

THAROLAX

(Hydroxyurea USP Hard Capsules)

Please read this leaflet carefully before you start taking your medicine. This leaflet provides a summary of information about your medicine. This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours. If you want to know more or are not sure ask your Doctor or Pharmacist.

What is Hydroxyurea

THAROLAX Capsules (Hydroxyurea) is a medicine you take once a day that can make your sickle cell disease less severe. Taking it regularly can raise your hemoglobin level and lower the number of times you get pain and acute chest syndrome. This can decrease the number of admissions to the hospital and the number of transfusions you may need. No, it is not a cure but it can improve your quality of life.

What is in this leaflet

This leaflet answers some common questions about THAROLAX (Hydroxyurea). It does not contain all the available information. It does not take the place of talking to your doctor or pharmacist.

All medicines have risks and benefits. Your doctor has weighed the risks of you taking THAROLAX (Hydroxyurea) against the benefits they expect it will have for you. This leaflet does not contain everything about THAROLAX (Hydroxyurea).

Your doctor has been provided with full information and can answer any questions you may have. Follow your doctor's advice even if it differs from what is in this leaflet.

Please read this leaflet carefully and keep it in a safe place so you may refer to it later.

What THAROLAX is used For

THAROLAX (Hydroxyurea) is used to treat various types of cancers such as **melanoma, leukemia and cancer of the ovary.**

THAROLAX (Hydroxyurea) contains hydroxyurea, an anti-cancer medicine. It interferes with the replication of cells and causes cell death, particularly in cancer cells.

THAROLAX (Hydroxyurea) may be used alone or in combination with other treatments for cancer.

Your doctor will inform you if this is necessary. Your doctor may have prescribed

THAROLAX (Hydroxyurea) for another reason. Ask your doctor if you have any questions about why THAROLAX was prescribed for you. This medicine is available only with a doctor's prescription.

THAROLAX (Hydroxyurea) is not recommended for use in children as its safety and effectiveness in patients under 18 years of age has not been established.

Before you are given THAROLAX

When you must not take THAROLAX

- You must not take THAROLAX if you have an allergy to THAROLAX, or any of the ingredients listed at the end of this leaflet.
- Do not take THAROLAX if you have marked depression of white blood cells (bone marrow depression) or red blood cells (severe anaemia).

Your doctor will be able to advise whether THAROLAX (Hydroxyurea) is appropriate in this situation.

• Do not take THAROLAX if you are pregnant or intend to become pregnant.

THAROLAX (Hydroxyurea) may cause harm to the unborn baby if it is given to a pregnant woman. You should use some kind of birth control while you are having THAROLAX (Hydroxyurea) and for at least 12 weeks after you stop using it. THAROLAX (Hydroxyurea) may cause birth defects if either the male or female is using it at the time of conception.

Do not take THAROLAX after the expiry date printed on the pack.

If you take this medicine after the expiry date has passed, it may not work as well.

Do not take THAROLAX if the packaging shows signs of tampering

Before you start to take THAROLAX

Tell your doctor if you have allergies to:

Any other medicines

Any other substances, such as foods, preservatives or dyes

Tell your doctor if you have or have had any medical conditions, especially the following:

- Liver problems
- Kidney problems
- Blood problems or anaemia
- Lowered immunity due to treatment with other medicines used to treat cancer (including Radiation therapy)
- Your immune system is not working properly (you get a lot of infections requiring Treatment

Tell your doctor if you have an infection or high temperature.

Your doctor may decide to delay your treatment until the infection has gone.

Do not have THAROLAX with any medicine that lowers your immune system, unless you have discussed this with your doctor.

Tell your doctor if you are pregnant or intend to become pregnant.

Tell your doctor if you are breastfeeding or plan to breastfeed.

THAROLAX (Hydroxyurea) passes into breast milk. Therefore there is a possibility that the breast-fed baby may be affected.

Taking THAROLAX with food or drink

You should check with your doctor before drinking alcohol to find out if it is advisable for you.

Driving or operating machinery

It is safe to drive or operate machinery, however, if you feel drowsy or unwell you should not do so until you have discussed it with your doctor.

Tell your doctor if you are asexually active man.

