Merck Product Launch

Public

Merck would like to inform you that WELIREG™ (belzutifan) 40-mg tablets has received FDA approval. 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.

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.**

Anemia

- WELIREG can cause severe anemia that can require blood transfusion. In Study 004, anemia occurred in 90% of patients and 7% had Grade 3 anemia. In Study 001, a clinical trial in patients with advanced solid tumors (n=58) treated at the recommended dose, anemia occurred in 76% of patients and 28% had Grade 3 anemia.
- Monitor for anemia before initiation of and periodically throughout treatment. Closely monitor patients who are dual UGT2B17 and CYP2C19 poor metabolizers due to potential increases in exposure that may increase the incidence or severity of anemia.
- Transfuse patients as clinically indicated. For patients with hemoglobin (Hb) <9g/dL, withhold WELIREG until Hb ≥9g/dL, then resume at reduced dose or permanently discontinue depending on the severity of anemia. For life threatening anemia or when urgent intervention is indicated, withhold WELIREG until Hb ≥9g/dL, then resume at a reduced dose or permanently discontinue.
- The use of erythropoiesis stimulating agents (ESAs) for treatment of anemia is not recommended in patients treated with WELIREG.

Selected Safety Information continues below.

Read Press Release

See Prescribing Information

SELECTED SAFETY INFORMATION (*continued*)

Hypoxia

- WELIREG can cause severe hypoxia that may require discontinuation, supplemental oxygen, or hospitalization. In Study 004, hypoxia occurred in 1.6% of patients. In Study 001, a clinical trial in patients with advanced solid tumors (n=58) treated at the recommended dose, hypoxia occurred in 29% of patients; 16% were Grade 3 hypoxia.
- Monitor oxygen saturation before initiation of and periodically throughout treatment. For decreased oxygen saturation with exercise (e.g., pulse oximeter <88% or P_aO_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 (e.g., pulse oximeter <88% or P_aO_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.

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

- In Study 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).
- The most common adverse reactions (≥25%) were decreased hemoglobin (93%), anemia (90%), fatigue (64%), increased creatinine (64%), headache (39%), dizziness (38%), increased glucose (34%), and nausea (31%).
- In Study 001, a clinical trial in patients with advanced solid tumors (n=58) treated at the recommended dose, the following additional adverse reactions have been reported: edema, cough, musculoskeletal pain, vomiting, diarrhea, and dehydration.

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, including hormonal contraceptives, decreases concentrations of CYP3A4 substrates, which may reduce the efficacy of these substrates. 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.

Pediatric Use

- Safety and effectiveness of WELIREG in pediatric patients under 18 years of age have not been established.

Before prescribing WELIREG™ (belzutifan), please read the accompanying Prescribing Information, including the Boxed Warning. The Medication Guide also is available.

Sincerely,

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For prescribers: please click here for state-required price disclosures.

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US-BEL-00058 08/21