# BC Cancer Protocol Summary of Belzutifan Therapy for von Hippel Lindau Disease-Associated Renal Cell Carcinoma, Hemangioblastomas and Pancreatic Neuroendocrine Tumours

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| ***Protocol Code*** | *UGUVHLBEL* |
| ***Tumour Group*** | *Genitourinary* |
| ***Contact Physician*** | *Dr Maryam Soleimani* |

## ELIGIBILITY:

Patients must have:

- One of the following conditions associated with von Hippel Lindau (vHL) disease and not requiring immediate surgery:
  - Non-metastatic renal cell carcinoma,
  - Central nervous system hemangioblastomas, or
  - Nonmetastatic pancreatic neuroendocrine tumours, and
- A BC Cancer "Compassionate Access Program" request approval prior to treatment
- Note: patients must have access to a home pulse oximeter for home monitoring of oxygen saturations
- **Treatment should be initiated by specialists with expertise in the management of vHL disease in collaboration with the BC Cancer vHL Clinic**

## EXCLUSIONS:

- Pheochromocytoma

## TESTS:

- Baseline: CBC & Diff, creatinine, total bilirubin, ALT, alkaline phosphatase, random glucose, iron studies, pulse oximetry
  - Person of child-bearing potential:
    - Confirm negative pregnancy test results via a quantitative beta-hCG blood test obtained 7 days prior to initial prescription
- Before each physician visit: CBC & Diff, creatinine, total bilirubin, ALT, alkaline phosphatase, random glucose, pulse oximetry
- Patients must be instructed to check oxygen saturation at home daily for the first two weeks of treatment, then as directed by provider
- If clinically indicated: serum beta-hCG test

## PREMEDICATIONS:

- Prophylactic antiemetic not typically required, but at provider discretion, may use antiemetic protocol for therapy with low emetogenicity (see SCNAUSEA)

**TREATMENT:**

| Drug | Dose | BC Cancer Administration Guideline |
|---|---|---|
| belzutifan | 120 mg once daily | PO once daily |

- One cycle consists of 4 weeks (30 days)
- Treat until clinical disease progression or unacceptable toxicity

**DOSE MODIFICATIONS:**

**Dose Levels:**

| Starting Dose | Dose level -1 | Dose level -2 | Dose level -3 |
|---|---|---|---|
| 120 mg | 80 mg | 40 mg | Discontinue |

**1. Anemia:**

* Ensure any concurrent iron deficiency anemia is addressed for all patients

| Hemoglobin (g/L) | Dose |
|---|---|
| Greater than or equal to 80 | 100 % |
| Less than 80 | ▪ Hold until hemoglobin 80 g/L<br>▪ Transfuse as required.<br>▪ Restart at next lower dose level or discontinue depending on severity and persistence of anemia |
| Life-threatening consequences; urgent intervention indicated | • Permanently discontinue |

2. **Hypoxia:**

| Hypoxia | Management |
|---|---|
| Decreased oxygen saturation with exertion (e.g., pulse oximeter less than 88%) | • Consider holding until resolved<br>• If held, consider restarting at next lower dose level depending on severity and persistence of hypoxia |
| Decreased oxygen saturation at rest (e.g., pulse oximeter less than 88%) | • Hold until resolved<br>• Restart at next lower dose level or discontinue depending on the severity and persistence of hypoxia |
| Life-threatening hypoxia; urgent intervention indicated | • Permanently discontinue |

3. **Renal impairment:** No dose modification for mild and moderate renal impairment. Belzutifan has not been studied in severe renal impairment (Creatinine Clearance less than 30 mL/min).

4. **Hepatic impairment:** No dose modification for mild hepatic impairment. Belzutifan has not been studied in moderate or severe hepatic impairment (total bilirubin greater than 1.5 x ULN and any ALT or AST).

**PRECAUTIONS:**

1. **Anemia:** Belzutifan can cause severe anemia that may require transfusion support. Patients who are dual UGT2B17 and CYP2C19 poor metabolizers may experience increase incidence or severity of anemia. Erythropoiesis stimulating agents are not recommended for the treatment of anemia secondary to belzutifan.
2. **Hypoxia**: Belzutifan has been associated with severe hypoxia requiring discontinuation, supplemental oxygen, or hospitalization. Asymptomatic hypoxia has been reported. Patients should be advised to check oxygen saturation daily for the first two weeks of treatment, then as directed by provider. Advise patients to report signs and symptoms of hypoxia and monitor oxygen saturation periodically throughout treatment.
3. **Drug Interactions:** Drug interactions may occur during treatment with belzutifan, including failure of hormonal contraceptives. See Cancer Drug Manual.
4. **Embryo-fetal toxicity**: Belzutifan can cause fetal harm. Advise patients to use effective non-hormonal contraception during treatment and for 1 week after the last dose. Some hormonal contraceptives are ineffective when used with belzutifan. If pregnancy is suspected, hold belzutifan and order a quantitative beta-hCG blood test. Do not restart belzutifan until negative pregnancy test is confirmed.

**Call Dr. Maryam Soleimani or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.**

## References


1. Jonasch E, Donskov F, Iliopoulos O, et al. Belzutifan for renal cell carcinoma in von Hippel-Lindau disease. N Engl J Med 2021;385:2036-46.
2. Belzutifan (Welireg) CADTH [Canada's Drug Agency (CDA-AMC)] Reimbursement Recommendation. Canadian Journal of Health Technologies Sep 2023; 3(9): 1-24.