Men who take THAROLAX (Hydroxyurea) are advised to use a condom to avoid pregnancy in their partner.

Important information about some of the ingredients of THAROLAX

If you have been told you have intolerance to some sugars, contact your doctor before taking this medicines, as it contains a type of sugar called lactose.

Pregnancy and Breastfeeding

You should not take this medicine if you are pregnant, planning to become pregnant or are breastfeeding, unless your doctor recommends it.

In addition, if you are pregnant, planning to be or breastfeeding you should not handle the capsules.

If you have not told your doctor about any of the above, tell them before you start THAROLAX. If you are not sure whether you should have THAROLAX, talk to your doctor. If you have not told your doctor about any of the above, tell them before you start having THAROLAX.

Taking other medicines

Tell your doctor if you are taking any other medicines, including any that you buy without prescription from your pharmacy, supermarket or health food shop.

Some medicines and THAROLAX (Hydroxyurea) may interfere with each other. These include:

- Some other medicines that are used to treat other forms of cancer
- Medicines used to treat gout
- Medicines used to treat HIV infection including Videx® (didanosine) and Zerit®(stavudine)

These medicines may be affected by THAROLAX, (Hydroxyurea) or affect how well it works. You may need different amounts of your medicine, or you may need to have different medicines. Your doctor will advise you.

Your doctor may have more information on medicines to be careful with or avoid while having THAROLAX (Hydroxyurea).

Hydroxyurea is also called as Hydroxycarbamide

How to take THAROLAX

How much to take

Your doctor will decide what dose you will receive. Your dose of THAROLAX capsules is worked out based on your body weight and height and on the type of cancer you have. The dose worked out for you may be different to the dose for another patient.

THAROLAX (Hydroxycarbamide)

may be given alone or together with other anti-cancer treatments or drugs. Ask your doctor if you want to know more about the dose of THAROLAX you receive.

How to take it

THAROLAX (Hydroxyurea) capsules may be given to you at the hospital or surgery, or you may take them yourself at home.

Swallow THAROLAX capsules with a glass of water.

Or if you have problems with swallowing the capsules, you can empty the capsule contents into a glass of water, stir and drink it straight away. Some of the materials present in the capsule may float to the surface of the water.

When to take it

THAROLAX (Hydroxyurea) is taken as a single dose and can be taken each day, or once every three days. Your doctor will decide how you should take the capsules and will explain this to you.

Take THAROLAX at about the same time each day that you are to take it.

THAROLAX (Hydroxyurea) may or may not be given at the same time as other anti-cancer treatments or agents.

If you forget to take it

If it is almost time for your next dose, skip the dose you missed and take your next dose when you are meant to.

Otherwise, take it as soon as you remember, and then go back to taking your medicine as you would normally.

Do not take a double dose to make up for the dose that you missed.

This may increase the chance of you getting an unwanted side effect.

How long it is given

Several courses of THAROLAX (**Hydroxycarbamide**) therapy may be needed depending on your response to treatment.

Additional treatment may not be repeated until your blood cell numbers return to acceptable levels and any side effects have been controlled.

Do not stop taking THAROLAX (Hydroxyurea) unless your doctor tells you to - even if you feel better.

If you take too much (Overdose)

If you are in hospital THAROLAX (Hydroxyurea) will be given to you by the hospital staff, so it is most unlikely that too many capsules would be given. However, if an overdose should be given, your doctor will give you the appropriate Treatment.

If you are taking THAROLAX at home - Immediately telephone your doctor or pharmacist or the Poisons Information Centre (telephone 13 11 26) or go to Accident or Emergency at your nearest hospital, if you think that you or someone else may have taken too many THAROLAX capsules.

Do this even if there are no signs of discomfort or poisoning. You may need urgent medical attention.

Symptoms of overdose may include acute skin inflammation, soreness, and discolouration of the skin, fluid retention associated with the hands & feet followed by scaling of the skin in these areas, soreness & inflammation of the mouth.

While you are taking THAROLAX

Things you must do

Be sure to keep all your doctor's appointments so your progress can be checked.

Your doctor may want to check your blood pressure and do some blood and other tests from time to time to check on your progress and detect any unwanted side effects.

