New Drug Fact Blast

Clinical Services

Drug/Manufacturer:	**Pyrukynd® (mitapivat) [Agios Pharmaceuticals, Inc.]**
Dosage Formulations:	Tablets: 5 mg, 20 mg, and 50 mg
FDA Approval Date: **FDB File Date:**	FDA: February 17, 2022 FDB: March 6, 2022
Indication:	The treatment of hemolytic anemia in adults with pyruvate kinase deficiency (PKD)
Mechanism of Action:	Pyrukynd is a pyruvate kinase (PK) activator that allosterically binds to the PK tetramer and increases PK activity. The red blood cell form of PK (PK-R) is mutated in PK deficiency, leading to reduced adenosine triphosphate (ATP), shortened red blood cell lifespan, and chronic hemolysis.
Dose/ Administration:	• Pyrukynd tablets are to be swallowed whole – do not split, crush, chew, or dissolve the tablets. • The starting dose of Pyrukynd is 5 mg twice daily. The dose may then be gradually tapered up every 4 weeks to a maximum dose of 50 mg twice daily based on hemoglobin (Hb) and transfusion requirements.

Duration	Dosage
Week 1 through Week 4	• 5 mg twice daily
Week 5 through Week 8	• If Hb is below normal range or patient has required a transfusion within the last 8 weeks: Increase to 20 mg twice daily and maintain for 4 weeks • If Hb is within normal range and patient has not required a transfusion within the last 8 weeks: Maintain 5 mg twice daily
Week 9 through Week 12	• If Hb is below normal range or patient has required a transfusion within the last 8 weeks: Increase to 50 mg twice daily and maintain thereafter • If Hb is within normal range and patient has not required a transfusion within the last 8 weeks: Maintain current dose (5 mg twice daily or 20 mg twice daily)
Maintenance	• If Hb decreases, consider up-titration to the maximum of 50 mg twice daily as per the above schedule

- If a dose is missed by 4 hours or less, administer the dose as soon as possible. If a dose is missed by more than 4 hours, wait until the next scheduled dose.
- Due to risk of acute hemolysis, avoid abrupt interruption or discontinuation of Pyrukynd.
  - Taper the dose gradually if Pyrukynd needs to be discontinued and monitor the patient for signs of acute hemolysis and worsening anemia.
  - If dose reduction is required due to an adverse event, tolerability, or Hb level above normal, the dose may be reduced to the next lower dose (20 mg or 5 mg twice daily)

Current Dose	Dose Taper Schedule		
	Day 1 – 7	Day 8 – 14	Day 15
5 mg twice daily	5 mg once daily	Discontinue	
20 mg twice daily	20 mg once daily	5 mg once daily	Discontinue
50 mg twice daily	50 mg once daily	20 mg once daily	Discontinue

- Avoid use in patients with moderate or severe hepatic impairment

	• Avoid use with strong CYP3A inhibitors or inducers • When used concomitantly with a moderate CYP3A inhibitor, do not titrate beyond 20 mg twice daily. • Consider alternative therapies with moderate CYP3A inducers. If concomitant therapy is necessary, monitor Hb and titrate beyond the 50 mg twice daily dose but do not exceed 100 mg twice daily.

Disease State Clinical Highlights:	• Pyruvate kinase deficiency (PKD) is a rare, autosomal recessive congenital disorder characterized by the premature destruction of red blood cells, or hemolytic anemia, caused by variants in the pyruvate kinase liver and red blood cell (*PKLR*) gene. The PK activity in cell types other than red blood cells is normal as the enzyme expressed in other cell types is encoded on a separate gene.
	• The prevalence of *PKLR* heterozygous carriers ranges from 1 to 3%. The estimated disease prevalence is 1 per 20,000 in the United States. Over 200 individuals with PKD are enrolled in an ongoing natural history study.
	• PKD is the most frequent enzyme deficiency in the Emben-Meyerhod pathway (EMP), the energy-producing glycolytic pathway which metabolizes glucose to generate ATP for the cell.
	  ○ In the last step of glycolysis, pyruvate kinase catalyzes the conversion of phosphoenolpyruvate (PEP) to pyruvate by removal of a phosphate group. This phosphate group is transferred to ADP (adenosine diphosphate) to create one molecule of ATP (adenosine triphosphate). ATP plays a major role in maintaining a cation gradient in the red blood cell, protecting the cell from premature death. In PKD, red blood cells last a few days to weeks instead of the normal lifespan of 120 days.
	  ○ The enzyme deficiency also leads to an increase in 2,3-diphosphoglycerate (2,3-DPG), a proximal glycolytic intermediate. Levels of 2,3-DPG may be elevated up to 2 times normal in PKD, resulting in decreased Hb oxygen affinity and improved oxygen delivery allowing a better tolerance of anemia than otherwise expected.
	• Hemolytic anemia in PKD is characterized by an increased reticulocyte count, increased indirect bilirubin, possibly increased lactate dehydrogenase (LDH), and possibly decreased haptoglobin.
	• Symptoms of PKD range from mild to severe and may include fatigue, unusually pale skin, jaundice, shortness of breath, and fast heart rate. Patients may also develop an enlarged spleen, iron overload from frequent blood transfusions, osteoporosis, and gallstones. The condition may be life threatening at birth or go undiagnosed into adulthood.
	• The Pyruvate Kinase Deficiency Natural History Study (PKD NHS) found patients with PKD had higher lifetime rates of pulmonary hypertension, osteoporosis, and liver cirrhosis, and higher 8-year rates of splenectomy, gallstones, and cholecystectomy than age and sex matched individuals from the general insured US population who did not have PKD.
	• A diagnosis of PKD should depend on the detection of the deficient PK enzyme and detection of compound heterozygous or homozygous variants in the *PKLR* gene. Testing for reduced PK enzyme activity, however, requires specialized laboratories and is not widely available. Molecular genetic testing can detect variants in the *PKLR* gene known to cause the disorder and can confirm a diagnosis. Agios Pharmaceuticals is offering Anemia-ID, a free genetic testing program for patients with unspecified chronic hemolysis where PKD is suspected. Anemia-ID provides a next-generation sequencing (NGS) panel consisting of approximately 50 genes known to cause hereditary anemias, including PKD.

Drug Clinical Highlights:

- Pyrukynd has been granted orphan drug designation by the FDA for PKD, thalassemia, and sickle cell disease. It is a first-in-class, oral small molecule allosteric activator of the PK enzyme. It is currently only FDA-approved for the treatment of hemolytic anemia in PKD, but clinical studies are underway in thalassemia and sickle cell disease.
  - In PKD, Pyrukynd targets the defective enzyme, restoring adequate PK-R activity. This corrects the underlying defect in red blood cell ATP production, increasing red blood cell lifespan, reducing hemolysis, and improving anemia.
  - In thalassemia, Pyrukynd increases red blood cell ATP, improving the ability of the red blood cell to survive in a setting of ongoing oxidative damage, thereby reducing hemolysis, ineffective erythropoiesis, and anemia.
  - In sickle cell disease, Pyrukynd increases red blood cell ATP, improving red blood cell energy metabolism and membrane integrity and reducing hemolysis. Pyrukynd also lowers 2,3-DPG, which reduces sickling by increasing Hb oxygenation. Improved red blood cell hydration through the ATP-dependent Gardos channel may also improve red blood cell survival.
- Contraindications: none
- Warnings and Precautions: Acute hemolysis with subsequent anemia has been observed with abrupt interruption or discontinuation of Pyrukynd. Gradually taper the dose if possible when discontinuation of therapy is required. Monitor patients for signs of acute hemolysis and anemia including jaundice, scleral icterus, dark urine, dizziness, confusion, fatigue, or shortness of breath.
- Adverse Reactions (≥ 10%): estrone deficiency (males), increased urate, back pain, reduced estradiol (males), and arthralgia. Of note, studies have found Pyrukynd also has mild to moderate inhibition of the aromatase enzyme (an off-target effect); no adverse events related to this inhibition have been described, but there are potential implications for patients with long-term treatment.
- Drug Interactions:
  - Effect of Other Agents on Pyrukynd:
    - Strong CYP3A Inhibitors (e.g., itraconazole, ketoconazole) – avoid coadministration
    - Moderate CYP3A Inhibitors (e.g., fluconazole)– do not titrate Pyrukynd beyond 20 mg twice daily and monitor Hb
    - Strong CYP3A Inducers (e.g., rifampin) – avoid coadministration
    - Moderate CYP3A Inducers (e.g., efavirenz) – consider alternative therapies. If no alternative therapy may be found, monitor Hb and titrate beyond 50 mg twice daily if necessary, but do not exceed 100 mg twice daily
  - Effect of Pyrukynd on Other Agents:
    - CYP3A Substrates (e.g., midazolam)
      - Pyrukynd induces CYP3A, so coadministration will decrease systemic concentrations of other CYP3A substrates including hormonal contraceptives
      - Monitor patients for loss of therapeutic effect of CYP3A substrates when co-administered with Pyrukynd
      - Advise patients using hormonal contraceptives to use an alternative non-hormonal contraceptive method or add a barrier method of contraception
    - CYP2B6 and CYP2C Substrates:
      - Pyrukynd induces CYP2B6, CYP2C8, CYP2C9, and CYP2C19 enzymes *in vitro*
      - Monitor patients for loss of therapeutic effect of these substrates when co-administered with Pyrukynd
    - UGT1A1 Substrates:
      - Pyrukynd induces UGT1A1 *in vitro*
      - Monitor patients for loss of therapeutic effect of UGT1A1 substrates when co-administered with Pyrukynd
    - P-gp Substrates:
      - Pyrukynd inhibits the P-gp transporter *in vitro*

- Monitor patients for adverse reactions with P-gp substrates when co-administered with Pyrukynd

- Clinical Studies:

	ACTIVATE (NCT03548220) N=80	ACTIVATE-T (NCT03559699) N=27
Study Design	Randomized, double-blind, placebo-controlled	Single-arm, open-label
Inclusion Criteria	• Aged ≥ 18 years with PKD • Documented presence of at least 2 variant alleles in the *PKLR* gene, of which at least 1 was a missense variant • Hb ≤ 10 g/dL	
	Not regularly transfused (defined as having ≤ 4 transfusions in the year prior to treatment and no transfusions 3 months prior to treatment)	History of a minimum of 6 transfusion episodes in the year prior to informed consent
Exclusion Criteria	Homozygous for the c.1436G>A (p.R479H) variant or 2 non-missense variants (without the presence of another missense variant) in the *PKLR* gene [these patients did not achieve Hb response (change from baseline in Hb ≥ 1.5 g/dL at > 50% assessments) in the dose-ranging study]	
Baseline Patient Characteristics	• Median age: 33 years (range, 18–78 years) • Median baseline Hb: 8.5 g/dL (range, 6.4–10.2 g/dL) • History of splenectomy: 73% • 55 patients (69%) had the missense/missense *PKLR* gene variant • 25 patients (31%) had the missense/non-missense *PKLR* gene variant	• Median age: 36 years (range, 18–68 years) • Median baseline Hb: 9.1 g/dL (range, 7.4–10.9 g/dL) • History of splenectomy: 78% • 20 patients (74%) had the missense/missense *PKLR* gene variant • 7 patients (26%) had the missense/non-missense *PKLR* gene variant • Median of 9 transfusion episodes (range: 6 to 17) in the year before the first dose • Median of 7 RBC units transfused (range, 3–20 units) standardized to 24 weeks prior to treatment
Associated PKD Complications/ Comorbidities	• Use of iron chelation therapy: 19% • Decrease in bone mineral density: 80% • History of cholecystectomy: 73%	• Use of iron chelation therapy: 89% • Decrease in bone mineral density: 74% • History of cholecystectomy: 85%
Interventions	• Randomization was stratified by average screening Hb (< 8.5 vs. ≥ 8.5 g/dL) and *PKLR* gene variant category (missense/missense vs. missense/non-missense) • Patients randomized 1:1 to: ○ Pyrukynd (n = 40) up to 50 mg twice daily for 12 weeks following a 12-week dose titration phase ○ Placebo (n = 40)	Patients were administered 50 mg twice daily for 24 weeks following a 16-week dose titration phase
Endpoints	• Primary Endpoint: Percentage of patients achieving a Hb response, defined as ≥ 1.5 g/dL increase in Hb from baseline sustained at 2 or more scheduled assessments (weeks 16, 20, and 24) during the fixed dose period without transfusions	• Primary Endpoint: Percentage of patients achieving a reduction in transfusion burden, defined as ≥ 33% reduction in the number of red blood cell units transfused during the fixed dose period compared with the patient's historical transfusion burden.

	• Key Secondary Endpoints – change from baseline at weeks 16, 20, and 24 in : ○ Hb concentration ○ bilirubin ○ lactate dehydrogenase (LDH) ○ reticulocyte percentages ○ haptoglobin	• Key Secondary Endpoint: Percentage of patients who were transfusion free

- ACTIVATE Study Results:
  - Median duration of treatment was 24.1 weeks; 75% (30 out of 40 patients) were exposed to Pyrukynd for > 24 weeks and < 28 weeks.
  - Of the 40 patients randomized to Pyrukynd therapy, 88% were maintained on 50 mg twice daily.
  - The majority of Pyrukynd-treated patients experienced an increase in Hb, while the majority of placebo-treated patients experienced a decrease in Hb.
  - 15 of the 16 Pyrukynd-treated patients with a Hb response continued in a long-term study and were evaluable for maintenance of response.
    - 13 patients maintained increases in Hb without requiring any transfusions
    - Median duration of response for all 16 patients was 6.9 months (range: 3.3, 18.4+)

ACTIVATE (NCT03548220) Endpoint	Pyrukynd N=40	Placebo N=40	Difference[1,2] p-value
Hb Response, n (%)	16 (40%)	0	39 (24, 55) <0.0001
Hemoglobin (g/dL) Baseline Mean (SD) LS Mean Change (95% CI)	 8.6 (1.0) 1.7 (1.3, 2.1)	 8.5 (0.8) -0.1 (-0.6, 0.3)	 1.8 (1.2, 2.4) <0.0001
Indirect bilirubin (mg/dL) Baseline Mean (SD) LS Mean Change (95% CI)	 4.8 (3.6) -1.2 (-1.7, -0.7)	 5.2 (3.6) 0.3 (-0.2, 0.8)	 -1.5 (-2.2, -0.9) <0.0001
Reticulocyte (fraction of 1) Baseline Mean (SD) LS Mean Change (95% CI)	 0.37 (0.24) -0.10 (-0.13, -0.07)	 0.40 (0.22) 0 (-0.02, 0.03)	 -0.10 (-0.14, -0.06) <0.0001
LDH (U/L) Baseline Mean (SD) LS Mean Change (95% CI)	 348 (276) -92 (-124, -60)	 260 (140) -21 (-53, 11)	 -71 (-116, -26) 0.003
Haptoglobin (mg/dL) Baseline Mean (SD) LS Mean Change (95% CI)	 8.2 (10.7) 16.9 (8.8, 25.1)	 8.3 (13.8) 1.2 (-7.0, 9.4)	 15.8 (4.3, 27.3) 0.008

CI: confidence interval, LS Mean Change: least square mean change from baseline, SD: standard deviation

[1] All results are statistically significant.

[2] For Hb response, the difference is adjusted for randomization stratification factors, which included average screening Hb (<8.5, ≥8.5 g/dL) and *PKLR* gene variant category (missense/missense, missense/non-missense). The two-sided p-value is based on the Mantel-Haenszel stratum weighted method adjusting for the randomization stratification factors. For the endpoints of average change from baseline at Weeks 16, 20, and 24 for hemoglobin, indirect bilirubin, reticulocytes, LDH, and haptoglobin, the two-sided p-value is based on the mixed-effect model repeat measurement (MMRM) method, which included change from baseline as the dependent variable, baseline as a covariate, and treatment arm, visit, treatment-by-visit interaction, and the randomization stratification factors as fixed factors and subject as the random effect. All scheduled visits were included in the model.

