Please note that patients must take Siklos® once a day at the same time each day. Siklos® is toxic to certain cells in the body. Therefore, anyone handling Siklos® tablets or bottles containing Siklos® tablets MUST follow these instructions at all times:

Before you get started, assemble the following items:
- Bottle of Siklos® tablets
- Disposable gloves
- Teaspoon and water to dissolve tablets
- Paper towel
- Plastic bag or other closed disposable container
- Detergent solution

1. Wash your hands with soap and water.
2. Put on disposable gloves. You must wear disposable gloves AT ALL TIMES when handling Siklos® tablets or bottles containing Siklos® tablets.
3. Immediately wipe up any powder spilled from Siklos® tablets with a damp disposable paper towel, using a detergent solution followed by clean water.
4. Remove disposable gloves only after administering Siklos® and cleaning up any spills.
5. Throw away the disposable paper towel and gloves in a closed container, such as a plastic bag or other disposable container, to avoid harm to other people.
6. Wash hands again with soap and water after removing gloves.

Please see Important Safety Information, including Boxed Warning, on following pages.

In case of accidental contact with Siklos® tablets or powder from tablets:
- Immediately wash any skin that comes into contact with a crushed or broken Siklos® tablet thoroughly with soap and water.
- Immediately flush eyes thoroughly with water or isotonic eyewash for at least 15 minutes if contact with crushed or broken tablets happens in the eyes.
**Siklos® 1,000 mg tablet** has three separation lines (score lines) and can be broken at these score lines to provide smaller doses. Each 1,000 mg tablet can be divided into 4 equal parts (each part is 250 mg).

**Siklos® 100 mg tablet** has one separation line (score line) and can be broken at this score line to provide smaller doses. Each 100 mg tablet can be divided into 2 equal parts (each part is 50 mg).

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**Breaking Instructions**

You will need the following supplies to break a Siklos® 100 mg or 1,000 mg tablet:
- A damp disposable paper towel
- A tablet cutter
- Disposable gloves

1. Place a damp disposable paper towel on a flat surface where the tablets will be broken.
2. Wash and dry your hands before handling Siklos® tablets or bottles containing the tablets.
3. Put on disposable gloves.
4. Remove the number of Siklos® tablets from the bottle needed to get the prescribed dose.
5. Use your index fingers and thumbs to hold each end of the Siklos® tablet.
6. While holding the ends of the Siklos® 1,000 mg or 100 mg tablet, push down on the tablet to break the tablet on the score line to get your prescribed dose.
**New!**

**SCORED TABLET**

**TRIPLE SCORED TABLET**

**BREAKING INSTRUCTIONS**

**Siklos® 1,000 mg tablets** can be broken as:
- 1/4 of a tablet for a dose of 250 mg of Siklos®
- 1/2 of a tablet for a dose of 500 mg of Siklos®
- 3/4 of a tablet for a dose of 750 mg of Siklos®
- a whole tablet for a dose of 1,000 mg of Siklos®

(no breaking needed)

Note: You may need to use a tablet cutter.

**Siklos® 100 mg tablets** can be broken as:
- 1/2 of a tablet for a dose of 50 mg of Siklos®
- a whole tablet for a dose of 100 mg of Siklos®

(no breaking needed)

Note: You may need to use a tablet cutter.

**Throw away the damp disposable paper towel in the trash and immediately wipe up any powder spilled from Siklos® tablets with a damp disposable paper towel, using a detergent solution followed by clean water.**

**After administering Siklos®, pull off disposable gloves and throw away in the trash.**

**Wash and dry your hands.**

**Store any unused broken tablets in the bottle and put the bottle back in the box. Broken tablets must be used within three months.**

**INDICATION AND IMPORTANT SAFETY INFORMATION**

**SIKLOS® (hydroxyurea) tablets, for oral use**

**INDICATION**

SIKLOS is an antimetabolite indicated to reduce the frequency of painful crises and to reduce the need for blood transfusions in pediatric patients 2 years of age and older with sickle cell anemia with recurrent moderate to severe painful crises.

**IMPORTANT SAFETY INFORMATION**

**WARNING: MYELOSUPPRESSION and MALIGNANCIES**

See Full Prescribing Information for complete Boxed Warning.

