UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2025 P 1370-6
Program	Prior Authorization/Notification
Medication	Welireg™ (belzutifan)
P&T Approval Date	10/2021, 10/2022, 10/2023, 2/2024, 7/2024, 7/2025
Effective Date	10/1/2025

1. Background:

Welireg™ (belzutifan) is a hypoxia-inducible factor inhibitor indicated for treatment of adult patients with von Hippel-Lindau (VHL) disease who require therapy for associated renal cell carcinoma (RCC), central nervous system (CNS) hemangioblastomas, or pancreatic neuroendocrine tumors (pNET), not requiring immediate surgery. Welireg is also indicated for the treatment of adult patients with advanced renal cell carcinoma (RCC) 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). Welireg is also indicated for the treatment of adult and pediatric patients 12 years and older with locally advanced, unresectable, or metastatic pheochromocytoma or paraganglioma (PPGL).

Coverage Information:
Members will be required to meet the criteria below for coverage. For members under the age of 19 years, the prescription will automatically process without a coverage review.

Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances. Some states also mandate usage of other Compendium references. Where such mandates apply, they supersede language in the benefit document or in the notification criteria.

2. Coverage Criteria[a]:

A. <u>Patients less than 19 years of age</u>

1. **Welireg** will be approved based on the following criterion:

   a. Patient is less than 19 years of age

   Authorization will be issued for 12 months.

B. <u>Von Hippel-Lindau (VHL) Disease</u>

1. **<u>Initial Authorization</u>**

   a. **Welireg** will be approved based on **<u>all</u>** the following criteria:

      (1) Diagnosis of von Hippel-Lindau (VHL) disease

-AND-

(2) Patient requires therapy for **one** of the following:

(a) Renal cell carcinoma (RCC)
(b) Central nervous system (CNS) hemangioblastoma
(c) Pancreatic neuroendocrine tumor (pNET)

-AND-

(3) Patient does not require immediate surgery

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Welireg** will be approved based on the following criterion:

(1) Patient does not show evidence of disease progression while on Welireg.

Authorization will be issued for 12 months.

C. Advanced Renal Cell Carcinoma

1. **Initial Authorization**

a. **Welireg** will be approved based on **both** the following criteria:

(1) Diagnosis of advanced renal cell carcinoma (RCC)

-AND-

(2) Disease has progressed after treatment with **both** of the following:

(a) Programmed death receptor 1 (PD-1) or programmed death ligand 1 (PD-L1) checkpoint inhibitor [e.g.,Keytruda (pembrolizumab), Opdivo (nivolumab)]

-AND-

(b) Vascular endothelial growth factor tyrosine kinase inhibitor (VEGF-TKI) [e.g., Cabometyx (cabozantinib), Inlyta (axitinib), Lenvima (lenvatinitb)]

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Welireg** will be approved based on the following criterion:

(1) Patient does not show evidence of disease progression while on Welireg.

Authorization will be issued for 12 months.

D. Pheochromocytoma/Paraganglioma

1. **Initial Authorization**

   a. **Welireg** will be approved based on **both** the following criteria:

      (1) Diagnosis of pheochromocytoma or paraganglioma (PPGL)

      -AND-

      (2) Disease is **one** of the following:

         (a) Advanced
         (b) Unresectable
         (c) Metastatic

      Authorization will be issued for 12 months.

2. **Reauthorization**

   a. **Welireg** will be approved based on the following criterion:

      (1) Patient does not show evidence of disease progression while on Welireg.

      Authorization will be issued for 12 months.

E. NCCN Recommended Regimens

The drug has been recognized for treatment of the cancer indication by The National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium with a Category of Evidence and Consensus of 1, 2A, or 2B

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. References:

1. Welireg [package insert]. Rathway, NJ: Merck & Co., Inc.; May 2025.
2. The NCCN Drugs and Biologics Compendium (NCCN Compendium™). Available at www.nccn.org. Accessed June 4, 2025.

Program	Prior Authorization/Notification – Welireg (belzutifan)
Change Control	
10/2021	New program
10/2022	Annual review with no changes to clinical coverage criteria. Added state mandate footnote. Updated references.
10/2023	Annual review with no changes to coverage criteria. Updated references.
2/2024	Added criteria for advanced renal cell carcinoma. Updated background and references.
7/2024	Updated examples of PD-L1 checkpoint inhibitors and VEGF-TKIs within advanced RCC criteria.
7/2025	Annual review. Added criteria for pheochromocytoma/paraganglioma.