Aqvesme and Pyrukynd (mitapivat)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Aqvesme and Pyrukynd (mitapivat) drug policy is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

- Aqvesme is indicated for treatment of anemia in adults with alpha- or beta-thalassemia.
- Pyrukynd is indicated for the treatment of hemolytic anemia in adults with pyruvate kinase (PK) deficiency.

POLICY

Documentation

Submission of the following information is necessary to initiate the prior authorization review:

Anemia with Alpha- or Beta-Thalassemia

1. Initial requests:
    A. Chart notes or medical record documentation of blood transfusion history and pretreatment or pretransfusion hemoglobin (Hgb) level
    B. Chart notes or medical record documentation of at least one of the following:
        1) Hemoglobin electrophoresis or high-performance liquid chromatography (HPLC) results
        2) Molecular genetic testing results

C. Chart notes or medical record documentation of baseline liver function tests (e.g., ALT, AST, alkaline phosphatase, and total bilirubin with fractionation)

2. Continuation requests: Documentation (e.g., chart notes) that the member has experienced a positive clinical response to therapy (e.g., increase in hemoglobin of at least 1.5 g/dL from baseline or reduction in blood transfusions from baseline)

Hemolytic anemia with pyruvate kinase deficiency

1. Initial requests:
   A. Chart notes or medical record documentation of at least one of the following:
      1) Enzyme assay demonstrating deficiency of pyruvate kinase (PK) enzyme activity
      2) Genetic testing demonstrating presence of at least 2 mutant alleles in the PKLR gene, of which at least 1 is a missense mutation
   B. Chart notes or medical record documentation of enzyme assay or genetic testing demonstrating member is not homozygous for the R479H mutation or does not have 2 non-missense variants, without the presence of another missense mutation, in the PKLR gene.
   C. Chart notes or medical record documentation of blood transfusion history or hemoglobin (Hb) levels.
2. Continuation requests: Documentation (e.g., chart notes) that the member has experienced a positive clinical response to therapy (e.g., increase in hemoglobin of at least 1.5 g/dL from baseline or reduction in blood transfusions from baseline).

Criteria for Initial Approval

Anemia with Alpha- or Beta-Thalassemia

Aqvesme (mitapivat) may be considered **medically necessary** for the treatment of hemolytic anemia with alpha- or beta-thalassemia when all of the following criteria are met:

1. Member has symptomatic anemia evidenced by a pretreatment or pretransfusion Hgb level less than or equal to 11 grams per deciliter (g/dL)
2. Member has a diagnosis of thalassemia (beta-thalassemia [β-thalassemia] with or without alpha-globin [α-thalassemia] gene mutations, hemoglobin E [HbE]/β-thalassemia, or α-thalassemia/hemoglobin H [HbH] disease) confirmed by either of the following:
   A. Hemoglobin electrophoresis or high-performance liquid chromatography (HPLC)
   B. Molecular genetic testing
3. Member does not have ANY of the following diagnoses:
   A. Homozygous or heterozygous sickle hemoglobin (HbS)
   B. Homozygous or heterozygous hemoglobin C (HbC)
   C. Hepatic cirrhosis (Child-Pugh Class A, B or C)
4. Members with non-transfusion-dependent beta-thalassemia must meet either of the following:
   A. Has had an inadequate response, intolerance, or contraindication to compliant use of hydroxyurea
      OR
   B. Genetic variant is not anticipated to benefit from hydroxyurea treatment
5. Members with transfusion-dependent beta-thalassemia must meet ALL of the following:
   A. Has had an inadequate response, intolerance, or contraindication to compliant use of Reblozyl (luspatercept-aamt)
   B. The requested medication will not be used in combination with Reblozyl
   C. History of requiring at least 6 red blood cell (RBC) units to be transfused in the previous 24 weeks
6. Prescribed by or in consultation with a hematologist or specialist in the treatment of alpha- or beta-thalassemia
7. Member is 18 years of age or older

Approval will be for **6 months**

Hemolytic anemia with pyruvate kinase deficiency
Pyrukynd (mitapivat) may be considered **medically necessary** for the treatment of hemolytic anemia with pyruvate kinase (PK) deficiency when all of the following criteria are met:

