Iptacopan

Adjudication Guideline

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Daman	Pharmaceutical Standards & Governance	

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1. Abstract

1.1 For Members

Iptacopan is used to treat certain rare blood and kidney disorders. It works by blocking part of the complement system, helping to prevent damage to blood cells and kidneys and reduce symptoms.

1.2 For Medical Professionals

Iptacopan is an oral, selective factor B inhibitor of the alternative complement pathway. It inhibits the formation of C3 and C5 convertases, thereby reducing complement-mediated hemolysis and inflammation in complement-driven disorders.

Mechanism of Action:

Iptacopan is an oral, selective inhibitor of complement factor B, a key component of the alternative pathway of the complement system. By inhibiting factor B, Iptacopan prevents the formation and activity of the C3 convertase (C3bBb), thereby blocking downstream complement activation.

This results in:

- Reduced amplification of complement activation
- Decreased production of inflammatory mediators (C3a, C5a)
- Prevention of membrane attack complex (MAC, C5b-9) formation

Overall, Iptacopan controls complement-mediated inflammation and hemolysis by targeting the proximal alternative complement pathway.

Indications:

Iptacopan is indicated for:

- **Paroxysmal Nocturnal Hemoglobinuria (PNH)**
  Treatment of adult patients with PNH

- **Primary Immunoglobulin A Nephropathy (IgAN)**
  Reduction of proteinuria in adults with primary IgA nephropathy

- **Complement 3 Glomerulopathy (C3G)**
  Treatment of adult patients with complement 3 glomerulopathy (C3G), specifically for the reduction of proteinuria

Dose and Administration:

- The recommended dose of Iptacopan is 200 mg taken orally twice daily, with or without food. Capsules should be swallowed whole and must not be opened, broken, or chewed.

- If a dose is missed, the patient should be instructed to take one dose as soon as possible (even if it is close to the next scheduled dose) and then resume the regular dosing schedule thereafter.

Vaccination Requirements Prior to Initiation of Iptacopan

- Complete or update vaccination for encapsulated bacteria at least 2 weeks prior to the first dose of Iptacopan, unless the risks of delaying FABHALTA therapy outweigh the risk of developing a serious infection.
- Administer vaccines in accordance with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for patients receiving complement inhibitors, including vaccination against Neisseria meningitidis, Streptococcus pneumoniae, and Haemophilus influenzae type b.
- If urgent initiation of FABHALTA is indicated and vaccination cannot be completed at least 2 weeks in advance, monitor patients closely for signs and symptoms of serious infection.

2. Scope

The scope of this adjudication rule outlines the coverage criteria and medical necessity of Iptacopan, in accordance with best clinical practice and the policy terms and conditions of each health insurance plan administered by Daman.

3. Adjudication Policy

3.1 Eligibility / Coverage Criteria

3.1.1 Iptacopan for Paroxysmal Nocturnal Hemoglobinuria

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired blood disorder in which a PIGA gene mutation leads to loss of protective GPI-anchored proteins on red blood cells, making them vulnerable to complement-mediated destruction. This results in chronic hemolysis, anemia, dark urine, and an increased risk of thrombosis.

Criteria for Initiation: **(should meet all criteria (A,B,C,D,E)**

A. The patient is 18 years of age or older; AND

B. The diagnosis of paroxysmal nocturnal hemoglobinuria is confirmed by peripheral blood flow cytometry (gold standard) demonstrating absence or deficiency of glycosylphosphatidylinositol-anchored proteins (GPI-APs) on at least two cell lineages (documentation required); AND

C. Eligible clinician: Hematologist.

D. Evidence of active disease, defined by one or more of the following:

- Persistent anemia with hemoglobin (Hb) < 10 g/dL;
- Elevated lactate dehydrogenase (LDH) ≥ 1.5 × upper limit of normal (ULN), indicating ongoing intravascular hemolysis;
- History of transfusion dependence (e.g., ≥ 1 transfusion in the past 6–12 months);
- Clinical symptoms attributable to hemolysis (e.g., fatigue, hemoglobinuria, abdominal pain, dyspnea, dysphagia)

E. For patients Switching from a C5 inhibitor (e.g., eculizumab or ravulizumab) to Iptacopan:

- Documentation of suboptimal response, intolerance, or breakthrough hemolysis, including one or more of the following:
    - Persistent anemia with hemoglobin < 10 g/dL despite an adequate trial of a C5 inhibitor, defined as at least 6 months of continuous therapy
    - Ongoing transfusion requirement despite therapy;
    - Evidence of breakthrough hemolysis (e.g., rising LDH with symptoms);
    - Documented C5 inhibitor intolerance or contraindication

Re-assessment and continuation Criteria:

A reassessment of therapy effectiveness will be conducted after 3 months of treatment to determine the appropriateness of ongoing therapy.

