PACKAGE LEAFLET: INFORMATION FOR THE USER

CYTARABINE TEVA 100 mg/ml SOLUTION FOR INJECTION/INFUSION

cytarabine

Read all of this leaflet carefully before you start using 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, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1 What Cytarabine Teva is and what it is used for

Cytarabine Teva is used in adults and children. The active ingredient is cytarabine.
Cytarabine is one of a group of medicines known as cytotoxics; these medicines are used in the treatment of acute leukaemias (cancer of blood where you have too many white blood cells). Cytarabine interferes with the growth of cancer cells, which are eventually destroyed.

Remission induction is an intensive treatment to force leukaemia into retreat. When it works, the balance of cells in your blood becomes more normal and your health improves. This relatively healthy spell is called a remission.

Maintenance therapy is a milder treatment to make your remission last as long as possible. Quite low doses of Cytarabine Teva are used to keep the leukaemia under control and stop it flaring up again.

2 What you need to know before you are given Cytarabine Teva

Do not use Cytarabine Teva:
- If you are allergic to cytarabine, or any of the other ingredients of this medicine (listed in section 6).
- If the cell count in your blood report is very low due to some cause other than cancer, or as decided by your doctor.
- If you are feeling increasing difficulties in body coordination after radiation treatment with another anticancer drug such as methotrexate.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before using Cytarabine Teva. Take special care with Cytarabine Teva:
- If your bone marrow is in low state, therapy should be initiated under close medical supervision.
- If you have problems with your liver.
- Cytarabine strongly reduces blood cell production in the bone marrow. This can make you more prone to infections or bleeding. The blood cell numbers can continue to fall for up to a week after stopping treatment. Your doctor will test your blood regularly and examine your bone marrow if required.
- Serious and sometimes life-threatening side effects can occur in the central nervous system, the bowels or lungs.
- Your liver and kidney functions should be monitored during cytarabine therapy. If your liver is not working well before treatment, cytarabine should be given only with utmost care.
- The levels of uric acid (showing that the cancer cells are destroyed) in your blood (hyperuricaemia) may be high during treatment. Your doctor will tell you if you need to take any medicine to control this.
- During treatment with cytarabine administration of live or attenuated vaccine can lead to serious or life-threatening infections. If required, consult your doctor. Use of killed or inactivated vaccine may not have the desired effect due to suppressed immune system while on cytarabine.
- Do not forget to tell your doctor if you have received radiotherapy.

Other medicines and Cytarabine Teva
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. In particular, tell your doctor if you are using medicines containing any of the following:
- 5-Fluorocytosine (a medicine used to treat fungal infections).
- Digitoxin or beta-acetyldigoxin, which are used to treat certain heart conditions.
- Gentamicin (an antibiotic used to treat bacterial infections).
- Cyclophosphamide, vincristine and prednisone which are used in cancer treatment programmes.

Pregnancy, breast-feeding and fertility
Pregnancy
Avoid becoming pregnant while you or your partner is being treated with Cytarabine Teva. If you are sexually active, you are advised to use effective birth control to prevent pregnancy during treatment, whether you are male or female. Cytarabine Teva may cause birth defects, so it is important to tell your doctor if you think you are pregnant. Men and women have to use effective contraception during and up to 6 months after treatment.

Breast-feeding
You should stop breast-feeding before starting treatment with Cytarabine Teva because this medicine may be harmful to infants being breast-fed.

Fertility
Cytarabine Teva may lead to suppression of menstrual cycles and ammenorrhoea in female patients, and may suppress sperm production in male patients. Male patients undergoing cytarabine treatment should use a reliable contraceptive method.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines
Cytarabine Teva does not affect your ability to drive or use machinery. However, cancer treatment in general can affect the ability of some patients to drive or operate machines. If you are affected, you should not drive or use machinery.

3 How to use Cytarabine Teva

Method and routes of administration
Cytarabine Teva will be given to you either by infusion into a vein (through a 'drip'), by injection into a vein or by subcutaneous injection under the direction of specialists in hospital. Your doctor will decide what dose to give and the number of days' treatment you will receive depending on your condition.

