



**Commercial/Healthcare Exchange PA Criteria**  
**Effective: December 9<sup>th</sup> 2021**

**Prior Authorization:** Welireg™

**Products Affected:** Welireg™ (belzutifan) tablets, for oral use

**Medication Description:**

Belzutifan is an inhibitor of hypoxia-inducible factor 2 alpha (HIF-2-alpha). HIF-2-alpha is a transcription factor that plays a role in oxygen sensing by regulating genes that promote adaptation to hypoxia. Under normal oxygen levels, HIF-2-alpha is targeted for ubiquitin-proteasomal degradation by VHL protein. Lack of functional VHL protein results in stabilization and accumulation of HIF-2-alpha. Upon stabilization, HIF-2-alpha translocates into the nucleus and interacts with hypoxia-inducible factor 1 beta (HIF-1-beta) to form a transcriptional complex that induces expression of downstream genes, including genes associated with cellular proliferation, angiogenesis, and tumor growth. Belzutifan binds to HIF-2-alpha, and in conditions of hypoxia or impairment of VHL protein function, belzutifan blocks the HIF-2-alpha-HIF-1-beta interaction, leading to reduced transcription and expression of HIF-2-alpha target genes.

**Covered Uses:** Von Hippel-Lindau disease, associated renal cell carcinoma, central nervous system hemangioblastomas, or pancreatic neuroendocrine tumors, not requiring immediate surgery

**Exclusion Criteria:** None

**Required Medical Information:**

1. Diagnosis
2. Medical history

**Age Restrictions:** 18 years of age and older

**Prescriber Restrictions:** Prescribed by, or in consultation with, an oncologist

**Coverage Duration:** 12 months

**Other Criteria:**

**I. Initial Approval Criteria**

**1. Von Hippel-Lindau Disease:** Approve if Patient meets all of the following criteria:

- A. 18 years of age and older; **AND**
- B. Patient has a von Hippel-Lindau (VHL) germline alteration as detected by genetic testing; **AND**
- C. Patient does not require immediate surgery; **AND**

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- D. Prescribed by, or in consultation with, an oncologist; **AND**
- E. Patient requires therapy for ONE of the following conditions (i, ii, iii, or iv):
  - i. Central nervous system hemangioblastomas; **OR**
  - ii. Pancreatic neuroendocrine tumors; **OR**
  - iii. Renal cell carcinoma; **OR**
  - iv. Retinal hemangioblastoma

## II. Continued Therapy

### 1. Von Hippel-Lindau Disease:

- A. Member has responded positively to the treatment as determined by the prescribing physician; **AND**
- B. Member has not experienced unacceptable toxicity from the drug.

### References:

1. Welireg™ tablets [package insert]. Whitehouse Station, NJ, Merck & Co., Inc. Updated August 2021. Accessed Sep 17, 2021.
2. Welireg™ tablets. IBM Micromedex® [database online]. Greenwood Village, CO. Truven Health Analytics. Available at: <https://www.micromedexsolutions.com>. Updated Sep 10, 2021. Accessed Sep 17, 2021.

### Policy Revision history

Rev #	Type of Change	Summary of Change	Sections Affected	Date
1	New Policy	New Policy	All	12/9/2021