B) Continuation of Iptacopan therapy should only proceed if the patient demonstrates meaningful clinical benefit, which may include one or more of the following:

- Increase or stabilization of hemoglobin levels
- Reduction in transfusion requirements or achievement of transfusion independence
- Reduction in hemolysis markers (e.g., LDH improvement)
- Improvement in Functional Assessment of Chronic Illness Therapy (FACIT)–Fatigue score, indicating enhanced quality of life.

Exclusion Criteria:

- Hypersensitivity to iptacopan or its excipients
- Presence of an unresolved or active, uncontrolled serious infection, particularly infections caused by encapsulated bacteria (e.g., meningococcal, pneumococcal, Haemophilus influenzae)
- Incomplete vaccination against encapsulated bacteria prior to treatment initiation
- Concomitant use of Iptacopan with other complement inhibitors, including but not limited to C3 inhibitors (e.g., pegcetacoplan or other C3-targeted therapies)

3.1.2 Iptacopan for Primary IgA Nephropathy (IgAN)

Primary IgA nephropathy (IgAN) is an immune-mediated kidney disease in which galactose-deficient IgA1-containing immune complexes deposit in the glomerular mesangium, leading to inflammation and progressive kidney injury.

Criteria for Initiation: :(should meet all criteria (A,B,C,D,E,F,G)

Use of Iptacopan for Primary Immunoglobulin A Nephropathy is approved only when all criteria (A–G) are met:

A. The patient is ≥ 18 years of age; AND

B. The diagnosis of primary IgA nephropathy is confirmed by renal biopsy (documentation required); AND

C. The patient is considered at high risk of disease progression if:

- UPCR ≥ 1 g/g, confirmed by at least two first-morning urine (FMU) samples, obtained ≥ 4 weeks apart; **AND**
- At least one of the following:
    1. Sustained reduction in estimated glomerular filtration rate (eGFR) despite optimized supportive care, defined as:

        • A decline in eGFR of ≥ 5 mL/min/1.73 m² within 12 months; **OR**
        • A decline in eGFR of ≥ 10 mL/min/1.73 m² over 5 years

    2. Active urine sediment, defined as evidence of glomerular hematuria on urinalysis, including ANY ONE of the following findings, as assessed by the treating nephrologist:

        • Microscopic hematuria on urine examination; **OR**

        • Presence of red blood cells consistent with glomerular origin (e.g., dysmorphic red blood cells); **OR**
        • Presence of red blood cell casts on urine microscopy.

    3. Kidney biopsy demonstrating active inflammatory lesions

D. The patient has received the maximum or maximally tolerated dose of ONE of the following medications for at least 3 months prior to initiating iptacopan:

    1. Angiotensin-converting enzyme inhibitor (ACE-I); OR

    2. Angiotensin receptor blocker (ARB); AND

E. The patient has an estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73 m²; AND

F. Therapy is prescribed by an eligible clinician: Nephrologist

G. Blood Pressure Control

The patient has controlled blood pressure or has undergone optimization of antihypertensive therapy, defined as meeting ANY ONE of the following criteria:

- Blood pressure ≤ 130/80 mmHg where achievable, documented on at least two readings taken ≥ 2 weeks apart; OR
- Blood pressure remains above 130/80 mmHg despite optimized antihypertensive therapy, at maximally tolerated doses; OR
- Further blood pressure reduction is clinically contraindicated, as documented by the treating nephrologist.

Re-assessment and continuation Criteria:

A reassessment of therapy effectiveness must be conducted after 6 months of treatment to determine whether continuation of Iptacopan therapy is appropriate.