The recommended dose is
Your doctor will decide the dose of Cytarabine Teva, based on your condition, whether you are in induction or maintenance therapy and your body surface area. Your body weight and height will be used to calculate your body surface area.

During treatment you will need regular checks including blood tests. Your doctor will tell you how often this should be done. He/she will be making regular checks of:
- Your blood, to check for low blood cell counts that may need treatment.
- Your liver (again using blood tests) to check that Cytarabine Teva is not affecting the way it functions in a harmful way.
- Your kidneys (again using blood tests) to check that Cytarabine Teva is not affecting the way it functions in a harmful way.
- Blood uric acid levels, as cytarabine may increase uric acid levels in the blood. Another medicine may be given if your uric acid levels are too high.

If you are on dialysis, the doctor may alter the time of drug administration as dialysis may decrease the effectiveness of the medicine.

If you receive high doses of cytarabine
High doses can worsen side effects such as sores in the mouth or may decrease the number of white blood cells and platelets (these help the blood to clot) in the blood. Should this happen, you may need antibiotics or blood transfusions. Mouth ulcers can be treated to make them less uncomfortable as they heal.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4 Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The side effects of Cytarabine Teva are dependent on the dose. The digestive tract is most commonly affected, but also the blood.

Tell your doctor or nursing staff immediately if you suffer from the following symptoms after you are given this medicine:
- An allergic reaction such as sudden wheeziness, difficulty in breathing, swelling of eyelids, face or lips, rash or itching (especially affecting the whole body) (frequency cannot be estimated from the available data).
- Severe allergic reaction (anaphylaxis): Skin rash (including red itchy skin); swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing); bronchospasm (narrowing of the airways); and you may feel you are going to faint (a spontaneous loss of consciousness caused by insufficient blood to the brain). It can be life-threatening (may affect up to 1 in 100 people).
- Clinical signs of pulmonary oedema / Acute Respiratory Distress Syndrome (ARDS): Sudden, distressing breathing difficulties and water in the lungs. These are more likely to develop with high dose therapy (frequency cannot be estimated from the available data).
- You are feeling tired and lethargic. These are symptoms of low numbers of red blood cells (may affect up to 1 in 10 people).
- You have flu like symptoms e.g. raised temperature, fever and chills. These are symptoms of low numbers of white blood cells (may affect up to 1 in 10 people).
- You bruise more easily or bleed more than usual if you hurt yourself. These are symptoms of low numbers of blood platelets (may affect up to 1 in 10 people).
- Severe pain in the chest (may affect up to 1 in 100 people).
- Severe pain in the abdomen (frequency cannot be estimated from the available data).
- Loss of vision (frequency cannot be estimated from the available data), loss of sense of touch, mental disturbance or loss of ability to move normally (this medicine may cause side effects to the brain and eyes which are usually reversible but may be very serious).

These are serious side effects. You may need urgent medical attention.

The following information is intended for healthcare professionals only:

Method of administration
By intravenous infusion or injection, or subcutaneous injection only.
Cytarabine Teva 100 mg/ml should not be administered by any other route.

Instruction for Use/Handling
For single use only.
The undiluted/diluted solution should be clear, colourless to pale yellow and free from visible particles.
If the solution contains visible particles, it should be warmed to 55°C, for 30 minutes, with adequate shaking, and allowed to cool to room temperature.

Once opened, the contents of each vial must be used immediately. Discard any unused contents.
Cytarabine Teva 100 mg/ml can be diluted with 0.9 % sodium chloride solution for infusion or 5 % glucose solution.

Cytotoxic Handling Guidelines

Administration
Cytarabine Teva should be administered by, or under the direct supervision of a qualified physician who is experienced in the use of cancer chemotherapeutic agents.

