Xromi® (Hydroxycarbamide)
100 mg/ml oral solution

Healthcare Professional Guide

Important information on minimising the risk of medication errors and serious adverse events

This document has been reviewed and approved by The Saudi Food and Drug Authority (SFDA)

Keep this guide in a safe place for further reference.
A patient guide is available. You are requested to provide the patient guide to every patient/caregiver when treatment with Hydroxycarbamide is initiated.

Contents

1. Indication, dosage and dose adjustment

Indication

Hydroxycarbamide is indicated for the prevention of vaso-occlusive complications of Sickle Cell Disease in patients over 2 years of age.

Dosage and dose adjustment

Hydroxycarbamide is for oral use.

Treatment should be supervised by a physician or other healthcare professionals experienced in the management of patients with Sickle Cell Disease.

The posology should be based on the patient's body weight (kg)

- **Hydroxycarbamide may be taken with or after meals at any time of the day but patients should standardise the method of administration and time of day.**
- **Water should be taken after each dose of Hydroxycarbamide to assist accurate and consistent dose delivery to the stomach.**
- **In adults without swallowing difficulties, solid oral formulations may be more appropriate and convenient.**

The table below summarises the recommended dosage and adjustments according to the patient's features:

Cases	Recommended dosage and adjustment
Adults	◇ Usual starting dose: 15 mg/kg/day ◇ Usual maintenance dose: between 20-25 mg/kg/day ◇ Maximum dose: 35 mg/kg/day **Hydroxycarbamide causes bone marrow suppression and haematological status must be monitored**
Children and adolescents (2-18 years of age)	No dose adjustments are necessary
Children less than 2 years of age	**Not indicated** for children less than 2 years of age
Elderly	Lower dosage regimen may be required

Cases	Recommended dosage and adjustment
Renal impairment	◇ If creatinine clearance > 60 ml/min: 15-35 mg/kg per day Since renal excretion is a pathway of elimination, consideration should be given to decreasing the dosage of Hydroxycarbamide in renally impaired patients ◇ If creatinine clearance ≤ 60 ml/min: initial dose should be decreased by 50% ◇ Blood parameters for renal impairment should be checked before starting treatment and closely monitored during treatment ◇ Hydroxycarbamide should be discontinued if necessary ◇ If appropriate, restart at a lower dose ◇ Hydroxycarbamide must not be administered to patients with severe renal impairment (creatinine clearance < 30 ml/min)
Hepatic impairment	◇ There are no data that support specific dose adjustments in patients with hepatic impairment ◇ Blood parameters for hepatic impairment should be checked before starting treatment and closely monitored during treatment ◇ Hydroxycarbamide should be discontinued if necessary ◇ If appropriate, restart at a lower dose ◇ Hydroxycarbamide is contraindicated in patients with severe hepatic impairment (Child-Pugh classification C)
If abnormality of blood cells count	If neutropenia or thrombocytopenia occurs, temporarily withhold Hydroxycarbamide dosing and monitor full blood cell count with white cell differential weekly

2. Handling of Hydroxycarbamide

Each pack contains:

- ◇ One 150 ml bottle capped with a child-resistant closure.
- ◇ A bottle adaptor.
- ◇ Two dosing syringes for accurate measurement of the prescribed dose of the oral solution.

	Syringe Type	
Syringe volume	3 ml	10 ml
Colour	Violet	Violet
Graduations	Each graduation of 0.1 ml contains 10 mg of Hydroxycarbamide	Each graduation of 0.5 ml contains 50 mg of Hydroxycarbamide
Dose volume	Doses less than or equal to 3 ml	Doses more than 3 ml

Please advise the patient or parent which syringe to use to ensure that the correct volume is administered

IMPORTANT

- ◇ **Store in a refrigerator (2 °C - 8 °C). After first opening of the bottle, discard any unused contents after 12 weeks**
- ◇ **Women who are pregnant, planning to be or breastfeeding should not handle Hydroxycarbamide**

Ensure that the patient or parent is well informed about the precautions for proper handling

- ◇ **Wash hands before and after administering a dose.**
- ◇ **Wipe up spillages immediately.**
- ◇ **Use disposable gloves when handling Hydroxycarbamide.**
- ◇ **Wash immediately and thoroughly with soap and water if Hydroxycarbamide comes into contact with the skin, eyes or nose.**

3. Avoiding medication errors

When switching patients from capsule or tablet to liquid formulation, there is a potential for medication errors to occur.

To avoid potential medication errors, please note the following:

◇ Hydroxycarbamide 100 mg/ml oral solution is bioequivalent to tablet and capsule formulations. No alteration in dose is necessary when switching formulations.

