MEDICATION GUIDE
WELIREG® (Well-ih-reg)
(belzutifan)
tablets

What is the most important information I should know about WELIREG?

WELIREG can cause serious side effects, including:

- **Low red blood cell counts (anemia).** Low red blood cell counts can be severe. You may need a blood transfusion if your red blood cell counts drop too low. Your healthcare provider will do blood tests to check your red blood cell counts before you start and during treatment with WELIREG. Tell your healthcare provider if you get any symptoms of low red blood cell counts, including tiredness, feeling cold, shortness of breath, chest pain, or fast heartbeat.
- **Low oxygen levels in your body.** WELIREG can cause low oxygen levels in your body that can be severe and may require you to stop treatment with WELIREG, receive oxygen therapy, or be hospitalized. Your healthcare provider will monitor your oxygen levels before you start and during treatment with WELIREG. Tell your healthcare provider or get medical help right away if you get symptoms of low oxygen in your body, including shortness of breath or fast heartbeat.
- **Heart problems when WELIREG is taken together with lenvatinib.** Serious heart problems, including heart failure, can happen when WELIREG is taken in combination with lenvatinib. Your healthcare provider will check your heart function before and during treatment with WELIREG. Tell your healthcare provider right away if you get symptoms of heart problems, including shortness of breath, swelling of your ankles, unusual weight gain, chest pain, or feeling faint.
- **Harm to your unborn baby.** Treatment with WELIREG during pregnancy can cause harm to your unborn baby.
  Females who are able to become pregnant:
  - Your healthcare provider will do a pregnancy test before you start treatment with WELIREG.
  - Use an effective form of non-hormonal birth control (contraception) during treatment with WELIREG and **for 1 week** after your last dose.
  - If you are taking WELIREG in combination with another medicine, your healthcare provider will tell you how long you should use birth control (contraception).
  - Birth control methods that contain hormones (such as birth control pills, injections, or transdermal system patches) may not work as well during treatment with WELIREG.
  - Talk to your healthcare provider about birth control methods that may be right for you during treatment with WELIREG.
  - Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with WELIREG.

  Males with female partners who are able to become pregnant:
  - Use effective birth control (contraception) during treatment with WELIREG and **for 1 week** after your last dose.
  - Tell your healthcare provider right away if your partner becomes pregnant or thinks she is pregnant during your treatment with WELIREG.

See **"What are the possible side effects of WELIREG?"** for more information about side effects.

What is WELIREG?

WELIREG is a prescription medicine used to treat:

- von Hippel-Lindau (VHL) disease in adults who need treatment for a type of kidney cancer called renal cell carcinoma (RCC), tumors in the brain and spinal cord called central nervous system (CNS) hemangioblastomas, or a type of pancreatic tumor called pancreatic neuroendocrine tumors (pNET), that do not require surgery right away.
- RCC with a clear cell component (ccRCC).
  - WELIREG can be used in adults with the medicine pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph, who are at intermediate-high or high risk of kidney cancer coming back after surgery to:
    - remove all or part of the kidney, **or**
    - remove all or part of the kidney and also surgery to remove cancer that has spread to other parts of the body (metastatic lesions).
  - WELIREG can be used with the medicine lenvatinib following treatment with a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) anti-cancer medicine in adults whose kidney cancer has spread (advanced ccRCC).
  - WELIREG can be used alone following treatment with a PD-1 or PD-L1 inhibitor and a vascular endothelial growth factor tyrosine kinase inhibitor (VEGF-TKI) anti-cancer medicines in adults whose kidney cancer has spread (advanced ccRCC).
- a type of tumor that starts in nerve and hormone making cells (neuroendocrine tumors) called pheochromocytoma or paraganglioma (PPGL) in adults and children 12 years of age and older that have spread to areas near the adrenal glands (locally advanced), or cannot be removed by surgery (unresectable), or that has spread to other parts of the body (metastatic).

It is not known if WELIREG is safe and effective in children with VHL or ccRCC, or in children younger than 12 years of age with PPGL.

Before taking WELIREG, tell your healthcare provider about all of your medical conditions, including if you:

- have low red blood cell counts (anemia)
- have heart problems (if you will take WELIREG in combination with lenvatinib)
- are pregnant or plan to become pregnant. See **"What is the most important information I should know about WELIREG?"**
- are breastfeeding or plan to breastfeed. It is not known if WELIREG passes into your breast milk. **Do not** breastfeed during treatment with WELIREG and for 1 week after your last dose. If you are taking WELIREG in combination with another medicine, your healthcare provider will tell you how long you should not breastfeed.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking WELIREG with certain other medicines may affect how WELIREG or those medicines work and may increase the risk of side effects.