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Design Department Harlow

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Other side effects:

Common (may affect up to 1 in 10 people):
- Abnormal red blood cells (megaloblastosis)
- Loss of appetite (anorexia)
- Stomach ache (abdominal pain)
- Difficulty in swallowing
- Feeling sick (Nausea)
- Vomiting
- Diarrhoea
- Inflammation or ulceration of the mouth or anus
- Reversible effects on the skin such as reddening (erythema), blistering, rash, hives, blood vessel inflammation (vasculitis), hair loss
- Reversible effects on the liver such as increased enzyme levels
- Reversible effects on the eyes such as sore eyes with bleeding (haemorrhagic conjunctivitis) with vision disturbance, sensitivity to light (photophobia), watery or burning eyes and inflammation of the cornea (keratitis)
- Fever
- Inflammation of the vein at the site of injection
- Abnormally high blood uric acid levels (hyperuricaemia)
- Impaired kidney function
- Inability to pass urine (urinary retention).

Uncommon (may affect up to 1 in 100 people):
- Sore throat
- Headache
- Blood poisoning (sepsis)
- Inflammation and ulcers of the gullet
- Severe bowel inflammation (necrotising colitis)
- Bowel cysts
- Inflammation of the inner lining of the stomach (peritonitis)
- Ulceration of the skin
- Itching
- Brown/black spots on the skin (lentigo)
- Yellowish skin and eye balls (jaundice)
- Lung infection (pneumonia)
- Breathing difficulty
- Damage to peripheral nerves causing symptoms such as tingling, weakness or pain in your hands or feet (peripheral neuropathy)
- Muscle and joint pain
- Inflammation of the lining that surrounds the heart (pericarditis)
- Chest pain
- Burning pain of palms and soles
- Bacterial infection of the skin (cellulitis) at the site of injection.

Very rare (may affect up to 1 in 10,000 people):
- Inflammation of the sweat glands
- Irregular heart beat (arrhythmias).

Not known (frequency cannot be estimated from the available data):
- Damage to nervous tissue (neural toxicity) and inflammation of one or more nerves (neuritis)
- Reduced number of immature red blood cells (reticulocytes)
- Dizziness
- Inflammation of the pancreas (pancreatitis)
- Sore eyes (conjunctivitis)
- Impaired liver function
- Liver abscess
- Freckling
- Skin rash.

The following side effects have also been reported with the use of Cytarabine Teva but how often they occur is not known:
- A so-called 'Cytarabine Syndrome' may occur 6-12 hours after the start of treatment. The symptoms include: Fever, bone and muscle pain, occasional chest pain, rash, sore eyes (conjunctivitis), nausea (feeling sick). Your doctor may prescribe corticosteroids (anti-inflammatory medicines) to prevent or treat these symptoms. If they are effective, treatment with cytarabine may be continued.
- Heart muscle disease (cardiomyopathy)
- Abnormal muscle breakdown (rhabdomyolysis)
- Loss of sperm and menstrual cycle
- Paralysis of the legs and lower body can occur when cytarabine is given into the space surrounding the spinal cord. This method of administration is not recommended.

Additional reactions observed with higher dose therapy

Blood disorders
A severe reduction in blood cells (pancytopenia), which can cause weakness, bruising and make infections more likely.

Central nervous system
The following symptoms, which are usually reversible, may develop in up to one third of patients after treatment with high cytarabine doses:
- Personality changes, changed alertness, difficulty in speaking, problems of coordination, tremor, abnormal eye movements (nystagmus), headache, peripheral motor and sensory neuropathies (damage to nerves of the peripheral nervous system), confusion, sleepiness, dizziness, coma, convulsions.

Skin disorders
A skin rash leading to scaling and peeling of the skin has been observed with high- dose therapy.

Digestive tract
Especially in treatment with high doses of cytarabine more severe reactions may appear in addition to the common symptoms.
Perforation, death of tissue (necrosis) and obstruction of the bowel have been reported.

Lungs
Acute, distressing breathing difficulties and water in the lungs (pulmonary oedema) have been observed, particularly at high doses.

Liver problems
Liver abscesses, liver enlargement, blockage of liver veins and inflammation of the pancreas have been observed after high-dose therapy.

