BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

IWILFIN™ (eflornithine) oral
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**

Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for IWILFIN (eflornithine)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a physician specializing in the diagnosis or in consultation with an Oncologist

Indication
- Diagnosis of **ONE** of the following:
  - Individual with high risk neuroblastoma (HRNB) who has at least a partial response to prior multiagent, multimodality therapy including anti GD2 immunotherapy (e.g., Unituxin (dinutuximab)) and is used to reduce the risk for relapse

- Other oncologic direct treatment use listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

Age Requirement
- 1 year of age or older

Baseline Clinical Evaluation
- Audiogram
- Complete blood count
- Liver function tests (alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin)
- Negative pregnancy test for women of childbearing potential
- Lansky score is at least 60 or more

Brand Specific Criteria
- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Documentation Requirements
- A completed request form must be submitted including:
  - Chart notes
  - Lab results
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration
- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.

Prescriber Qualifications
- Continues to be seen by a physician specializing in the diagnosis or in consultation with an Oncologist

Clinical Response
- No evidence of disease progression
- No evidence of unacceptable drug toxicity

Adherence
- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria
- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

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Safety

- No significant adverse drug effects that may exclude continued use such as:
  - Severe/serious or life threatening myelosuppression (e.g., neutropenia, thrombocytopenia, bone marrow failure, anemia)
  - Hepatotoxicity
  - Hearing loss
  - Other life threatening adverse effects thought to be drug related that recurs after dose interruption and dose reduction

Additional Requirements

- Requested dose is at least 192 mg once daily

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use (as listed above)

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year *(Total duration of treatment is 2 years)*

Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications

2. Off-Label Use of Cancer Medications

Description:

Iwilfin (eflornithine) is an ornithine decarboxylase inhibitor indicated to reduce the risk of relapse in adult and pediatric individuals with high-risk neuroblastoma (HRNB) who have demonstrated at least a partial response to prior multiagent, multimodality therapy including anti-GD2 immunotherapy.

HRNB remains a challenge in pediatric oncology, accounting for 15% of all pediatric cancer deaths. While most patients are able to attain remission, approximately 50% will relapse. Once relapsed, there is currently no curative treatment for these children, and for these children the 5-year survival rate is <10%.

Neuroblastomas are neuroblastic tumors of children. Segmental chromosomal aberrations (SCAs), particularly segmental deletions of chromosome 1p, are associated with a poor prognosis. Deletions of chromosome 1p are associated with amplification of the *MYCN* oncogene (also called *N-myc*), the most common focal genetic lesion in sporadic neuroblastoma. The presence or absence of alterations in total DNA content and the amplification of MYCN are important in determining the appropriate therapy for newly diagnosed patients. The definitive diagnosis of neuroblastoma is made by histologic confirmation, either from biopsy of tumor tissue or evidence of metastases

to bone marrow on aspirate or biopsy with concomitant elevation of catecholamines in the urine. The treatment of neuroblastoma is determined based on low-, intermediate-, and high-risk categories based on tumor stage and other clinical characteristics at diagnosis (including age and molecular/pathologic features).

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Lansky Scale:

Score	Description
100	Fully active, normal
90	Minor restrictions in physical strenuous activity
80	Active, but tires more quickly
70	Both greater restriction of, and less time spent in, play activity
60	Up and around, but minimal active play; keeps busy with quieter activities
50	Gets dressed, but lies around much of the day; no active play; able to participate in all quiet play and activities
40	Mostly in bed, participates in quiet activities
30	In bed, needs assistance even for quiet play
20	Often sleeping, play entirely limited to very passive activities
10	No play, does not get out of bed
0	Dead

Resources:

Iwilfin (eflornithine) tab product information, revised by USWM, LLC. 11-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 24, 2025.

Shohet JM, Nuchtern JG. Epidemiology, pathogenesis, and pathology of neuroblastoma. In: UpToDate, Park JR, Shah SM (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through November 2025. Topic last updated on April 09, 2025. Accessed December 02, 2025.

Shohet JM, Nuchtern JG, Foster JH. Clinical presentation, diagnosis, and staging evaluation of neuroblastoma. In: UpToDate, Park JR, Shah SM (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through November 2025. Topic last updated on April 05, 2024. Accessed December 02, 2025 .

Shohet JM, Nuchtern JG, Foster JH. Treatment and prognosis of neuroblastoma. In: UpToDate, Park JR, Shah SM (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through November 2025. Topic last updated on October 15, 2025. Accessed December 02, 2025.

Osterheld J, Ferguson W, Kraveka JM, et al.: Eflornithine as Postimmunotherapy Maintenance in High-Risk Neuroblastoma: Externally Controlled, Propensity Score–Matched Survival Outcome Comparisons. J Clin Oncol 2023;42(1):90-102. Re-evaluated December 02, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Neuroblastoma Version 1.2025 – Updated April 16, 2025. Available at https://www.nccn.org. Accessed December 02, 2025.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT02395666: A Phase II Preventative Trial of DFMO (Efl ornithine HCl) as a Single Agent in Patients With High RiskNeuroblastoma in Remission. Available from: http://clinicaltrials.gov. Last update posted December 06, 2023. Last verified December 2023. Accessed February 08, 2024. Re-evaluated December 02, 2025.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.