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Section:	Prescription Drugs	**Effective Date:**	July 1, 2022
Subsection:	Hematological Agents	**Original Policy Date:**	January 26, 2018
Subject:	Siklos	**Page:**	1 of 5

Last Review Date: June 16, 2022

Siklos

Description

Siklos (hydroxyurea)

Background
Sickle cell anemia is a genetically inherited condition which causes red blood cells to become sickle shaped. These “sickled” red blood cells can cause many complications including infections, hypertension, renal disease, stroke, retinopathy, and other chronic conditions. Painful crises are an acute condition caused by chronic sickle cell disease that causes much distress to people with sickle cell anemia. Hydroxyurea has been used to prevent these acute painful crises from occurring, as well as to improve survival and reduce other complications. Siklos is a new formulation of hydroxyurea specifically designed for use in sickle cell patients to decrease the need for blood transfusions as well as decrease the frequency of painful crises (1-2).

Regulatory Status
FDA approved indication: Siklos is indicated to reduce the frequency of painful crises and to reduce the need for blood transfusions in adult and pediatric patients, 2 years of age and older, with sickle cell anemia with recurrent moderate to severe painful crises (2).

Siklos carries boxed warnings for myelosuppression and malignancies. Due to the risk of myelosuppression, blood counts should be monitored every 2 weeks throughout the duration of therapy. Hydroxyurea is a human carcinogen and secondary leukemia has been reported in patients receiving long-term. Skin cancer has also been reported in patients receiving long-term hydroxyurea. Advise protection from sun exposure and monitor for the development of secondary malignancies (2).

Initiation of therapy is started at 20 mg/kg/day and is based on the patient's actual or ideal body weight, whatever is less. Dosing adjustments are made based on blood counts, therefore, it is imperative to monitor patients' CBCs during therapy (2).

Siklos can cause fetal harm when administered to pregnant women. Verify the pregnancy status of females of reproductive potential prior to initiating Siklos therapy. Females and males with partners of reproductive potential should be advised to use effective contraception during and after treatment with Siklos for at least 6 months after therapy (2).

Safety and effectiveness in pediatric patients 2 years of age and older have been established (2).

Related policies
Adakveo, Endari, Oxbryta

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Siklos may be considered **medically necessary** for patients 2 years of age or older for the treatment of sickle cell disease (SCD) when the conditions indicated below are met.

Siklos may be considered **investigational** in patients less than 2 years of age and for all other indications.

Prior-Approval Requirements

Age 2 years of age or older

Diagnosis

Patient must have following:

Sickle Cell Disease (SCD)

AND ALL of the following:

1. History of moderate to severe painful crises

2. Inadequate treatment response, intolerance, or contraindication to generic hydroxyurea
3. Prescriber agrees to monitor blood counts at least every 4 weeks throughout therapy and adjust dose accordingly
4. Prescriber agrees to monitor for the development of secondary malignancies
5. Female patients of reproductive potential **only**: Prescriber agrees to advise patient to use effective contraception during treatment and for at least 6 months after therapy
6. Male patients with partners of reproductive potential **only**: Prescriber agrees to advise patient to use effective contraception during treatment and for at least 6 months after therapy
7. **NOT** given concurrently with live vaccines

Prior – Approval *Renewal* Requirements

Age 2 years of age or older

Diagnosis

Patient must have following:

Sickle Cell Disease (SCD)

AND ALL of the following:

1. Decrease in number of painful crises
2. Prescriber agrees to monitor blood counts at least every 4 weeks throughout therapy and adjust dose accordingly
3. Prescriber agrees to monitor for the development of secondary malignancies
4. Female patients of reproductive potential **only**: Prescriber agrees to advise patient to use effective contraception during treatment and for at least 6 months after therapy
5. Male patients with partners of reproductive potential **only**: Prescriber agrees to advise patient to use effective contraception during treatment and for at least 6 months after therapy
6. **NOT** given concurrently with live vaccines

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Painful crises are an acute condition caused by chronic sickle cell disease that causes much distress to people with sickle cell anemia. Hydroxyurea has been used to prevent these acute painful crises from occurring, as well as to improve survival and reduce other complications. Siklos is indicated to reduce the frequency of painful crises and to reduce the need for blood transfusions patients with sickle cell anemia with recurrent moderate to severe painful crises (1-2).

Prior authorization is required to ensure the safe, clinically appropriate and cost-effective use of Siklos while maintaining optimal therapeutic outcomes.

References

1. National Heart, Lung, and Blood Institute (NHLBI): Evidence-Based Management of Sickle Cell Disease. Expert Panel Report, 2014. Published by: U.S. Department of Health and Human Services, National Institutes of Health. https://www.nhlbi.nih.gov/sites/default/files/media/docs/sickle-cell-disease-report%20020816_0.pdf . Accessed on August 3, 2021.
2. Siklos [package insert]. Bryn Mawr, PA: Medunik USA Inc.; December 2021.

Policy History

Date	Action
January 2018	Addition to PA
March 2018	Annual review

November 2018	Annual review and reference update. Addition of effective contraception requirement and changed CBC monitoring from every 2 weeks to every 4 weeks per SME
September 2019	Annual review and reference update
September 2020	Annual review
September 2021	Annual review and reference update
June 2022	Annual editorial review and reference update. Revised contraception requirements for consistency

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 16, 2022 and is effective on July 1, 2022.