Evolent Clinical Guideline 3127 for Fabhalta™ (iptacopan)

Guideline Number: Evolent_CG_3127	**Applicable Codes**	
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STATEMENT

Purpose

To define and describe the accepted indications for Fabhalta (iptacopan) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Paroxysmal Nocturnal Hemoglobinuria (PNH)

- Fabhalta (iptacopan) may be used for the treatment of adult members with paroxysmal nocturnal hemoglobinuria (PNH).

CONTRAINDICATIONS/WARNINGS

- Contraindications
  - Serious hypersensitivity to iptacopan or any component of the formulation
  - Initiation in patients with unresolved serious infection caused by encapsulated bacteria, including *S. pneumoniae*, *N. meningitidis*, or *H. influenza* type B.
- US Boxed Warning
  - Serious infections caused by encapsulated bacteria
    - Iptacopan, a complement inhibitor, increases the risk of serious infections, especially those caused by encapsulated bacteria, such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type b. Life-

threatening and fatal infections with encapsulated bacteria have occurred in patients treated with complement inhibitors. These infections may become rapidly life-threatening or fatal if not recognized and treated early.

- Complete or update vaccination for encapsulated bacteria at least 2 weeks prior to the first dose of iptacopan, unless the risks of delaying therapy with iptacopan outweigh the risk of developing a serious infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against encapsulated bacteria in patients receiving a complement inhibitor.
- Patients receiving iptacopan are at increased risk for invasive disease caused by encapsulated bacteria, even if they develop antibodies following vaccination. Monitor patients for early signs and symptoms of serious infections and evaluate immediately if infection is suspected.
- Because of the risk of serious infections caused by encapsulated bacteria, iptacopan is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the FABHALTA REMS.

EXCLUSION CRITERIA

- Disease progression while taking Fabhalta (iptacopan).
- Concurrent use with other therapies used to treat PNH, e.g., eculizumab, ravulizumab.
- Dosing exceeds single dose limit of 200 mg.
- Treatment exceeds the maximum limit of 60 (200 mg) capsules/month.
- Investigational use of Fabhalta (iptacopan) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
  - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
  - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
  - Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of < 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
  - Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
  - That non-randomized clinical trials with a significant number of subjects may be a

basis for supportive clinical evidence for determining accepted uses of drugs.

- That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
- That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

CODING AND STANDARDS

Codes

- J8999 - iptacopan

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
June 2026	• Updated references
June 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1501 Fabhalta (iptacopan) • Updated indication section • Added maximum dosage form quantities in exclusion criteria • Updated exclusion criteria • Updated references

Date	Summary
June 2024	• New policy

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Services Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

REFERENCES

1. Peffault de Latour R, et al. Oral Iptacopan Monotherapy in Paroxysmal Nocturnal Hemoglobinuria. *N Engl J Med*. 2024 Mar 14;390(11):994-1008. doi: 10.1056/NEJMoa2308695.
2. Risitano AM, et al. Factor B inhibition with oral iptacopan monotherapy demonstrates sustained long-term efficacy and safety in anti-C5-treated patients (pts) with paroxysmal nocturnal hemoglobinuria (PNH) and persistent anemia: final 48-week results from the multicenter, phase III APPLY-PNH trial. Presented at the 2023 American Society of Hematology (ASH) Annual Meeting and Exposition; December 9-12; San Diego, CA; abstract 571.
3. Jang JH, et al. Iptacopan monotherapy in patients with paroxysmal nocturnal hemoglobinuria: a 2-cohort open-label proof-of-concept study. *Blood Adv*. 2022 Aug 9;6(15):4450-4460. doi: 10.1182/bloodadvances.2022006960.
4. Fabhalta prescribing information. Novartis Pharmaceuticals Corporation. East Hanover, NJ 2025.
5. Clinical Pharmacology Elsevier Gold Standard 2026.
6. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2026.
7. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2026.
8. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2026.
9. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.
10. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.
11. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm.