PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS REGULATIONS (PREPARATIONS) 1986

This medicine is marketed upon physician's prescription only

WELIREG® 40MG FILM-COATED TABLETS

Film-Coated Tablets

Each film-coated tablet contains:
belzutifan 40 mg
For the list of the inactive ingredients and allergens see section 6 'FURTHER INFORMATION'. See also section 2.10 'Important information about some of the ingredients of the medicine'.

Read the entire leaflet carefully before using the medicine.

- This leaflet contains concise information about the medicine. If you have any further questions, refer to the doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.

In addition to the leaflet, WELIREG has a Patient Alert Card.
This card includes important safety information, that you need to know before starting and during the treatment with WELIREG and act accordingly. Read the Patient Alert Card and the patient leaflet before you start using this medicine. Keep the Patient Alert Card for further reference if needed.

1. WHAT WELIREG IS INTENDED FOR?

WELIREG is a medicine used to treat adults with von Hippel-Lindau (VHL) disease who need treatment for a type of kidney cancer called renal cell carcinoma (RCC), tumours in the brain and spinal cord called central nervous system hemangioblastomas, or a type of pancreatic cancer called pancreatic neuroendocrine tumours, and for whom surgery or other local procedures are unsuitable or undesirable.

Therapeutic group: antineoplastic agents

WELIREG is a hypoxia-inducible factor 2 alpha (HIF-2α) inhibitor which may slow or stop the growth of tumours in patients with VHL disease.

2. BEFORE USING WELIREG

2.1 Do not use WELIREG if:

you are sensitive (allergic) to belzutifan or any of the other ingredients that this medicine contains. For a list of inactive ingredients, see section 6 'FURTHER INFORMATION'.

2.2 Special warnings regarding use of WELIREG

Before starting treatment with WELIREG, tell your doctor if:

- You have breathing problems
- You have heart problems
- You have low levels of red blood cells (anaemia)
- You are pregnant or plan to be pregnant (see section 2.8 'Pregnancy, breastfeeding and fertility')

- WELIREG may affect fertility, which may affect your ability to have children. Talk to your doctor if this is a concern for you.

If any of the above apply to you (or you are not sure) talk to your doctor before taking this medicine.

Additional warnings:
WELIREG may decrease your red blood cell level. Common symptoms include shortness of breath, fatigue, dizziness, and pale skin.

WELIREG may also decrease the oxygen level in your blood. Common symptoms include shortness of breath, increased heart rate, rapid breathing, and feeling anxious or restless. Although symptoms vary from person to person, low oxygen levels in your body that can be serious may require you to stop treatment with WELIREG, receive oxygen therapy or be hospitalised. Contact your doctor immediately if you develop any of the following symptoms: bluish discoloration of the skin around your mouth, inability to speak in full sentences without catching your breath, unusual tiredness, and confusion. In light of this risk, you should stop smoking while taking WELIREG.

2.3 Smoking
You should stop smoking while taking WELIREG.

2.4 Children and adolescents
Do not give WELIREG to children and adolescents below the age of 18 years.
There is no information regarding the use in this age group. The efficacy and safety of the medicine in this age group was not tested.

2.5 Tests and follow-up
Your doctor will regularly measure your oxygen level and do blood tests to check your red blood cell level during your treatment with WELIREG.

2.6 Interactions with other medicines
If you are taking, or have recently taken, other medicines including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. This is because WELIREG can affect the way some other medicines work. Also, some other medicines can affect the way WELIREG works.
Some medicines may increase the risk of side effects with WELIREG, for example:

- imatinib (used to treat cancer)
- fluconazole (used to treat fungal infections)
- fluoxetine, fluvoxamine (used to treat depressive disorders)

WELIREG may affect the way other medicines work, for example:

- hormonal contraceptives such as desogestrel, ethinylestradiol and levonorgestrel
- alfentanil (used as a supplement before or during anesthesia)
- lurasidone (used to treat schizophrenia or bipolar depression)
- sirolimus, tacrolimus (used as prophylaxis of organ rejection in transplants)

Your doctor will decide if the dose needs to be changed.

2.7 Using WELIREG with food
You can take WELIREG with or without food.

2.8 Pregnancy, breastfeeding and fertility
Pregnancy

If you are pregnant, think you may be pregnant, or are planning to have a baby, ask your doctor or pharmacist before taking this medicine.

For women of fertility age who may become pregnant, your doctor will carry out a pregnancy test before you start taking the medicine.

WELIREG may harm your unborn baby and cause a miscarriage. This means:

- You should not become pregnant while taking WELIREG
- You should not take WELIREG if you are pregnant.

Contraception in women and men

Women

If you are a woman who could get pregnant:

- 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. You should use an effective form of non-hormonal birth control (contraception) or have your male partner use a condom during treatment with WELIREG and for 1 week after your last dose.