1. Member meets at least one of the following:
   A. Deficiency of PK enzyme activity
   B. Presence of at least 2 mutant alleles in the PKLR gene, of which at least 1 is a missense mutation.
2. Member is not homozygous for the R479H mutation or does not have 2 non-missense variants, without the presence of another missense mutation, in the PKLR gene
3. Member meets at least one of the following criteria:
   A. History of a minimum of 6 blood transfusion episodes in the past 52 weeks OR
   B. Hb concentration less than or equal to 10.0 g/dL
4. Member is receiving concomitant treatment with at least 0.8 mg oral folic acid daily
5. Prescribed by or in consultation with a hematologist
6. Member is 18 years of age or older

Approval will be for **3 months**

Continuation of Therapy
Anemia with Alpha- or Beta-Thalassemia
Aqvesme (mitapivat) may be considered **medically necessary** for continued treatment of hemolytic anemia with alpha- or beta-thalassemia when all of the following criteria are met:

1. Member has achieved or maintained a positive clinical response to therapy as defined by ONE of the following:
   A. Increase in hemoglobin of at least 1.5 g/dL from baseline
   B. Reduction in blood transfusions from baseline
2. Member has not experienced unacceptable toxicity (e.g. new or worsening jaundice or ALT ≥10×baseline)
3. Prescribed by or in consultation with a hematologist or specialist in the treatment of alpha- or beta-thalassemia

Approval will be for **12 months**

Hemolytic anemia with pyruvate kinase deficiency
Pyrukynd (mitapivat) may be considered **medically necessary** for the continued treatment of hemolytic anemia with pyruvate kinase (PK) deficiency when all of the following criteria is met:

1. Member has achieved or maintained a positive clinical response to therapy as defined by ONE of the following:
   A. Increase in hemoglobin of at least 1.5 g/dL from baseline
   B. Reduction in blood transfusions from baseline
2. Member will continue to receive concomitant treatment with at least 0.8 mg oral folic acid daily
3. Prescribed by or in consultation with a hematologist

Approval will be for **6 months**

Aqvesme and Pyrukynd (mitapivat) are considered **not medically necessary** for members who do not meet the criteria set forth above.

Dosing and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limits

Medication	Quantity Limit	FDA-recommended dosing
Aqvesme 100 mg Tablet	56 tabs per 28 days	100 mg twice daily
Pyrukynd 50 mg-20 mg Taper Pack	1 pack per 14 days	**Initial:** 5 mg twice daily, titrated from 5 mg twice daily to 20 mg twice daily, then to maximum recommended dose of 50 mg twice daily, with dose increases every 4 weeks. **Maintenance:** 5 mg, 20 mg, or 50 mg twice daily depending on patient response. Some patients may reach and maintain normal hemoglobin (Hb) at 5 mg twice daily or 20 mg twice daily. *Dose tapering for medication interruption or discontinuation:* Patients currently taking 5 mg twice daily: • Days 1-7: 5 mg once daily • Days 8-14: Discontinue Patients currently taking 20 mg twice daily: • Days 1-7: 20 mg once daily • Days 8-14: 5 mg once daily • Day 15: Discontinue Patients currently taking 50 mg twice daily: • Days 1-7: 50 mg once daily • Days 8-14: 20 mg once daily • Day 15: Discontinue
Pyrukynd 20 mg-5 mg Taper Pack	1 pack per 14 days	
Pyrukynd 5 mg Taper Pack	1 pack per 7 days	
Pyrukynd 50 mg Maintenance Pack	1 pack per 28 days	
Pyrukynd 20 mg Maintenance Pack	1 pack per 28 days	
Pyrukynd 5 mg Maintenance Pack	1 pack per 28 days	

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- N/A

REFERENCES

- Pyrukynd [package insert]. Cambridge, MA: Agio Pharmaceuticals, Inc.; February 2022.
- A Study to Evaluate Efficacy and Safety of AG-348 in Not Regularly Transfused Adult Participants with Pyruvate Kinase Deficiency (PKD). ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/study/NCT03548220. Published November 10, 2020. Accessed March 1, 2022.

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- Aqvesme [package insert]. Cambridge, MA: Agios Pharmaceuticals, Inc.; December 2025.
- National Organization for Rare Disorders. Alpha thalassemia. Updated January 23, 2017. Accessed February 3, 2026. https://rarediseases.org/rare-diseases/alpha-thalassemia/
- National Organization for Rare Disorders. Beta thalassemia. Updated May 23, 2023. Accessed February 3, 2026. https://rarediseases.org/rarediseases/thalassemia-major/

POLICY HISTORY

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