Package leaflet: information for the user

Siklos 100 mg film-coated tablets
Siklos 1000 mg film-coated tablets
hydroxycarbamide

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, or pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Siklos is and what it is used for

Siklos is used to prevent painful crises, including sudden chest pain, caused by Sickle Cell disease, in adults, adolescents and children older than 2 years.

Sickle Cell disease is an inherited blood disorder that affects the disc shaped red cells of the blood. Some cells become abnormal, rigid and take a crescent or sickle shape which leads to anemia.
The sickle cells also get stuck in blood vessels, blocking blood flow. This can cause acute pain crises and organ damage.

For severe painful crises, most patients require hospitalisation.Siklos will decrease the number of painful crises as well as the need for hospitalisation linked with the disease.

The active substance of Siklos, hydroxycarbamide, is a substance which inhibits growth and proliferation of some cells, such as blood cells. These effects lead to a reduction of circulating red, white and coagulation blood cells (myelosuppressive effect). In Sickle Cell disease, hydroxycarbamide helps also to prevent red blood cells from taking abnormal shape.

2. What you need to know before you take Siklos

Do not take Siklos

- if you are allergic to hydroxycarbamide or any of the other ingredients of this medicine (listed in section 6),
- if you suffer from severe liver disease,
- if you suffer from severe kidney disease,

- if you are myelosuppressed (if you have decreased production of red, white, or coagulating blood cells) as described in section 3 “How to take Siklos, Treatment follow-up”,
- if you are breast-feeding (see section “Pregnancy,breast-feeding and fertility”).

Warnings and precautions

Talk to your doctor or pharmacist or nurse before taking Siklos

- if you have a liver disease,
- if you have a kidney disease,
- if you have leg ulcers,
- if you are taking other myelosuppressive medicines (decrease production of red, white, or coagulating blood cells) or receiving radiation therapy,
- if you have a known lack of vitamin B12 or folate.

If you experience (or have experienced) any of the above, please tell your doctor. If you have any question, please ask your doctor or pharmacist or nurse.

Patients and/or parents or the legal responsible person must be able to follow directions regarding the administration of this medicine, their monitoring and care.

Other medicines and Siklos

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.
Information sharing is especially required for
- antiretroviral medicines (those that inhibit or destroy a retrovirus such as HIV), e.g. didanosine, stavudine and indinavir (a drop in your white cell count may occur) ,
- myelosuppressive medicines (those that decrease production of red, white, or coagulating blood cells) and radiation therapy,
- some vaccines.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

Siklos is not recommended during pregnancy. Please contact your doctor if you think you may be pregnant. The use of effective contraception is strongly recommended.

If you become pregnant or plan to become pregnant while taking Siklos, your doctor will discuss with you the potential benefits and risks of continuing using Siklos.

For male patients taking Siklos, if your partner becomes pregnant or plans to become pregnant, your doctor will discuss with you the potential benefits and risks of continuing using Siklos.

The active substance of Siklos passes into human breast-milk. You must not breast-feed while taking Siklos.

Hydroxycarbamide may decrease sperm production in male patients while they are being treated.

Driving and using machines

Some people may experience dizziness when using Siklos. Do not drive or use any tools or machines if you experience dizziness whilst taking Siklos.

3. How to take Siklos

Always take Siklos exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Dose

Your doctor will tell you how much of Siklos to take each day and will describe the dose in whole, half or quarter tablets.

The prescribed dose of Siklos must be taken once daily, preferably in the morning before breakfast. It can be taken with a glass of water or a very small amount of food.
If you cannot swallow the tablets, you can disintegrate them in water **immediately before use**:

- Place the required dose (preferably broken if Siklos 1000 mg tablet is used) in a teaspoon and add some water.
- As soon as the tablet is disintegrated, swallow the content of the teaspoon. You can add a drop of syrup or mix the content with food to mask a possible bitter taste.
- Then drink a large glass of water or any other drink.

Handling

Siklos is a cytotoxic medicine that must be handled with care.
Any person, in particular pregnant women, who are not taking Siklos should avoid direct contact with the parts when breaking a tablet. Wash your hands before and after contact with the tablets.
In case the prescribed dose requires breaking the tablet in halves or quarters, this should be done out of the reach of food. Powder spilled from the broken tablet should be wiped up with a damp disposable towel which must be thrown out. For the storage of unused broken tablets, see section 5 “How to store Siklos”.