Talk to your doctor or pharmacists about birth control methods that may be right for you during this time.
If you become pregnant while using WELIREG, talk to your doctor straight away.

Men

WELIREG may be passed on to an unborn baby and harm it. If you are a man whose female partner could get pregnant:

- You and your partner should use effective contraception while taking WELIREG.
- Also do this for at least 1 week after your last dose of WELIREG.

If your partner becomes pregnant while you are using WELIREG, talk to your doctor straight away.
If you are a man whose female partner is pregnant:
Use a barrier method of contraception during treatment with WELIREG and 1 week after last dose.

Breastfeeding

Do not breastfeed during treatment with WELIREG. It is not known if WELIREG passes into your breast milk; it may harm your baby.

You should not breastfeed for at least one week after your last dose of WELIREG.

Fertility

WELIREG may impair fertility. If you are planning to have a baby with your partner - talk to your doctor about family planning before taking WELIREG.

2.9 Driving and using machines

You may feel dizzy or tired after taking WELIREG. If this happens, do not drive or use tools or machines until you no longer feel dizzy or tired.

2.10 Important information about some of the ingredients of the medicine

WELIREG contains less than 1 mmol sodium (23 mg) per film-coated tablet, that is to say essentially ‘sodium-free’.

3. HOW SHOULD YOU USE WELIREG?

Always use WELIREG according to the doctor's instructions.

You should check with the doctor or pharmacist if you are not sure regarding the dosage and treatment regimen.
The dosage and treatment regimen will be determined by the doctor only.
Usually, the acceptable dosage of WELIREG is 120 mg (three 40 mg tablets):

- Take your prescribed dose once a day, at the same time each day.
- Your doctor may change your dose if needed.

Do not exceed the recommended dose.

Method of administration

Swallow the tablet whole.

No information is available regarding crushing/splitting/chewing of the tablets.

You can take WELIREG with or without food.

If you have accidentally taken a higher dose than you should
If you have taken an overdose, or if a child has accidentally swallowed the medicine, proceed immediately to a doctor or to a hospital emergency room and bring the package of the medicine with you. Medical treatment may be necessary.

If you have forgotten to take WELIREG
If you forgot to take WELIREG at the specific time, take the missed dose as soon as possible on the same day. Take your regular dose of WELIREG the next day.

- If you vomit after taking WELIREG, do not take another WELIREG tablet. Take your regular dose of WELIREG the next day.
- Do not take a double dose to make up for forgotten or vomited dose.

Adhere to the treatment regimen as recommended by the doctor.
Even if there is an improvement in your health, do not discontinue use of WELIREG without consulting your doctor.

If you are not sure how to take WELIREG, call your doctor or pharmacist.

Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take a medicine. Wear glasses if you need them.

If you have further questions regarding the use of the medicine, consult with a doctor or a pharmacist.

4. SIDE EFFECTS
As with any medicine, WELIREG may cause side effects, in some users.
Do not be alarmed by reading the list of side effects, you may not suffer from any of them.

Very common side effects - appear in more than 1 in 10 people
- low red blood cells (anaemia)
- feeling tired
- feeling dizzy
- have difficulty breathing
- feeling sick (nausea)

- weight gain

Common side effects - appear in 1-10 people in 100
- abnormally low oxygen levels in the blood

If a side effect appears, if any of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by using the link 'Adverse Drug Reactions Report' at the home page of the Ministry of Health's web site (www.health.gov.il) which refers to the online side effects reporting form, or by using the link:
https://sideeffects.health.gov.il/

5. HOW TO STORE WELIREG?

- Avoid Poisoning! This medicine and any other medicine must be stored in a safe place out of the reach and sight of children and/or infants, in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the pack. The expiry date refers to the last day of the indicated month.
- **Storage conditions**:
  No special storage requirements, it is recommended to keep at room temperature.
  Do not use this medicine if the packaging is damaged or shows signs of tampering.
- Medicines should not be disposed of via wastewater or household waste. Ask the pharmacist how to dispose of medicines you no longer use. These measures will help to protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredient WELIREG also contains:
cellulose microcrystalline, mannitol, hypromellose acetate succinate, croscarmellose sodium, magnesium stearate and colloidal anhydrous silica.
The film-coat contains polyvinyl alcohol (part hydrolyzed), titanium dioxide, macrogol (macrogol 3350), talc and indigo carmine aluminum lake.

What WELIREG looks like and contents of the pack:
WELIREG is a blue, oval shaped, film-coated tablet, debossed with '177' on one side and plain on the other side.

Pack sizes: WELIREG is available in plastic (HDPE) bottles with a child-resistant closure, with 90 film-coated tablets.
The bottle also contains two desiccants.

Marketing authorization holder and importer:
Merck Sharp & Dohme (Israel-1996) Company Ltd., 34 Ha'charash St., Hod-Hasharon.

Approved in March 2024.

Drug registration no. listed in the official Registry of the Ministry of Health:
173-89-37469