Keep follow up appointments with your doctor in order to get the best effect from your treatments.

If you forget an appointment, contact your doctor immediately. Tell any other doctors, dentists and pharmacists who are treating you that you are having THAROLAX.

If you are about to be started on any new medicine, tell your doctor, dentist or pharmacist that you are having THAROLAX (Hydroxyurea).

If you plan to have surgery that needs a general anaesthetic, tell your doctor or dentist that you are having THAROLAX (Hydroxyurea).

If you become pregnant while having THAROLAX, tell your doctor. You must maintain an adequate fluid intake.

THAROLAX (**Hydroxycarbamide**) can lower the number of white blood cells and platelets in your blood. This means that you have an increased chance of getting an infection or bleeding. The following precautions should be taken to reduce your risk of infection or bleeding:

- Avoid people who have infections. Check with your doctor immediately if you think you may be getting an infection, or if you get a fever, chills, cough hoarse throat, lower back or side pain or find it painful or difficult to urinate.

Be careful when using a toothbrush, toothpick or dental floss. Your doctor, dentist, nurse or pharmacist may recommend other ways to clean your teeth and gums. Check with your doctor before having any dental work.

- Be careful not to cut yourself when you are using sharp objects such as a razor or nail cutters.
- Avoid contact sports or other situations where you may bruise or get injured.

Things you must not do

Do not give THAROLAX (Hydroxyurea) to anyone else, even if they have the same condition as you. Do not take THAROLAX (Hydroxyurea) to treat any other complaints unless your doctor tells you to. Do not stop taking THAROLAX (Hydroxyurea) or lower the dose, without checking with your doctor. If you empty the contents of the capsules into water for swallowing, do not allow the powder to come into contact with your skin. Also avoid inhaling the contents when opening the capsules. If the powder is accidentally spilled, you should wipe up the powder using a damp paper towel and the paper towel should be disposed of immediately. You should also dispose of the empty capsules immediately after taking your required dosage.

WARNING

Treatment of patients with THAROLAX may be complicated by severe, sometimes lifethreatening, adverse effects. THAROLAX should be administered under the supervision of a physician experienced in the use of this medication for the treatment of sickle cell anemia.

Hydroxyurea is mutagenic and clastogenic, and causes cellular transformation to a tumorigenic phenotype. Hydroxyurea is thus unequivocally genotoxic and a presumed transspecies carcinogen which implies a carcinogenic risk to humans. In patients receiving long-term hydroxyurea for myeloproliferative disorders, such as polycythemia vera and thrombocythemia, secondary leukaemia's have been reported. It is unknown whether this leukemogenic effect is secondary to hydroxyurea or is associated with the patient's underlying disease. The physician and patient must very carefully consider the potential benefits of THAROLAX relative to the undefined risk of developing secondary malignancies. Tharolax is used to treat chronic myeloid leukaemia or cervical cancer.

Your medical team will discuss with you the options for treating your cancer. They will take into account factors such as the type of cancer, where it is, which stage it is at and whether you have had treatment before. The results of blood tests and other investigations will also be considered. How well you feel and how you are likely to cope with treatment is also important.

Your cancer treatment will usually consist of a treatment session with Tharolax followed by a break of a number of days before the next treatment session with Tharolax. This cycle may be repeated many times as part of your cancer treatment. Tharolax works by damaging cancer cells in the body. Tharolax also affects healthy cells and treatment with Tharolax may damage your immune system. Your medical team may arrange for you to have some blood tests to check how well your immune system is working.

Do not share your medicine with other people. It may not be suitable for them and may harm them.

The pharmacy label on your medicine tells you how much medicine you should take. It also tells you how often you should take your medicine. This is the dose that you and your prescriber have agreed you should take. You should not change the dose of your medicine unless you are told to do so by your prescriber. If you feel that the medicine is making you unwell or you do not think it is working, then talk to your prescriber.

How does hydroxyurea work?

Hydroxyurea works in two ways. The first way is in the red blood cells. Red blood cells contain hemoglobin that carries oxygen to all parts of the body. People who have sickle cell disease make abnormal hemoglobin called sickle hemoglobin. Sickle haemoglobin causes the red blood cells to become stiff and sticky. The sickle cell can then cause a block in the flow of blood to important organs.