- **Myelosuppression:** SIKLOS may cause severe myelosuppression. Do not give if bone marrow function is markedly depressed. Monitor blood counts at baseline and throughout treatment. Interrupt treatment and reduce dose as necessary.
- **Malignancies:** Hydroxyurea is carcinogenic. Advise sun protection and monitor patients for malignancies.
## Risks with Concomitant Use of Antiretroviral Drugs

Avoid use of SIKLOS in patients with wounds on the legs (leg ulcers), leukocytoclastic vasculitis, spontaneous vasculitic ulcers reported in patients with myeloproliferative disease (a condition currently receiving interferon therapy. Due to potentially severe clinical outcomes for the cutaneous vasculitic toxicities were reported most often in patients with a history of, or currently receiving, interferon therapy. Due to potentially severe clinical outcomes for the cutaneous vasculitic ulcers reported in patients with myeloproliferative disease (4%) currently receiving interferon therapy. Due to potentially severe clinical outcomes for the cutaneous vasculitic ulcers reported in patients with myeloproliferative disease (4%), including headache (2.7%), fever (2.5%) and nervous system disorders (4%), including headache (2.7%).

### USE IN SPECIFIC POPULATIONS

- **Pregnancy:** SIKLOS can cause fetal harm based on findings from animal studies and the drug's mechanism of action. Advise pregnant women of the potential risk to a fetus.
- **Lactation:** It is not known whether SIKLOS is excreted in human milk, the effects of SIKLOS on the breastfed child, or the effects of SIKLOS on milk production. Because of the potential for serious adverse reactions in a breastfed child from SIKLOS, including carcinogenicity, advise patients not to breastfeed during treatment with SIKLOS.
- **Females and Males of Reproductive Potential:** Advise patients to inform their healthcare provider of a known or suspected pregnancy. Advise females and males of reproductive potential to use contraception during and after treatment with SIKLOS for at least 6 months after therapy. Based on findings in animals and humans, male fertility may be compromised by treatment with SIKLOS. Prior to therapy, advise male patients about the possibility of sperm conservation.
- **Pediatric Use:** Continuous follow-up of the growth of treated children is recommended. Pediatric patients aged 2-16 years had a higher risk of neutropenia than patients more than 16 years old. The safety and effectiveness of SIKLOS have not been established in pediatric patients less than 2 years of age.
- **Renal Impairment:** The exposure to SIKLOS is higher in patients with creatinine clearance of less than 60 mL/min. Reduce dosage and closely monitor the hematologic parameters when SIKLOS is to be administered to these patients.
- **Hepatic Impairment:** Monitor hematologic parameters more frequently in patients with hepatic impairment receiving SIKLOS.

### OVERDOSAGE

Acute mucocutaneous toxicity has been reported in patients receiving hydroxyurea at doses several times above the therapeutic dose. Soreness, violet erythema, oedema on palms and soles followed by scaling of hand and feet, severe generalized hyperpigmentation of the skin and stomatitis have been observed.

### DOSAGE AND ADMINISTRATION

SIKLOS dosing is based on patient’s actual or ideal weight, whichever is less. Specific parameters (blood counts) must be monitored every 2 weeks throughout treatment with SIKLOS and dosing must be adjusted accordingly. Dosing recommendation based on blood count:
- Initial recommended dose is 20 mg/kg once daily based on patient's actual or ideal weight.
- Increase dose 5 mg/kg/day every 8 weeks or if a painful crisis occurs, until a maximum tolerated dose of 35 mg/kg/day is reached.
- If blood counts are considered toxic, discontinue SIKLOS until hematologic recovery.
- Reduce the dose of SIKLOS by 50% in patients with renal impairment (creatinine clearance of less than 60 mL/min). Monitor the hematologic parameters closely in these patients.

SIKLOS is available in 100 mg and 1,000 mg tablets. The 100 mg tablets have 1 score line and can be split into 2 parts (each 50 mg). The 1,000 mg tablets have 3 score lines and can be split into 4 parts (each 250 mg).

The tablets should be taken once daily, at the same time each day, with a glass of water. For patients who are not able to swallow the tablets, these can be dispersed immediately before use in a small quantity of water in a teaspoon.

- **SIKLOS is a cytotoxic drug.**
- **Ensure patients follow applicable special handling and disposal procedures.**

To report suspected adverse reactions, contact Medunik USA at 1-844-884-5520 or medicalinfo@medunikusa.com.

Please read the Full Prescribing Information, including Boxed Warning at www.SIKLOSusa.com.