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# 5.85.027

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| <b>Section:</b>    | Prescription Drugs   | <b>Effective Date:</b>       | July 1, 2023     |
| <b>Subsection:</b> | Hematological Agents | <b>Original Policy Date:</b> | January 26, 2018 |
| <b>Subject:</b>    | Siklos               | <b>Page:</b>                 | 1 of 5           |

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**Last Review Date:** June 15, 2023

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## 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).

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|                    |                      |                              |                  |
|--------------------|----------------------|------------------------------|------------------|
| <b>Section:</b>    | Prescription Drugs   | <b>Effective Date:</b>       | July 1, 2023     |
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| <b>Subject:</b>    | Siklos               | <b>Page:</b>                 | 2 of 5           |

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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 and 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** if the conditions indicated below are met.

Siklos may be considered **investigational** 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

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|                    |                      |                              |                  |
|--------------------|----------------------|------------------------------|------------------|
| <b>Section:</b>    | Prescription Drugs   | <b>Effective Date:</b>       | July 1, 2023     |
| <b>Subsection:</b> | Hematological Agents | <b>Original Policy Date:</b> | January 26, 2018 |
| <b>Subject:</b>    | Siklos               | <b>Page:</b>                 | 3 of 5           |

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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

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|                    |                      |                              |                  |
|--------------------|----------------------|------------------------------|------------------|
| <b>Section:</b>    | Prescription Drugs   | <b>Effective Date:</b>       | July 1, 2023     |
| <b>Subsection:</b> | Hematological Agents | <b>Original Policy Date:</b> | January 26, 2018 |
| <b>Subject:</b>    | Siklos               | <b>Page:</b>                 | 4 of 5           |

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## 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](https://www.nhlbi.nih.gov/sites/default/files/media/docs/sickle-cell-disease-report%20020816_0.pdf)
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 |

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|                    |                      |                              |                  |
|--------------------|----------------------|------------------------------|------------------|
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| <b>Subject:</b>    | Siklos               | <b>Page:</b>                 | 5 of 5           |

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| 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 |
| June 2023      | Annual review. Changed policy number to 5.85.027   |

## Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 15, 2023 and is effective on July 1, 2023.**