Know the medicines you take. Keep a list of them to show to your healthcare provider and pharmacist when you get a new medicine.

How should I take WELIREG?

- Take WELIREG exactly as your healthcare provider tells you.
- **Do not** stop taking WELIREG or change your dose without talking to your healthcare provider.
- Take your prescribed dose of WELIREG 1 time a day, at the same time each day.
- Take WELIREG with or without food.
- Swallow WELIREG tablets whole. **Do not** chew, crush, or split WELIREG tablets.
- If you miss a dose of WELIREG, take it as soon as possible on the same day. Then take your next dose of WELIREG at your regular time the next day. **Do not** take extra tablets to make up for the missed dose.
- If you vomit after taking a dose of WELIREG, **do not** take an extra dose. Take your next dose at your regular time the next day.
- If you take too much WELIREG, call your healthcare provider or go to the nearest emergency room right away.

What are the possible side effects of WELIREG?

WELIREG can cause serious side effects, including:

- See **"What is the most important information I should know about WELIREG?"**

The most common side effects of WELIREG in adults with VHL disease include:

- low red blood cell counts
- tiredness
- increased blood creatinine (kidney function test)
- headache
- dizziness
- increased blood sugar (glucose) levels
- nausea

The most common side effects of WELIREG when taken with pembrolizumab in adults with ccRCC include:

- low red blood cell counts
- increased blood liver enzymes (liver function tests)
- tiredness
- decreased white blood cell counts

The most common side effects of WELIREG when taken with lenvatinib in adults with advanced ccRCC include:

- low red blood cell counts
- tiredness
- increased blood liver enzymes (liver function tests)
- high blood pressure
- muscle and joint pain
- diarrhea
- decreased white blood cell counts
- decreased blood salts (sodium) levels
- increased creatinine (kidney function test)
- nausea
- decreased levels of thyroid hormone
- decreased appetite
- decreased platelet counts
- increased blood potassium levels
- increased blood levels of lipase (a digestive enzyme made by the pancreas)
- protein in your urine
- decreased blood magnesium levels
- decreased blood calcium levels
- increased blood clotting time
- rash
- vomiting
- weight loss
- constipation
- stomach-area (abdomen) pain
- mouth sores

The most common side effects of WELIREG when taken alone in adults with advanced ccRCC include:

- low red blood cell counts
- tiredness
- muscle and joint pain
- increased blood creatinine (kidney function test)
- decreased white blood cell counts
- increased blood liver enzymes (liver function tests)
- decreased blood salts (sodium) levels
- increased blood potassium levels

The most common side effects of WELIREG in adults and children 12 years of age and older with PPGL include:

- low red blood cell counts
- tiredness
- muscle and joint pain
- decreased white blood cell counts
- increased blood liver enzymes (liver function tests)
- increased blood calcium levels
- shortness of breath
- increased blood potassium levels
- headache
- dizziness
- nausea

Your healthcare provider may change your dose, temporarily stop, or permanently stop treatment with WELIREG if you get certain side effects.

WELIREG may cause fertility problems in males and females, which may affect your ability to have children. Talk to your healthcare provider if this is a concern for you.

These are not all of the possible side effects of WELIREG.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store WELIREG?

- Store WELIREG at room temperature between 68°F to 77°F (20°C to 25°C).
- The WELIREG bottle has a child-resistant closure.
- The WELIREG bottle contains 2 desiccant canisters that help keep your medicine dry. **Do not** eat the desiccant canisters.

Keep WELIREG and all medicines out of the reach of children.

General information about the safe and effective use of WELIREG.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use WELIREG for a condition for which it was not prescribed. Do not give WELIREG to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about WELIREG that is written for health professionals.

What are the ingredients in WELIREG?

Active ingredient: belzutifan

Inactive ingredients: croscarmellose sodium, hypromellose acetate succinate, magnesium stearate, mannitol, microcrystalline cellulose, and silicon dioxide. The film-coating contains FD&C Blue #2 aluminum lake, polyethylene glycol, polyvinyl alcohol, talc, and titanium dioxide.

Manufactured for: Merck Sharp & Dohme LLC
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