

Xromi[®] (Hydroxycarbamide)

100 mg/ml oral solution

Patient / Parent Guide

Important safety information about serious side effects that you need to be aware of before, during and after treatment

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1. Why your doctor has prescribed Hydroxycarbamide

Your doctor has prescribed Hydroxycarbamide for you or your child to treat a condition called sickle cell disease. This is an inherited disease that affects the red cells of the blood. Some cells become abnormal, rigid and take a crescent or sickle shape which leads to anaemia. The sickle cells also get stuck in blood vessels, blocking blood flow. This can cause acute pain crises and organ damage

Hydroxycarbamide is used to prevent the complications of blocked blood vessels caused by sickle cell disease in patients over 2 years of age

Hydroxycarbamide will decrease the number of painful crises as well as the need for hospitalisation as a result of the disease

- ◇ Hydroxycarbamide has been prescribed for you. Never give it to someone else, even if he or she has the same disorder for which you are being treated
- ◇ Take this medication exactly as it has been prescribed for you by your doctor. Take your treatment regularly and do not change the dose yourself

Hydroxycarbamide may interact with other medicines and live virus vaccines. Please tell your doctor if you are taking or have recently taken any other medicines, even those obtained without a prescription. Please tell your doctor if you have had or are due to have any vaccinations (e.g. measles, mumps, rubella (MMR), chicken pox)

Before starting the treatment, read the package leaflet present in each box of Hydroxycarbamide

2. Hydroxycarbamide must be handled with care

Please use the syringe as advised by your doctor or pharmacist
Ask your doctor or pharmacist if you have any questions

Each pack contains one bottle 150 ml capped with a child-resistant closure, a bottle adaptor and two dosing syringes (a red syringe graduated to 3 ml and a white syringe graduated to 12 ml)



	Syringe Type	
Syringe volume	3 ml	12 ml
Colour	Red	White
Measurements	0.5 ml to 3 ml	1 ml to 12 ml

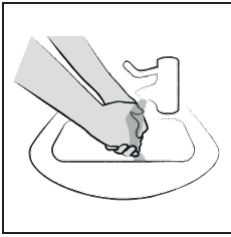
Your doctor or pharmacist will advise which syringe to use depending on the dose that has been prescribed

IMPORTANT

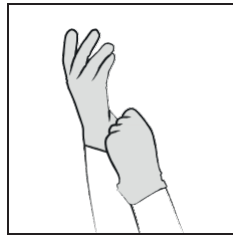
- ◇ **Women who are pregnant, planning to be or breastfeeding should not handle Hydroxycarbamide**
- ◇ **Hydroxycarbamide may be taken with or after meals at any time of the day.** However, the choice of method and time of day should be consistent from day to day
- ◇ **Water should be taken after each dose of Hydroxycarbamide, to assist accurate and consistent dose delivery to the stomach**

- ◇ Keep out of the sight and reach of children. Accidental ingestion can be lethal for children
- ◇ Store in a refrigerator (2°C - 8°C). After first opening of the bottle, discard any unused contents after 12 weeks
- ◇ Keep the bottle tightly closed to prevent spoilage of the medicine and reduce the risk of accidental spillage. To minimise air bubbles, the bottle should **not** be shaken prior to dosing

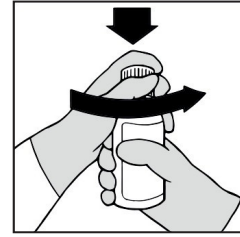
Handling



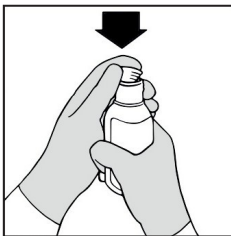
1. Wash your hands before and after administering a dose. Wipe up spillages immediately



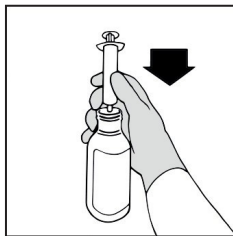
2. Put on disposable hand gloves to decrease the risk of exposure



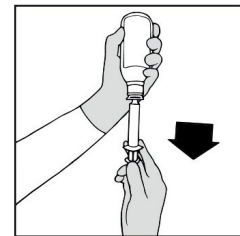
3. Remove the bottle cap



4. Push the adaptor firmly into the top of the bottle and leave in place for future doses

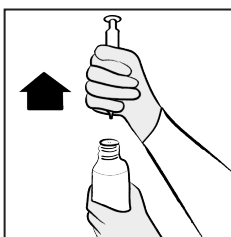


5. Push the tip of the dosing syringe into the hole in the adaptor. Your doctor or pharmacist will advise you of the correct syringe to use, either the 3 ml (red syringe) or the 12 ml (white syringe) in order to give the correct dose



6. Turn the bottle upside down. Pull the plunger of the syringe back so that the medicine is drawn from the bottle into the syringe. Pull the plunger back to the point on the scale that corresponds to the dose prescribed

If you are not sure about how much medicine to draw into the syringe, always ask your doctor or nurse for advice



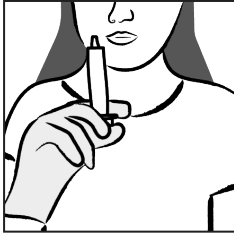
7. Turn the bottle back the right way up and carefully remove the syringe from the adaptor, holding it by the barrel rather than the plunger



8. Gently put the tip of the syringe into your mouth and to the inside of your cheek



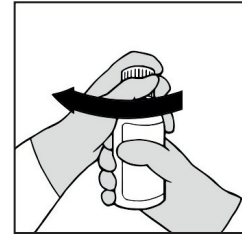
9. Slowly and gently push the plunger down to gently squirt the medicine into the inside of your cheek and swallow it. DO NOT forcefully push down the plunger, or squirt the medicine to the back of your mouth or throat, as you may choke



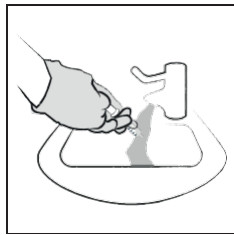
10. Remove the syringe from your mouth



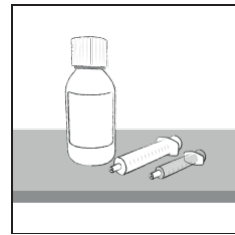
11. Swallow the dose of oral solution then drink some water, making sure no medicine is left in your mouth



12. Put the cap back on the bottle with the adaptor left in place. Ensure that the cap is tightly closed



13. Wash the syringes with cold or warm tap water and rinse well. Hold the syringe under water and move the plunger up and down several times to make sure the inside of the syringe is clean. Let the syringe dry completely before you use it again



14. Store the syringe in a hygienic place with the medicine

Wash immediately and thoroughly with soap and water if Hydroxycarbamide comes into contact with skin, eyes or nose

3. When you are treated with Hydroxycarbamide, it is very important to be regularly monitored by your doctor

3.1 Reduced production of blood cells in the bone marrow (the soft, organic, sponge like material in the cavities of bones)

When you take Hydroxycarbamide your doctor will need to take regular blood tests, to check the number and type of cells in your blood

These tests may be performed

- ◇ Initially every two weeks and then every 2-3 months

Depending on these results your doctor may change your dose or temporarily withhold the dosing

- Other medicines that reduce the production of blood cells in the bone marrow and radiotherapy treatment

You will have to talk to your doctor, pharmacist or nurse before taking Hydroxycarbamide

- ◇ **If you are taking other myelosuppressive medicines (medicines that decrease production of red, white, or coagulating blood cells)**
- ◇ **If you are receiving radiation therapy, chemotherapy, or are currently taking any medicines for cancer treatment (especially interferon therapy)**

When used with Hydroxycarbamide

- ◇ There is greater chance of bone marrow depression, gastro-intestinal disturbances and soreness and inflammation of the mouth and gut