Others
- Effects on the surface of the eye (corneal toxicity)
- Viral, bacterial etc infections

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5 How to store Cytarabine Teva

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

Unopened container
Do not store above 25ºC.
Do not refrigerate or freeze.
Keep the vial in the outer carton in order to protect from light.

Solution for infusion
Chemical and physical in-use stability of the diluted solution has been demonstrated in 0.9% sodium chloride solution for infusion between 0.1 mg/ml and 21.6 mg/ml for up to 28 days at temperature below 25°C and for up to 28 days at 2-8° C.
Chemical and physical in-use stability of the diluted solution has been demonstrated in 5% glucose solution between 5.4 mg/ml and 21.6 mg/ml for up to 10 days at temperature below 25°C and for up to 28 days at 2-8°C.
The diluted solutions do not require protection from light at 25°C storage conditions.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2-8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Do not use this medicine after the expiry date which is stated on the vial or carton label after EXP. The expiry date refers to the last day of that month.

Do not use this medicine if you notice that the solution is not clear, colourless to pale yellow and free from particles.

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

6 Contents of the pack and other information

What Cytarabine Teva contains
- The active substance is cytarabine. One ml solution contains 100 mg cytarabine.
  - Each 1 ml vial contains 100 mg cytarabine.
  - Each 5 ml vial contains 500 mg cytarabine.
  - Each 10 ml vial contains 1 g cytarabine.
  - Each 20 ml vial contains 2 g cytarabine.
- The other ingredients are:
  - macrogol 400
  - trometamol
  - water for injections

What Cytarabine Teva looks like and contents of the pack
Cytarabine Teva is a clear, colourless to pale yellow solution for injection or infusion.

Colourless glass vial with rubber stopper coated with Fluorotec and an aluminium metallic cap with propylene disk.
The vial may or may not be sheathed in a protective sleeve.

100 mg/1 ml (butyl, 3 ml nominal fill volume)
500 mg/5 ml (bromobutyl, 5 ml nominal fill volume)
1 g/10 ml (bromobutyl, 10 ml nominal fill volume)
2 g/20 ml (bromobutyl, 20 ml nominal fill volume)

Pack sizes
Each pack contains 1 single-use vial.

Pack sizes:
1x 1 ml
1x 5 ml
1x 10 ml
1x 20 ml

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Teva B.V.
Swensweg 5
2031GA Haarlem
Netherlands

Manufacturer
S.C. SINDAN-PHARMA S.R.L.
11, Ion Mihalache Ave, the 1st district,
011171, Bucharest 1
Romania

Actavis Italy S.p.A
Via Pasteur 10, Nerviano (Milan)
20014
Italy

This medicinal product is authorised in the Member States of the EEA under the following names:

Sweden	Cytarabin Actavis
Denmark	Cytarabin Actavis
Croatia	Citarabin Actavis 100 mg/ml otopina za injekciju
Ireland	Cytarabine Teva 100 mg/ml Solution for Injection/ Infusion
Italy	Citarabina Actavis
Poland	Cytarabine Teva
Romania	Citarabină Teva 100mg/ml soluţie injectabilă
United Kingdom	Cytarabine 100mg/ml Solution for Injection or Infusion

This leaflet was last revised in December 2016.

Preparation
- Chemotherapeutic agents should be prepared for administration only by professionals trained in the safe use of the preparation.
- Operations such as dilution and transfer to syringes should be carried out only in the designated area.
- The personnel carrying out these procedures should be adequately protected with clothing, gloves and eye shield.
- Pregnant personnel are advised not to handle chemotherapeutic agents.

Disposal and Contamination
To destroy, place in a high risk (for cytotoxics) waste disposal bag and incinerate at 1100ºC.

If spills occur, restrict access to the affected area and adequate protection including gloves and safety spectacles should be worn. Limit the spread and clean the area with absorbent paper/material. Spills may also be treated with 5% sodium hypochlorite. The spill area should be cleaned with copious amounts of water. Place the contaminated material in a leak proof disposal bag for cytotoxics and incinerate at 1100ºC.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements for cytotoxic agents.

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