Continuation of Iptacopan therapy should include the following required clinical improvements:

- Estimated glomerular filtration rate (eGFR) must remain ≥ 30 mL/min/1.73 m². Values below this level indicate advanced kidney impairment where continuation of therapy is not recommended.
- Reduction in urine protein-to-creatinine ratio (UPCR) from baseline

  (defined as a clinically meaningful reduction e.g., ≥ 50% reduction from baseline and/or reduction to < 0.7 g/day, where clinically appropriate)

- No evidence of accelerated decline in renal function, defined as a rate of eGFR decline that does not exceed the pre-treatment (baseline) rate

1.1.3 Iptacopan for complement 3 Glomerulopathy (C3G)

Complement 3 glomerulopathy (C3G) is a rare, chronic kidney disease caused by uncontrolled activation of the alternative complement pathway, leading to deposition of complement protein C3 in the glomeruli. This results in inflammation and progressive kidney injury, typically presenting with proteinuria, hematuria, and declining kidney function.

Criteria for Initiation: :(should meet all criteria (A,B,C,D,E,)

A. The patient is 18 years of age or older.

B. The diagnosis of Complement 3 Glomerulopathy (C3G) is confirmed by renal biopsy.

C. Disease Severity Criteria:

1. The patient has a urine protein-to-creatinine ratio (UPCR) ≥ 1.0 g/g, confirmed in at least two first-morning urine (FMU) samples obtained more than 4 weeks apart.

2. The patient has an estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73 m².

D. The patient has received the maximum or maximally tolerated dose of ONE of the following medications for at least 3 months prior to initiating Iptacopan:

   a. Angiotensin-converting enzyme inhibitor (ACE-I); OR
   b. Angiotensin receptor blocker (ARB).

E. Eligible clinician: **Nephrologist**

Re-assessment and continuation Criteria:

A. A reassessment of therapy effectiveness must be conducted after 6 months of treatment to determine whether continuation of Iptacopan therapy is appropriate.

B. Continuation of Iptacopan therapy should include the following required clinical improvements:

- Estimated glomerular filtration rate (eGFR) must remain ≥ 30 mL/min/1.73 m². Values below this level indicate advanced kidney impairment where continuation of therapy is not recommended.
- Reduction in urine protein-to-creatinine ratio (UPCR) from baseline

(defined as a clinically meaningful reduction e.g., ≥ 50% reduction from baseline and/or reduction to < 0.7 g/day, where clinically appropriate)

- Evidence of reduction or clearance of C3 deposits on repeat kidney biopsy, if available, as supportive evidence of treatment response

Exclusion Criteria for Primary IgA Nephropathy and complement 3 Glomerulopathy

- Known hypersensitivity to iptacopan or any of its excipients
- Presence of an unresolved or active, uncontrolled serious infection, particularly infections caused by encapsulated organisms
- Incomplete vaccination against encapsulated bacteria prior to treatment initiation, unless the clinical benefit outweighs the risk of delaying therapy
- End-stage kidney disease, including patients on dialysis or with a prior kidney transplant
- Estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m²
- Crescentic or rapidly progressive glomerulonephritis (RPGN)
- Concomitant use with another complement inhibitor

3.2 Requirements for Coverage

- Kindly code the ICD-10 and the CPT codes to the highest level of specificity

Eligible clinician Specialties
Nephrology
Haematology

3.3 Non-Coverage

- Not covered for visitor plan
- Age less than 18 years

3.4 Payment and Coding Rules

- Kindly apply DOH payment rules and regulations and relevant coding manuals for ICD, Drugs.

4. Denial Codes

Code	Code Description
CODE-010	Activity/diagnosis inconsistent with clinician specialty
MNEC-004	Service is not clinically indicated based on good clinical practice
MNEC-005	Service/supply may be appropriate, but too frequent
CODE-014	Activity/diagnosis is inconsistent with the patient's age/gender
AUTH-001	Prior approval is required and was not obtained
MNEC-006	Alternative service should have been utilized

5. Appendices

5.1 References

- https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/218276s004lbl.pdf
- uptodate/Iptacopan
- https://www.medicines.org.uk/emc/product/15853/smpc#gref
- https://www.ema.europa.eu/en/medicines/human/EPAR/fabhalta
- Immunoglobulin A nephropathy-uptodate

5.2 Revision History

Date	Change(s)
1/09/2026	New AR release

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