Redness of the skin may reoccur when Hydroxycarbamide is given to patients who have received irradiation therapy in the past

3.2 Use with medicines that inhibit or destroy a retrovirus such as HIV

Tell your doctor, nurse or pharmacist if you are taking any antiretroviral medicines (those that inhibit or destroy a retrovirus such as HIV), e.g. didanosine, stavudine and indinavir

Hydroxycarbamide should not be used in combination with antiretroviral agents for HIV disease

A drop in your white cell count, severe liver damage and failure and peripheral neuropathy may occur

3.3 Ulcers of the skin and inflammation of blood vessels

Ulcers

Talk to your doctor, pharmacist or nurse before taking Hydroxycarbamide if you have leg ulcers or wounds

Leg ulcers are a common complication of sickle cell disease, but have also been reported in patients treated with hydroxycarbamide. In patients with leg ulcers, hydroxycarbamide should be used with caution

Talk to your doctor if you develop inflammation or ulceration of the mouth (oral mucositis) when treated with Hydroxycarbamide

Inflammation of the blood vessels (vasculitis)

During therapy with hydroxycarbamide, vasculitis in the skin (which can sometimes lead to ulcers and gangrene) has occurred in patients with myeloproliferative disorders

The risk is increased in patients who have previously received or are receiving interferon therapy

Hydroxycarbamide should be discontinued if skin ulcers develop

3.4 Long term safety

- Hydroxycarbamide may affect the DNA synthesis. Development of cancer such as skin cancer and secondary cancers e.g. secondary leukaemia in elderly patients

Hydroxycarbamide may potentially affect DNA synthesis causing damage to the cells

In patients receiving long-term hydroxycarbamide there have been reports of

◇ **Skin cancer**

Please protect your skin from sun exposure, conduct self-inspection of the skin and be screened for secondary malignancies during your routine follow-up visits to the doctor (especially if you are older)

◇ **Isolated cases of cancer of blood cells (leukaemia)**

In some patients receiving long-term therapy with hydroxycarbamide for various types of blood tumours, secondary leukaemia has been reported

It is unknown whether this is due to hydroxycarbamide or is a consequence of the patient's underlying disease

3.5 Use of hydroxycarbamide if you have liver and/or kidney disease

- ◇ **Please talk to your doctor pharmacist or nurse if you have any liver or kidney disease**
- ◇ If you have kidney disease your doctor may need to give you a lower dose
- ◇ Hydroxycarbamide should be used with caution in patients with marked kidney disease
- ◇ Do not take Hydroxycarbamide if you suffer from severe liver disease or/and severe kidney disease
- ◇ **Your kidney and liver function should be checked prior to, and repeatedly during treatment with hydroxycarbamide**
- ◇ Discontinue Hydroxycarbamide immediately if jaundice becomes apparent

3.6 Effect of hydroxycarbamide on the development of the foetus (birth defects); male fertility; need for contraception; breastfeeding

Talk to your doctor, nurse or pharmacist concerning the use of contraceptive measures before and during treatment with Hydroxycarbamide

Hydroxycarbamide is an active substance which may cause changes to the DNA (mutagenic)

The use of effective contraception before and during treatment is strongly recommended for both male and female patients

(i) If you are a man

Hydroxycarbamide may decrease your ability to father children (fertility) while you are treated

It is important for you to know that Hydroxycarbamide may decrease sperm production and harm your sperm

Absence or low amount of sperm in the semen (azoospermia or oligospermia) is a very common side effect of hydroxycarbamide. These disorders can be also associated with the underlying disease. Although in general reversible, it has to be taken into account when fatherhood is desired

Talk to your doctor or nurse if this is a concern for you. Your doctor can inform you about the possibility of sperm conservation (cryopreservation) before the start of therapy

(ii) If you are a woman of childbearing potential

Do not take Hydroxycarbamide if you are planning to have a baby without first speaking to your doctor for advice

Hydroxycarbamide should be stopped 3 to 6 months prior to becoming pregnant, if possible

