients' treatment needs when starting WELIREG and over time. To manage patient expectations, remind them of the following:

- It may take time to see results with WELIREG, and everyone responds differently to treatment
- Patients should continue taking WELIREG as prescribed, and not stop treatment on their own
- Patients may experience side effects, so they should pay attention to how they feel and let you know as soon as possible
- Side effects may be managed, depending on severity, by dose reduction, dose interruptions, or discontinuation

Encourage your patients to explore helpful information and resources at welireg.com

- Tips for managing treatment with WELIREG
- Patient-friendly clinical trial results
- Side effects that may occur
- How to make WELIREG part of their routine
- How to take WELIREG
- Co-pay assistance and financial support

Help make WELIREG part of their routine

Encourage patients to set daily reminders on their devices to help them remember to take WELIREG.

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SELECTED SAFETY INFORMATION

WARNING: EMBRYO-FETAL TOXICITY

- **Exposure to WELIREG® (belzutifan) during pregnancy can cause embryo-fetal harm.**
- **Verify pregnancy status prior to the initiation of WELIREG® (belzutifan).**
- **Advise patients of these risks and the need for effective non-hormonal contraception as WELIREG® (belzutifan) can render some hormonal contraceptives ineffective.**

Anemia

- WELIREG can cause severe anemia that can require blood transfusion.
  - Monitor for anemia before initiation of, and periodically throughout, treatment. Transfuse patients as clinically indicated. For patients with hemoglobin <8 g/dL, withhold WELIREG until ≥8 g/dL, then resume at the same or reduced dose or permanently discontinue WELIREG, depending on the severity of anemia. For life-threatening anemia or when urgent intervention is indicated, withhold WELIREG until hemoglobin ≥8 g/dL, then resume at a reduced dose or permanently discontinue WELIREG.
- In LITESPARK-004 (N=61), decreased hemoglobin occurred in 93% of patients with VHL disease and 7% had Grade 3 events. Median time to onset of anemia was 31 days (range: 1 day to 8.4 months).
- The safety of erythropoiesis-stimulating agents (ESAs) for treatment of anemia in patients with VHL disease treated with WELIREG has not been established.
- In LITESPARK-005 (n=372), decreased hemoglobin occurred in 88% of patients with advanced RCC with a clear cell component and 29% had Grade 3 events. Median time to onset of anemia was 29 days (range: 1 day to 16.6 months). Of the patients with anemia, 22% received transfusions only, 20% received erythropoiesis-stimulating agents (ESAs) only, and 12% received both transfusion and ESAs.

Hypoxia

- WELIREG can cause severe hypoxia that may require discontinuation, supplemental oxygen, or hospitalization.
- Monitor oxygen saturation before initiation of, and periodically throughout, treatment. For decreased oxygen saturation with exercise (eg, pulse oximeter <88% or PaO_2 ≤55 mm Hg), consider withholding WELIREG until pulse oximetry with exercise is greater than 88%, then resume at the same or a reduced dose. For decreased oxygen saturation at rest (eg, pulse oximeter <88% or PaO_2 ≤55 mm Hg) or when urgent intervention is indicated, withhold WELIREG until resolved and resume at a reduced dose or discontinue. For life-threatening or recurrent symptomatic hypoxia, permanently discontinue WELIREG. Advise patients to report signs and symptoms of hypoxia immediately to a health care provider.
- In LITESPARK-004, hypoxia occurred in 1.6% of patients.
- In LITESPARK-005, hypoxia occurred in 15% of patients and 10% had Grade 3 events. Of the patients with hypoxia, 69% were treated with oxygen therapy. Median time to onset of hypoxia was 30.5 days (range: 1 day to 21.1 months).

Embryo-Fetal Toxicity

- Based on findings in animals, WELIREG can cause fetal harm when administered to a pregnant woman.
- Advise pregnant women and females of reproductive potential of the potential risk to the fetus. Advise females of reproductive potential to use effective non-hormonal contraception during treatment with WELIREG and for 1 week after the last dose. WELIREG can render some hormonal contraceptives ineffective. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with WELIREG and for 1 week after the last dose.