◇ It is very important that precise instructions are provided to patients/parents/carers. Patients and parents/carers should be advised on the exact volume to administer and the correct syringe (3 ml or 10 ml) to use.

For example:

- for 100 mg dose give 1.0 ml using the SMALL 3 ml syringe
- for 500 mg dose give 5.0 ml using the LARGE 10 ml syringe

4. Need for contraception

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

Both male and female patients should understand the need for contraception before and during treatment with Hydroxycarbamide

Hydroxycarbamide may be a potent mutagenic active substance and has been described as teratogenic in animals. Male and female patients should be informed that Hydroxycarbamide may harm their sperm and eggs.

5. Risk to male fertility, potential risk to foetus and breastfeeding

5.1 Male fertility

- Male patients should be informed that fertility might be affected by treatment.
- Very common reversible oligo- and azoospermia have been observed in man, although these disorders are also associated with the underlying disease.

Healthcare professionals should discuss about the possibility of sperm conservation (cryopreservation) before the start of therapy

5.2 Women of childbearing potential

- There is limited amount of data from the use of Hydroxycarbamide in pregnant women.
- Female patients on Hydroxycarbamide wishing to conceive should stop treatment 3 to 6 months before pregnancy if possible.
- Hydroxycarbamide can cause foetal harm when administered to a pregnant woman, as it crosses the placental barrier.

Hydroxycarbamide must not be administered to patients who are pregnant

The patient should be instructed to immediately contact a doctor in case of suspected pregnancy.

The patient should discuss with the doctor and must be informed of the potential risk to the foetus.

Careful follow-up of the pregnant patient should be planned, including appropriate clinical examinations, laboratory tests and ultrasound scans

Breastfeeding

Hydroxycarbamide is excreted in human breast milk. Patients should not breastfeed during the treatment because of the potential for serious adverse reactions in the breastfeeding infant.

6. Management of adverse drug reactions

The table below summarises the adverse effects most frequently reported during treatment with Hydroxycarbamide.
An assessment of the risks and benefits should be carried out whenever any adverse effect occurs.

Recommendations for the management of some adverse drug reactions with known frequency

Side Effect	Frequency	Management
Bone marrow depression including neutropenia (< 1,500 /µl) **Reticulocytopenia (< 80,000 /µl)**	Very common	• The effective dose may be the maximal tolerated dose • Discontinuation until blood counts return to normal, then resume at reduced doses • Blood counts usually return to normal within two weeks of discontinuation of Hydroxycarbamide • Treatment at a dose which caused haematological toxicity must not be attempted more than twice • In case of anaemia, check for infection with Parvovirus, splenic or hepatic sequestration, renal impairment
Thrombocytopenia (< 80,000 /µl), anaemia (haemoglobin < 4.5 g/dl)	Common	
Macrocytosis	Very common	• The macrocytosis may mask the incidental development of folic acid deficiency; regular determinations of serum folic acid are recommended
Oligospermia, azoospermia	Very common	• Consider cryopreservation of sperm before starting treatment
Dizziness, Headaches	Common	• Check for a complication of Sickle Cell Disease such as anaemia or otorhinolaryngological manifestation • Discuss discontinuation of treatment
Skin reactions (such as skin ulcer, oral, nail and skin hyperpigmentation, dry skin, alopecia)	Common	• Discuss relationship with the treatment and discontinuation of treatment
Leg ulcers	Rare	• In case of history of leg ulcer, initiate with caution • Topical care • Prevention by surveillance of skin condition and avoidance of local injuries • Discuss dose reduction or discontinuation of treatment

For the full list of adverse reactions, please refer to the Summary of Product Characteristics.

Reporting of suspected adverse reactions

To report any side effect(s):

- **Saudi Arabia: The National Pharmacovigilance Centre (NPC) :**
  - **Fax: +966-11-205-7662**
  - **Toll free phone: 19999**
  - **E-mail: npc.drug@sfda.gov.sa**

Website: https://ade.sfda.gov.sa/

Or

Qomel Co Ltd reporting contact

- **Fax: +966-11-288-6668**
- **Phone Number: +966-11-288-6660**
- **E-mail: Hisham@qomel.com**
- **Qualified Person for Pharmacovigilance: Hisham Al Agla**

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

7. Summary of Product Characteristics

The Summary of Product Characteristics (SmPC) is available at: https://sdi.sfda.gov.sa/

Electronic copies of this Healthcare Professional Guide and the Patient/Carer Guide are available from the website of the Health Products Regulatory Authority or https://sdi.sfda.gov.sa/