Hydroxyurea helps the body make another hemoglobin called fetal hemoglobin or hemoglobin F which is usually only produced by babies in the fetal stages of life (before birth). With higher levels of hemoglobin F, red blood cells are less likely to sickle and cause problems.

The second way that hydroxyurea works is by lowering the number of neutrophils (infection—fighting white blood cells). This can be a good thing, because the increased neutrophil count makes the blood “thicker” and “stickier” which increases the chance that the sickled cells will get stuck in the veins and cause the blockage that causes the problems.

Things to be careful of

Be careful driving or operating machinery until you know how THAROLAX affects you.

As with other medicines used to treat cancer, THAROLAX (Hydroxyurea) may cause dizziness, light-headedness or tiredness in some people. Make sure you know how you react to THAROLAX before you drive a car, operate machinery, or do anything else that could be dangerous if you are dizzy or light-headed. If this occurs do not drive.

What are the benefits of taking hydroxycarbamide?

It should reduce the number and severity of crises.

- It should reduce the risk of sickle cell chest syndrome (chest crisis).
- You will need fewer blood transfusions.
- It can increase your life expectancy.
- It can improve quality of life.

Hydroxycarbamide **does not** reduce the frequency of, or prevent, the following sickle Cell complications:

- Leg ulcers
- bone damage (avascular necrosis)
- Infections.

The role of hydroxycarbamide in preventing stroke is not clear and is still being Researched. It is also uncertain if hydroxycarbamide is effective in preventing painful Erections of the penis (priapism).

Hydroxycarbamide is not a painkiller but it may help pain by reducing the number Of times you experience painful crises.

Side effects

Tell your doctor or nurse as soon as possible if you do not feel well while you are having THAROLAX.

Like other medicines that treat cancer, THAROLAX (Hydroxyurea) may have unwanted side effects, some of which may be serious. You may need medical treatment if you get some of the side effects.

Ask your doctor to answer any questions you may have. Tell your doctor or nurse if you notice any of the following and they worry you:

These are the more common side effects of THAROLAX (Hydroxyurea).

- Nausea, vomiting
- Diarrhoea or constipation
- Loss of appetite
- Dizziness
- feeling tired or sleepy
- Fever; high temperature, chills
- Stomach pain or discomfort
- Discolouration or ulcers on the skin
- Decay of the skin or nails

Tell your doctor or nurse as soon as possible if you notice any of the following:

These are very rare side effects, which might possible occur. You may need medical attention.

- Sore mouth
- Frequent infections such as fever, severe chills
- Tiredness, headaches, being short of breath, dizziness
- Convulsions
- Pain in lungs or difficulty breathing.

Less serious side effects may include:

- hair loss;
- skin peeling or discoloration, mild rash;
- upset stomach, constipation, diarrhea, vomiting;
- headache, dizziness, drowsiness; or
- Weight gain.

If any of the following happen, tell your doctor or nurse immediately, or go to Accident and Emergency at your nearest hospital:

These are very serious side effects. You may need urgent medical attention or hospitalisation sudden life-threatening allergic reactions; sudden signs of allergy such as rash, itching or hives on the skin, swelling of the face, tongue or other parts of the body, shortness of breath, wheezing or trouble breathing.

If you are receiving radiation treatment with THAROLAX (Hydroxyurea) or are taking other medications as well as THAROLAX, the side effects listed above may occur more frequently or be more severe.

Other side effects not listed above may occur in some patients. Tell your doctor or nurse if you notice anything that is making you feel unwell.

The benefits and side effects of THAROLAX (Hydroxyurea) may take some time to occur. Therefore even after you have finished your THAROLAX (Hydroxyurea) treatment you should tell your doctor immediately if you notice any of the side effects listed above

Do not store THAROLAX (Hydroxyurea) or any other medicine in the bathroom or near a sink. Do not leave it in the car on hot days. Heat and dampness can destroy some medicines. Keep it where children cannot reach it.

A locked cupboard at least one-and-a-half metres above the ground is a good place to store medicines. Pay particular attention to this when you are opening the capsules to dissolve the contents in water.

Disposal

If your doctor tells you to stop taking THAROLAX (Hydroxyurea), return any that you have not taken to your treating clinic/ hospital, doctor or pharmacist, so they can be disposed of safely.

Who should take hydroxyurea?

We recommend hydroxyurea for anyone with sickle cell disease who has had two or more episodes of pain or acute chest syndrome in their lifetime. Your sickle cell team will offer the medication if we feel it could help you, but the final choice is made by you and your family.

Is hydroxyurea the only treatment for sickle cell disease?

Hydroxyurea is the only non-invasive option at this time. Chronic red blood cell transfusions have been used for many years to treat severe problems of sickle cell disease; however, this introduces the slim but still real chance of transfusion-acquired HIV or Hepatitis C as well as other problems such as iron overload with liver and heart damage. Also, bone marrow or stem cell transplantation (replacing a patient's bone marrow with normal bone marrow) can cure sickle cell disease, but requires a suitable donor and can be associated with many severe complications.

What it looks like

THAROLAX (Hydroxyurea) capsules are opaque aqua / opaque pink, with BMS 303 printed on each capsule. They are supplied in bottles of 100 capsules.

Ingredients

Active:

The active ingredient in THAROLAX (Hydroxyurea) capsules is hydroxyurea. Each capsule contains 500mg of hydroxyurea.

Inactive:

Each capsule also contains citric acid, lactose, magnesium stearate, sodium phosphate & capsule colourants.

What do I need to know about hydroxyurea and pregnancy?

People who take hydroxyurea must not get pregnant or father a child. Hydroxyurea is a known teratogen, which means that if you get pregnant or father a child the baby might be deformed. The malformation can range from life limiting to life threatening. If you are of child-bearing age, then you must always use some type of birth control or not have sex at all. If you want to have a baby, you must stop hydroxyurea for several months before getting pregnant.

This applies to both men and women as the hydroxyurea can affect the sperm.

A mother can start taking hydroxyurea again after the baby is born and breast feeding is completed. You should not use hydroxyurea if you are allergic to it, or if you have severe bone marrow suppression, severe anemia, or low levels of platelets in your blood. Wash your hands before and after you handle a hydroxyurea capsule or the bottle that contains the pills. For best protection, wear disposable gloves when handling the pills.

Do not open the hydroxyurea capsule. Do not use a pill that has been accidentally opened or broken. The medicine from an open capsule can be dangerous if it gets in your eyes, mouth, or nose, or on your skin. If this occurs, wash your skin with soap and water or rinse your eyes with water.

If any powder from an open capsule is spilled, wipe it up at once with a damp paper towel and throw the towel away in a sealed plastic bag where children and pets cannot get to it.

Hydroxyurea can lower blood cells that help your body fight infections and help your blood to clot. Your blood may need to be tested often. Avoid being near people who are sick or have infections. Avoid activities that may increase your risk of bleeding injury. Tell your doctor at once if you develop signs of infection

How will I know that hydroxyurea is working?

You will not feel better right away, because it takes a few months for hydroxyurea to start working. If you take it once a day every day, then you will eventually notice that you feel better and have fewer problems like pain.

Your doctors can also see changes in your lab work that shows the medication is working. There are a few people who won't respond, so the medication doesn't help. But, you should try the hydroxyurea for at least six months before stopping it.

Is hydroxyurea safe?

Hydroxyurea is safe when prescribed and monitored by doctors who know how to care for patients with sickle cell disease. It may cause a temporary upset stomach, but taking it with food helps. There is also the increased risk for infection when the neutrophils count drops. This risk is minimized by your monthly lab work.

The long-term side effects of hydroxyurea are not fully known. Some people wonder if hydroxyurea could cause cancer if taken for a long time, but this has not been seen in people with sickle cell disease who have been treated for as long as 20 years.

Actually, adults with sickle cell disease who take hydroxyurea seem to live longer than those who do not. There is no known limit to how long you can be on the medication so you should take it as long as it is working.

Is taking hydroxyurea easy?

Yes and no. Hydroxyurea is a medication that only has to be taken once a day. If you are able to swallow pills, it is even easier although liquid is also available. However, taking hydroxyurea is a big commitment.