Adverse Reactions

Adverse Reactions in LITESPARK-004

- Serious adverse reactions occurred in 15% of patients, including anemia, hypoxia, anaphylaxis reaction, retinal detachment, and central retinal vein occlusion (1 patient each).
- WELIREG was permanently discontinued due to adverse reactions in 3.3% of patients for dizziness and opioid overdose (1.6% each).
- Dosage interruptions due to an adverse reaction occurred in 39% of patients. Those which required dosage interruption in >2% of patients were fatigue, decreased hemoglobin, anemia, nausea, abdominal pain, headache, and influenza-like illness.
- Dose reductions due to an adverse reaction occurred in 13% of patients. The most frequently reported adverse reaction which required dose reduction was fatigue (7%).
- The most common adverse reactions (≥25%), including laboratory abnormalities, that occurred in patients who received WELIREG were decreased hemoglobin (93%), fatigue (64%), increased creatinine (64%), headache (39%), dizziness (38%), increased glucose (34%), and nausea (31%).

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SELECTED SAFETY INFORMATION (*continued*)

Adverse Reactions (*continued*)

Adverse Reactions in LITESPARK-005

- Serious adverse reactions occurred in 38% of patients. The most frequently reported serious adverse reactions were hypoxia (7%), anemia (5%), pneumonia (3.5%), hemorrhage (3%), and pleural effusion (2.2%). Fatal adverse reactions occurred in 3.2% of patients who received WELIREG, including sepsis (0.5%) and hemorrhage (0.5%).
- WELIREG was permanently discontinued due to adverse reactions in 6% of patients. Adverse reactions which resulted in permanent discontinuation (≥0.5%) were hypoxia (1.1%), anemia (0.5%), and hemorrhage (0.5%).
- Dosage interruptions due to an adverse reaction occurred in 39% of patients. Of the patients who received WELIREG, 28% were 65 to 74 years, and 10% were 75 years and over. Dose interruptions occurred in 48% of patients ≥65 years of age and in 34% of younger patients. Adverse reactions which required dosage interruption in ≥2% of patients were anemia (8%), hypoxia (5%), COVID-19 (4.3%), fatigue (3.2%), and hemorrhage (2.2%).
- Dose reductions due to an adverse reaction occurred in 13% of patients. Dose reductions occurred in 18% of patients ≥65 years of age and in 10% of younger patients. The most frequently reported adverse reactions which required dose reduction (≥1.0%) were hypoxia (5%) and anemia (3.2%).
- The most common adverse reactions (≥25%), including laboratory abnormalities, were decreased hemoglobin (88%), fatigue (43%), musculoskeletal pain (34%), increased creatinine (34%), decreased lymphocytes (34%), increased alanine aminotransferase (32%), decreased sodium (31%), increased potassium (29%), and increased aspartate aminotransferase (27%).

Drug Interactions

- Coadministration of WELIREG with inhibitors of UGT2B17 or CYP2C19 increases plasma exposure of belzutifan, which may increase the incidence and severity of adverse reactions. Monitor for anemia and hypoxia and reduce the dosage of WELIREG as recommended.
- Coadministration of WELIREG with CYP3A4 substrates decreases concentrations of CYP3A4 substrates, which may reduce the efficacy of these substrates or lead to therapeutic failures. Avoid coadministration with sensitive CYP3A4 substrates. If coadministration cannot be avoided, increase the sensitive CYP3A4 substrate dosage in accordance with its Prescribing Information. Coadministration of WELIREG with hormonal contraceptives may lead to contraceptive failure or an increase in breakthrough bleeding.

Lactation

- Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with WELIREG and for 1 week after the last dose.

Females and Males of Reproductive Potential

- WELIREG can cause fetal harm when administered to a pregnant woman. Verify the pregnancy status of females of reproductive potential prior to initiating treatment with WELIREG.
- Use of WELIREG may reduce the efficacy of hormonal contraceptives. Advise females of reproductive potential to use effective non-hormonal contraception during treatment with WELIREG and for 1 week after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with WELIREG and for 1 week after the last dose.
- Based on findings in animals, WELIREG may impair fertility in males and females of reproductive potential and the reversibility of this effect is unknown.

Renal Impairment

- For patients with severe renal impairment (eGFR 15-29 mL/min estimated by MDRD), monitor for increased adverse reactions and modify the dosage as recommended.

Hepatic Impairment

- For patients with moderate and severe hepatic impairment, monitor for increased adverse reactions and modify the dosage as recommended.

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