Treatment follow-up

Your doctor will tell you how long to take Siklos.

When taking Siklos you will have regular blood tests and check your liver and kidney. Depending on the dose you take, these tests may be performed every two weeks or every two months. Depending on these results your doctor will adjust your dose of Siklos.

The growth of children using Siklos should be regularly monitored by the treating doctor.

If you take more Siklos than you should

If you take more Siklos than you should or if a child has taken any, contact your doctor or the nearest hospital immediately as you may need urgent medical treatment. The most common symptoms of overdose with Siklos are:

- Redness of the skin,
- Soreness (touch is painful) and swelling of the palms of hands and soles of feet followed by the hands and feet becoming scaly,
- Skin becoming strongly pigmented (locally changes of colour),
- Soreness or swelling in the mouth.

If you forget to take Siklos

Do not take a double dose to make up for a forgotten tablet. Continue as normal when it is time to take the next dose as prescribed by your doctor.

If you stop taking Siklos

Do not stop your treatment unless advised by your doctor.
If you have any further question on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, Siklos can cause side effects, although not everybody gets them.

Tell your doctor immediately if you notice any of the following serious side effects:
- A severe infection,
- Tiredness and/or looking pale,
- Unexplained bruising (accumulation of blood under the skin) or bleeding,
- Unusual headache,
- Difficulties in breathing.

Tell your doctor as soon as possible if you notice any of the following side effects:
- Fever or chills,
- Feeling sick, or a general feeling of being unwell,
- Rash (itching red eruption of the skin),
- Ulcers or wounds on your legs,
- Sore (open skin infection) on your skin,
- Disorientation (confusion) and dizziness.

DETAILS OF SIDE EFFECTS

Very common side effects (may affect more than 1 in 10 people):
Low blood cell counts (myelosuppression), enlargement of red blood cells, decreased resistance to infections.
Absence or low amount of sperm in the semen (azoospermia or oligospermia). Siklos may hence decrease the ability of men to father children.

Common side effects (may affect up to 1 in 10 people):
Reduced number of red blood cells (anaemia), low platelet count, headache, skin reactions, inflammation or ulceration of the mouth (oral mucositis).

Uncommon side effects (may affect up to 1 in 100 people):
Dizziness, nausea, itching red eruption of the skin (rash), black nails (melanonychia), and hair loss.

Rare side effects (may affect up to 1 in 1,000 people):
Wounds on the legs (leg ulcers), and modification of liver function.

Very rare side effects (may affect up to 1 in 10,000 people) or unknown frequency (frequency cannot be estimated from the available data):
Inflammation of the skin causing red scaly patches and possibly occurring together with pain in the joints.

Isolated cases of malignant disease of blood cells (leukaemia), skin cancer in elderly patients, viral infection with *Parvovirus B19*, bleeding, gastrointestinal disturbances, vomiting, skin dryness, fever, absence of menstrual cycles (amenorrhoea), and weight gain.

Reporting of side effects
If you get any side effects, talk to your doctor or, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Siklos

Keep this medicine out of the sight and reach of children.

Do not use Siklos after the expiry date which is stated on the carton and the bottle after EXP.

Store below 30°C.

Unused broken tablets must be replaced in the bottle and must be used within three months.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Siklos contains

- The active substance is hydroxycarbamide.
  Each Siklos 100 mg film-coated tablet contains 100 mg hydroxycarbamide.
  Each Siklos 1000 mg film-coated tablet contains 1,000 mg hydroxycarbamide.

- The other ingredients are sodium stearyl fumarate, silicified microcrystalline cellulose and basic butylated methacrylate copolymer.

What Siklos looks like and contents of the pack

Siklos 100 mg film-coated tablets are off-white, oblong-shaped tablets with a break line on both sides. The tablet can be divided into two equal parts.
Each half of tablet is embossed “H” on one side.
Siklos 100 mg is supplied in plastic bottles containing 60, 90 or 120 tablets.

Siklos 1000 mg film-coated tablets are off-white, capsule-shaped tablets marked with three score lines on both sides. The tablet can be divided into four equal parts.
Each quarter of tablet is embossed “T” on one side.
Siklos 1000 mg is supplied in plastic bottles containing 30 tablets.

All pack sizes may not be marketed.

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This leaflet was last approved in July 2019.

Detailed information on this medicine is available on the European Medicines Agency website http://www.ema.europa.eu/. There are also links to other websites about rare diseases and treatments.