	○ ACTIVATE-T Study Results: ▪ Median duration of treatment was 40.3 weeks; 74% (20 out of 27 patients) were exposed to Pyrukynd for > 40 weeks and < 47 weeks. ▪ 9 patients (33%) achieved the primary endpoint for reduction in transfusion burden ▪ 6 patients (22%) did not require any transfusions during the 24 week fixed dose treatment period ▪ All 6 patients who were transfusion free remained transfusion free in a long-term extension study. The median duration of response was 17 months (range: 11.5+, 21.8+).

ACTIVATE-T (NCT03559699) Endpoints	Pyrukynd N=27
Patients with Transfusion Reduction Response n (%) 95% CI	 9 (33) (17, 54)
Patients who were Transfusion Free n (%) 95% CI	 6 (22) (9, 42)

Price Per Unit (WAC):	• $460.00 per tablet across all strengths • Based on dosing of 1 tablet twice daily, annual cost of therapy is $335,800.00 • 28-Day Packs = $25,760.00 per pack ○ 56 of the 5 mg tablets ○ 56 of the 20 mg tablets ○ 56 of the 50 mg tablets • Taper Packs: ○ blister wallet containing 7 of the 5 mg tablets = $3,220.00 ○ blister wallet containing 7 tablets each of 20 mg and 5 mg tablets = $6,440.00 ○ blister wallet containing 7 tablets each of 50 mg and 20 mg tablets = $6,440.00
Therapeutic Alternatives:	• Pyrukynd is the first and only FDA-approved agent for PKD. • Therapeutic alternatives for PKD are supportive therapies for hemolytic anemia including blood transfusions, folic acid supplementation, splenectomy, and iron chelation therapy. ○ Increased red blood cell turnover in PKD may lead to folate deficiency. Routine administration however is not needed in those with adequate dietary intake. Discontinuation of folic acid therapy is reasonable for patients who no longer have ongoing hemolysis with Pyrukynd therapy. ○ Splenectomy can improve the hemolytic anemia and modestly improve Hb in about 50% of patients. It will now typically be reserved for those with severe transfusion dependent anemia not responsive to Pyrukynd therapy. ○ Iron chelation therapy is used frequently in PKD patients as they are at an increased risk of iron overload due not only to frequent blood transfusions, but also from increased iron absorption due to ineffective erythropoiesis. ○ For patients with severe transfusion-dependent PKD, especially after splenectomy, hematopoietic stem cell transplant may be offered. • In patients requiring frequent blood transfusions, Pyrukynd may reduce transfusion associated complications such as iron overload. However, only the reduction in transfusion burden was studied, not reductions in such related complications. • In patients who did not require regular transfusions, only changes in lab values such as Hb were measured and no objective indicators of disease severity. It is reasonable that real world benefits may be seen even in those with mild symptoms when hemolysis is reduced (i.e., improvement in fatigue and reduction in iron overload).

Prior Authorization Approval Criteria:	**Must meet the following criteria:** Initial Therapy: • Prescribed by or in consultation with a hematologist or other specialist in the treated disease state **AND** • Age ≥ 18 years **AND** • Documented diagnosis of symptomatic Pyruvate Kinase Deficiency (ICD-10 D55.21) **AND** • Documentation of genetic testing confirming presence of at least 2 variant alleles in the *PKLR* gene, of which at least 1 is a missense variant **AND** • Documentation of previous red blood cell transfusions for hemolytic anemia in the past year **AND** • Baseline Hemoglobin level of ≤ 10 g/dL **AND** • Lack of moderate to severe hepatic disease **AND** • Participant is not currently pregnant **AND** • Claim does not exceed 2 tablets per day • Initial approval for 3 months Continuation of Therapy: • Documentation of increase in Hb ≥ 1.5 g/dL from baseline **OR** • Documentation of reduction in transfusion burden from baseline **Additional Provider Diagnostic/Monitoring Criteria, if desired:** • Routine complete blood counts (CBC) and reticulocyte count • Routine iron studies as appropriate

Implication to State Medicaid Program:	• LOE: 2036 – 2038
	• Agios Pharmaceuticals has estimated a total of 3,000 to 8,000 patients to be eligible for treatment in the US and Europe combined.
	• Other Pyrukynd Clinical Trials in progress:
	  ○ ACTIVATE-Kids (NCT05175105) – Phase 3 trial in pediatric patients aged 1 – 17 years who are not regularly transfused
	  ○ ACTIVATE-KidsT (NCT05144256) – Phase 3 trial in pediatric patients aged 1 – 17 years who are regularly transfused
	  ○ ENERGIZE (NCT04770753) – Phase 3 trial in adult patients with non-transfusion dependent alpha or beta thalassemia
	  ○ ENERGIZE-T (NCT04770779) – Phase 3 trial in adult patients with transfusion dependent alpha or beta thalassemia
	  ○ NCT04610866 – Extension of a Phase 1 trial in adult patients with sickle cell disease who took part in and benefited from the initial study for long term safety and tolerability
	  ○ NCT05031780 – Phase 2/3 trial in patients aged 16 years or older with sickle cell disease
	• Another pyruvate kinase activator, FT-4202 from Forma Therapeutics, is in Phase 2 trials for thalassemia and sickle cell disease (NCT04987489). It is currently not being studied in PKD.
	• PKD is a potential candidate for gene therapy as the deficiency is the result of a defect in a single gene that primarily only affects one cell type. Clinical studies of gene therapy for PKD in mice have demonstrated increases in PK activity and Hb and reductions in reticulocyte count and spleen size. NCT04105166 is an open-label Phase I trial of gene therapy for PKD currently in recruitment status.

References:

- Pyrukynd® (mitapivat) [package insert]. Cambridge, MA: Agios Pharmaceuticals, Inc.; February 2022.
- Al-Samkari H, van Beers EJ. Mitapivat, a novel pyruvate kinase activator, for the treatment of hereditary hemolytic anemias. Ther Adv Hematol. 2021;12:20406207211066070. Published 2021 Dec 21. doi:10.1177/20406207211066070
- Grace RF, Mark Layton D, Barcellini W. How we manage patients with pyruvate kinase deficiency [published correction appears in Br J Haematol. 2019 May;185(4):807]. Br J Haematol. 2019;184(5):721-734. doi:10.1111/bjh.15758
- Prchal, J. Pyruvate kinase deficiency. UpToDate. Last updated March 3, 2022. Pyruvate kinase deficiency - UpToDate. Accessed March 18, 2022.
- Yaish, H. M. Pyruvate Kinase Deficiency. Medscape. Last updated February 23, 2022. Pyruvate Kinase Deficiency: Practice Essentials, Pathophysiology, Etiology (medscape.com). Accessed March 18, 2022.
- Know PK Deficiency: Testing Resources. Test to Confirm or Rule Out PK deficiency | For HCPs (knowpkdeficiency.com). Accessed March 10, 2022.
- IPD Analytics. Hematology: Pyruvate Kinase Deficiency. Accessed March 18, 2022.
- IPD Analytics. New Drug Review: Pyrukynd (mitapivat). March 2022.
- Al-Samkari H, Galactéros F, Glenthøj A, et al. Mitapivat versus Placebo for Pyruvate Kinase Deficiency. N Engl J Med. 2022;386(15):1432-1442. doi:10.1056/NEJMoa2116634
- NIH: U.S. National Library of Medicine. Pyruvate Kinase Deficiency Natural History Study (PKD NHS). Pyruvate Kinase Deficiency Natural History Study - Full Text View - ClinicalTrials.gov. Accessed March 18, 2022.
- NIH: U.S. National Library of Medicine. A Study to Evaluate Efficacy and Safety of AG-348 in Not Regularly Transfused Adult Participants With Pyruvate Kinase Deficiency (PKD). A Study to Evaluate Efficacy and Safety of AG-348 in Not Regularly Transfused Adult Participants With Pyruvate Kinase Deficiency (PKD) - Full Text View - ClinicalTrials.gov. Accessed March 18, 2022.
- NIH: U.S. National Library of Medicine. A Study Evaluating the Efficacy and Safety of AG-348 in Regularly Transfused Adult Participants With Pyruvate Kinase Deficiency (PKD). A Study Evaluating the Efficacy and Safety of AG-348 in Regularly Transfused Adult Participants With Pyruvate Kinase Deficiency (PKD) - Full Text View - ClinicalTrials.gov. Accessed March 18, 2022.
- NIH: U.S. National Library of Medicine. A Study to Evaluate the Efficacy and Safety of Mitapivat in Pediatric Participants With Pyruvate Kinase Deficiency (PKD) Who Are Not Regularly Transfused, Followed by a 5-Year Extension Period (ACTIVATE-Kids). A Study to Evaluate the Efficacy and Safety of Mitapivat in Pediatric Participants With Pyruvate Kinase Deficiency (PKD) Who Are Not Regularly Transfused, Followed by a 5-Year Extension Period - Full Text View - ClinicalTrials.gov. Accessed March 18, 2022.
- NIH: U.S. National Library of Medicine. A Study to Evaluate the Efficacy and Safety of Mitapivat in Pediatric Participants With Pyruvate Kinase Deficiency (PKD) Who Are Regularly Transfused, Followed by a 5-Year Extension Period (ACTIVATE-KidsT). A Study to Evaluate the Efficacy and Safety of Mitapivat in Pediatric Participants With Pyruvate Kinase Deficiency (PKD) Who Are Regularly Transfused, Followed by a 5-Year Extension Period - Full Text View - ClinicalTrials.gov. Accessed March 18, 2022.
- NIH: U.S. National Library of Medicine. A Study Evaluating the Efficacy and Safety of Mitapivat in Participants With Non-Transfusion-Dependent Alpha- or Beta-Thalassemia (α- or β-NTDT) (ENERGIZE). A Study Evaluating the Efficacy and Safety of Mitapivat in Participants With Non-Transfusion-Dependent Alpha- or Beta-Thalassemia (α- or β-NTDT) - Full Text View - ClinicalTrials.gov. Accessed March 18, 2022.
- NIH: U.S. National Library of Medicine. A Study Evaluating the Efficacy and Safety of Mitapivat in Participants With Transfusion-Dependent Alpha- or Beta-Thalassemia (α- or β-TDT) (ENERGIZE-T). A Study Evaluating the Efficacy and Safety of Mitapivat in Participants With Transfusion-Dependent Alpha- or Beta-Thalassemia (α- or β-TDT) - Full Text View - ClinicalTrials.gov. Accessed March 18, 2022.
- NIH: U.S. National Library of Medicine. Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Long-term Mitapivat Dosing in Subjects With Stable Sickle Cell Disease: An Extension of a Phase I Pilot Study of Mitapivat. Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Long-term Mitapivat Dosing in Subjects With Stable Sickle Cell Disease: An Extension of a Phase I Pilot Study of Mitapivat - Full Text View - ClinicalTrials.gov. Accessed March 18, 2022.
- NIH: U.S. National Library of Medicine. A Study Evaluating the Efficacy and Safety of Mitapivat (AG-348) in Participants With Sickle Cell Disease. A Study Evaluating the Efficacy and Safety of Mitapivat (AG-348) in Participants With Sickle Cell Disease - Full Text View - ClinicalTrials.gov. Accessed March 18, 2022.
- NIH: U.S. National Library of Medicine. A Study of FT-4202 in Patients With Thalassemia or Sickle Cell Disease. A Study of FT-4202 in Patients With Thalassemia or Sickle Cell Disease - Full Text View - ClinicalTrials.gov. Accessed March 18, 2022.
- NIH: U.S. National Library of Medicine. Gene Therapy for Pyruvate Kinase Deficiency (PKD). Gene Therapy for Pyruvate Kinase Deficiency (PKD) - Full Text View - ClinicalTrials.gov. Accessed March 18, 2022.