Hydroxycarbamide can potentially cause foetal harm (birth defects) when administered to a pregnant woman, as it can cross the placental barrier

It may affect the DNA synthesis and as it is toxic to the cells (cytotoxic) it can potentially produce birth defects (teratogenic effect)

Hydroxycarbamide must not be used during pregnancy

If you become pregnant while you are still taking Hydroxycarbamide, please contact your doctor immediately

Please contact your doctor immediately if you think you may be pregnant

Breastfeeding

Hydroxycarbamide is excreted in human breast milk. You should not breastfeed during the treatment

You should not handle Hydroxycarbamide if you are pregnant, planning to be or breastfeeding

3.7 Influence on the growth of the children and adolescents

The doctor will monitor growth (height and weight) in children and adolescents, as it can be affected in patients with sickle cell disease. Currently, it is not known whether Hydroxycarbamide can impact children's growth

4. Side effects which have been observed with Hydroxycarbamide

Like all medicines, Hydroxycarbamide can cause side effects (although not everybody gets them). If any of these side effects become serious, or if you notice any side effects not listed here, please tell your doctor or pharmacist

- Key signs and symptoms of serious adverse reactions

If you get any of the following side effects, talk to your doctor or go to hospital immediately

- ◇ A severe infection
- ◇ Fever or chills
- ◇ Tiredness and/or looking pale
- ◇ Unexplained bruising (accumulation of blood under the skin) or bleeding
- ◇ Any yellowing of the whites of the eyes or skin (jaundice)
- ◇ Inflammation of the skin causing red scaly patches and possibly occurring together with pain in the joints
- ◇ Ulcers or wounds on legs
- ◇ Sore (open skin infection) on your skin

5. Important signs and symptoms of the disease

Some signs and symptoms may require you to call a doctor or to visit an emergency department

These may be caused by disease progression or show that your treatment is not working or be a side effect linked to the medicinal product

You should never hesitate to discuss your condition, or your treatment with any doctor, especially if it is not your usual doctor. This will help the doctor to choose the right treatment and to administer it more rapidly

- Acute painful crises

This is referred to as an episode of extreme pain, and is the major symptom of the sickle cell disease which can start in childhood or adulthood

The pain which affects mainly the bones and joints, is often difficult to relieve by usual painkillers (analgesics). Other organs may be affected (lungs, kidneys, brain, inner ear, etc.), which explains why the symptoms vary greatly between patients. The crises may occur suddenly and resolve rapidly or last several days. The episodes of acute pain may occur several times a year. For severe painful crises, most patients require hospitalisation

- When to seek urgent attention from healthcare provider

Seek urgent attention from a healthcare provider in the following cases

- ◇ Pain which is not relieved by usual painkillers (analgesics)
- ◇ Your temperature is above 38.5°C, even if there is no pain
- ◇ Vomiting
- ◇ A sudden pallor, fatigue or impairment of your health status, a sudden increase of the volume of your spleen (your doctor will tell you how to palpate your spleen)
- ◇ If you are a man and you have an involuntary, painful erection which lasts for more than three hours (priapism)

When the vaso-occlusive crises affect the lungs, it is called “acute chest syndrome” (ACS): The patient has chest pains, fever and difficult breathing. He/she is out of breath. This can occur in both adults and children. If it does, a doctor must be seen **urgently**

- Infections

When you have sickle cell disease, you are more susceptible to infections (illness with fever). This is mainly because your spleen is less effective at filtering out certain types of bacteria. Any infection can trigger a vaso-occlusive crisis or an acute chest syndrome. It is therefore important for you to consult your doctor if you have a fever or any other sign or symptom of infection

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for **MHRA Yellow Card** in the Google Play or Apple App Store

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

6. Patient Information Leaflet

The patient information leaflet (PIL) is available
on the Electronic Medicines Compendium
(www.medicines.org.uk) at
<https://www.medicines.org.uk/emc/product/10549/pil>