VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Welireg Prior Authorization Policy
- Welireg® (belzutifan tablets – Merck)

REVIEW DATE: 05/07/2025; selected revision 05/21/2025

OVERVIEW

Welireg, a hypoxia-inducible factor inhibitor, is indicated for the treatment of:

- **Pheochromocytoma or paraganglioma**, locally advanced, unresectable, or metastatic disease in patients ≥ 12 years of age.
- **Renal cell carcinoma**, **advanced** with a clear cell component following a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and a vascular endothelial growth factor tyrosine kinase inhibitor (VEGF-TKI) in adults.
- **von Hippel-Lindau (VHL) disease,** in adults who require therapy for associated renal cell carcinoma, central nervous system (CNS) hemangioblastomas, or pancreatic neuroendocrine tumors, not requiring immediate surgery.[1]

The pivotal trial for VHL disease included patients with VHL disease-associated renal cell carcinoma, CNS hemangioblastomas, pancreatic neuroendocrine tumor, and retinal hemangioblastoma.[2]

Guidelines

Welireg is discussed in guidelines from the National Comprehensive Cancer Network (NCCN):

- **CNS Cancers:** NCCN guidelines (version 5.2024 – March 18, 2025) recommend Welireg for VHL-associated CNS hemangioblastoma not requiring immediate surgery or those for whom surgery is contraindicated due to location or prior surgery or comorbidities, growing or symptomatic as "useful in certain circumstances" (category 2A).[3] Welireg is used as a single-agent treatment for brain metastases in VHL-associated renal cell carcinoma (category 2B).
- **Kidney Cancer:** NCCN guidelines (version 3.2025 – January 9, 2025) recommend Welireg as a "preferred" regimen for VHL-associated renal cell carcinoma (category 2A). Welireg is also recommended as a single-agent therapy for relapse or stage IV disease as subsequent therapy for clear cell histology if prior history includes immuno-oncology therapy (PD-1 or PD-L1 inhibitor and a VEGF-TKI) as "other recommended regimens" (category 2A) and as immuno-oncology therapy naive as "useful in certain circumstances" (category 2B).[4]
- **Neuroendocrine and Adrenal Tumors:** NCCN guidelines (version 1.2025 – March 27, 2025) list VHL disease as a hereditary endocrine neoplasia. Welireg is recommended in a variety of settings for pancreatic neuroendocrine tumors with germline VHL alteration (category 2A).[5] Welireg is not addressed in the guidelines for the treatment of pheochromocytoma or paraganglioma.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Welireg. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Welireg is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Pheochromocytoma or Paraganglioma**. Approve for 1 year if the patient meets BOTH of the following (A and B):
   - **A)** Patient is ≥ 12 years of age; AND
   - **B)** Patient has locally advanced, unresectable, or metastatic disease.

2. **Renal Cell Carcinoma**. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has advanced disease; AND
   - **C)** The cancer has a clear cell histology; AND
   - **D)** Patient has tried at least one programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor; AND
     Note: Examples of PD-1 inhibitor or PD-L1 inhibitor include: Keytruda (pembrolizumab intravenous infusion), Opdivo (nivolumab intravenous infusion), and Bavencio (avelumab intravenous infusion).
   - **E)** Patient has tried at least one vascular endothelial growth factor tyrosine kinase inhibitor (VEGF-TKI).
     Note: Examples of VEGF-TKI include Cabometyx (cabozantinib tablets), Lenvima (lenvatinib capsules), Inlyta (axitinib tablets), Fotivda (tivozanib capsules), pazopanib, sunitinib, and sorafenib.

3. **Von Hippel-Lindau Disease.** Approve for 1 year if the patient meets ALL of the following (A, B, C and D):
   - **A)** Patient is ≥ 18 years of age; 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
   - **D)** 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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Welireg is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Welireg® tablets [prescribing information]. Whitehouse Station, NJ: Merck; May 2025.
2. Jonasch E, Donskov F, Iliopoulos O, et al. Belzutifan for renal cell carcinoma in von Hippel-Lindau disease. *N Eng J Med*. 2021; 385(22):2036-2046.
3. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 5.2024 – March 18, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 1, 2025.

4. The NCCN Kidney Cancer Clinical Practice Guidelines in Oncology (version 3.2025 – January 9, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 1, 2025.
5. The NCCN Neuroendocrine and Adrenal Tumors Clinical Practice Guidelines in Oncology (version 1.2025 – March 27, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 1, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	09/13/2023
Selected Revision	**Renal Cell Carcinoma**: Indication and criteria were added to the FDA-Approved Indications section due to new indication in advanced renal cell carcinoma following a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and a vascular endothelial growth factor tyrosine kinase inhibitor (VEGF-TKI) in adults.	12/20/2023
Annual Revision	No criteria changes.	06/19/2024
Annual Revision	**Renal Cell Carcinoma**: The requirement that the cancer has a clear cell histology was added.	05/07/2025
Selected Revision	**Pheochromocytoma or Paraganglioma:** Condition of approval and criteria was added to FDA approved indications section.	05/21/2025