Belzutifan

Indication
Adult patients with von Hippel-Lindau (VHL) disease who require therapy for VHL associated renal cell carcinoma (RCC) and for whom localised procedures are unsuitable or undesirable.

Regimen details
Belzutifan 120 mg (three 40 mg tablets) once daily

Cycle frequency
Every 28 days

Number of cycles
Until progression or unacceptable toxicity

Administration
Orally. Swallowed whole, with or without food

Pre-medication
Nil

Emetogenicity
Low

Additional supportive medication
Metochlopramide 10mg tds if required

Extravasation
N/a

Investigations – pre first cycle
Standard pre-SACT tests plus:
Pulse oximetry (oxygen saturation)
Erythropoietin
Iron studies, vitamin B12, folate

Investigations –pre subsequent cycles
FBC, U+E (including creatinine), LFT (including AST)
Pulse oximetry
Erythropoietin - Repeat as clinically appropriate if there is new onset anaemia or worsening of pre-existing anaemia
Iron studies, vitamin B12, folate - Repeat as clinically appropriate if there is new onset anaemia or worsening of pre-existing anaemia

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	Limit
Neutrophil count	≥ 1.0 x 10^9/L
Platelet count	≥ 100 x 10^9/L
Haemoglobin	≥ 8 g/dL
Creatinine clearance	≥ 30 mL/min
Bilirubin	≤ 1.5 x ULN
AST	< 1.5 x ULN
Oxygen saturation	See below

Dose modifications

Haematological Toxicities

Haemoglobin g/dL < 8 Withhold until resolved to ≤ Grade 2 (Hb ≥8 g/dL). Check erythropoietin levels, iron studies and consider blood transfusion. Resume at a reduced dose (reduce by 40 mg) or discontinue depending on the severity and persistence of anaemia.

Renal Impairment

GFR < 30 ml/min No information available

Hepatic Impairment

Not studied in patients with moderate to severe hepatic impairment.

Other Toxicities

Oxygen saturation
Grade 2: Decreased oxygen saturation with exercise (e.g., pulse oximeter <=55 mm Hg) Withhold until resolved to ≤ Grade 2. Look for other reversible causes of hypoxia. Consider supplemental oxygen. Resume at reduced dose (reduce by 40 mg) or discontinue depending on the severity and persistence of hypoxia.
Grade 4: Life-threatening Permanently discontinue.

Dose levels of belzutifan:

Starting dose 120 mg once daily
First dose reduction 80 mg once daily
Second dose reduction 40 mg once daily

Adverse effects - for full details consult product literature/ reference texts

For a detailed list of adverse effects see current Summary of Product Characteristics at Home - electronic medicines compendium

- **Serious side effects**

Hypoxia

- **Frequently occurring side effects**

Very common: Anaemia, Dizziness, Dyspnoea, Nausea and Fatigue

- **Other side effects**

Significant drug interactions – for full details consult product literature/ reference texts

In vitro and pharmacogenomic studies indicate that belzutifan is metabolised by UGT2B17 and by CYP2C19. Co-administration of belzutifan with hormonal contraceptives may lead to contraceptive failure or an increase in breakthrough bleeding. Co-administration of belzutifan with inhibitors of UGT2B17 or CYP2C19 increases plasma exposures of belzutifan, which may increase the incidence and severity of adverse reactions of belzutifan. Monitor for anaemia and hypoxia and reduce the dosage of belzutifan as recommended.

Additional comments

Pregnancy Testing

The pregnancy status of females of reproductive potential should be verified prior to initiating treatment with belzutifan.

Contraception

Belzutifan may cause embryo-foetal harm, including foetal loss, when administered to a pregnant woman.

Females

Females of reproductive potential should be advised to use highly effective contraception during treatment with belzutifan and for at least 1 week after the last dose. Use of belzutifan may reduce the efficacy of hormonal contraceptives. Patients using hormonal contraceptives should be advised to use an alternative non-hormonal contraceptive method or have their male partner use a condom during treatment with belzutifan

Males

Male patients and their female partner of reproductive potential should be advised to use highly effective contraception during male patient treatment with belzutifan and for at least 1 week after the last dose. Advise male patients with female partners who are pregnant to use barrier method of contraception during treatment with belzutifan and 1 week after the last dose.

References

Welireg SPC: https://www.medicines.org.uk/emc/product/14126/smpc

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THIS PROTOCOL HAS BEEN DIRECTED BY DR CHARNLEY, CONSULTANT ONCOLOGIST

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

Date: January 2025
Review: January2027
VERSION: 1