The medication only works if you take it every day so it has to be taken EVERY day. Lab work should be drawn monthly (or more often if needed) to monitor that the neutrophils do not get too low. If the neutrophils get too low, the risk of infection goes up.

When this happens, the hydroxyurea has to be held and more labs are needed to determine when a safe time to restart the medication is. There are also doctor visits every 3 months. It is a BIG commitment but for people who have frequent hospitalizations or pain, hydroxyurea can improve your quality of life.

What should I avoid while taking hydroxyurea?

Do not handle hydroxyurea pills or the medicine bottle without skin protection (disposable gloves). Avoid being near people who are sick or have infections. Tell your doctor at once if you develop signs of infection. This medicine can pass into body fluids (including urine, feces, vomit, semen, and vaginal fluid). For at least 48 hours after you receive a dose, avoid allowing your body fluids to come into contact with your hands or other surfaces.

Patients and caregivers should wear rubber gloves while cleaning up body fluids, handling contaminated trash or laundry or changing diapers.

Wash hands before and after removing gloves. Wash soiled clothing and linens separately from other laundry. Body fluids should not be handled by a woman who is pregnant or who may become pregnant. Use condoms during sexual activity to avoid exposure to body fluids.

What happens if I overdose

Seek emergency medical attention or call the Poison Help line at 1-800-222-1222. Overdose symptoms may include drowsiness, mouth sores, and swelling with pain and purple discoloration in your hands and feet.

Storage

THAROLAX (Hydroxyurea) capsules should be stored below 30°C in a cool dry place. The container must be tightly closed.

What other drugs will affect hydroxyurea?

Some medicines can increase your risk of certain side effects while taking hydroxyurea. Tell your doctor if you are also using:

- didanosine (Videx);
- stavudine (Zerit); or
- An interferon such as Actimmune, Alferon, Avonex, Betaseron, Extavia, Infergen, Intron, Rebetrone, Rebif, or Roferon.

This list is not complete and other drugs may interact with hydroxyurea. Tell your doctor about all medications you use.

This includes prescription, over-the-counter, vitamin, and herbal products. Do not start a new medication without telling your doctor.

WARNING:

Along with its benefits, hydroxyurea treatment may cause severe, sometimes fatal side effects (see also Side Effects section). Your doctor will follow you closely while you are taking this medication. Keep all medical and laboratory appointments. Cancers have been reported with the use of this medication but it is not known if these cancers are due to the drug or the disease being treated. Consult your doctor for more details.

How long should I take it for?

You should continue to take hydroxycarbamide, as advised, unless you're Haematologist or another doctor tells you not to.

If you want to stop taking it, please talk to your haematologist beforehand. If after a trial period of several months there has been no medical benefit to your sickle cell disease, despite taking the right dose of hydroxycarbamide, your doctors will advise you to stop taking the drug.

How will my health be monitored?

When you start taking hydroxycarbamide, you will need to see the haematologists and have blood tests (blood counts, HbF level, liver and kidney function) regularly.

At first, or if the dose is changed, you will be seen at least every two weeks. As soon as your blood measures are stable on the hydroxycarbamide you will be seen every eight to twelve weeks.

Your dose may be reduced if your blood count falls or if your liver and kidney blood tests show any changes.

We will not be able to prescribe hydroxycarbamide if you are not able to come for regular blood tests, as we need to be able to monitor you.

When will I notice any improvement in my sickle cell disease?

It usually takes at least three months before sickle cell patients can tell if the hydroxycarbamide is working, so it is important to give the medication time to work and for you to take it as prescribed. Hydroxycarbamide will not work if you only take it every now and again or only when you are ill or in pain.

Can I take other medications whilst I am taking Hydroxycarbamide?

You should tell your doctor about all the other medications you are taking when you start using hydroxycarbamide. Occasionally the dosage will need to be changed because of your other medications. You should also tell your doctor if you start any new medications. This includes medicines bought at a pharmacy or elsewhere.

Marketing Authorisation Holder and Manufacturer

Taj Pharma Group (India)

Taj Pharmaceuticals Ltd.

Mumbai, India

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