PACKAGE LEAFLET: INFORMATION FOR THE USER

Cytarabine 20 mg/ml Solution for Injection/Infusion
cytarabine

Read all of this leaflet carefully before you start using this medicine because it contain import information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this section. See section 4.

What is in this leaflet:

1. What Cytarabine solution for injection/infusion is and what it is used for
2. What you need to know before you use Cytarabine solution for injection/infusion
3. How to use Cytarabine solution for injection/infusion
4. Possible side effects
5. How to store Cytarabine solution for injection/infusion
6. Contents of the pack and other information

1. WHAT CYTARABINE SOLUTION FOR INJECTION/INFUSION IS AND WHAT IT IS USED FOR

Cytarabine solution for injection/infusion 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 treatment of acute leukaemias (cancer of blood where you have too many white blood cells) including prophylaxis and treatment of CNS involvement (meningeal leukaemia). Cytarabine interferes with the growth of cancer cells, which are eventually destroyed.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE CYTARABINE SOLUTION FOR INJECTION/INFUSION

Do not use Cytarabine solution for injection/infusion

- 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, unless your doctor decides that it is safe to take cytarabine
- if you are feeling increasing difficulties in body coordination after radiation treatment or treatment with another anticancer medicine such as methotrexate
- if you are pregnant

Warning and precautions
Talk to your doctor, pharmacist or nurse before taking Cytarabine solution for injection/infusion

- if your bone marrow is not functioning properly, as, therapy should only be initiated under close medical supervision.
- if you have any problems with your liver. If your liver is not working well before treatment, cytarabine should be given only under strict medical supervision.
- If you have received radiotherapy.
- if you are undergoing transfusion of certain type of blood cells (granulocyte).

- if you have had or are going to have a dialysis immediately before or after treatment with cytarabine. If you are on dialysis, the doctor may alter the time that this medicine is given as dialysis may decrease the effect of this medicine.

During treatment

- Your doctor will test your blood regularly and examine your bone marrow if required
- Your doctor may frequently monitor the functioning of your liver and kidneys.
- Your doctor may carry out tests to check the functioning of your nerves during treatment with this medicine.
- 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 vaccines is not advised. 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.

Cytarabine strongly reduce blood cell production in the bone marrow. This can make you more prone to infection or bleeding. The blood cell numbers can continue to fall after stopping treatment.

Other medicines and Cytarabine solution for injection/infusion

Tell your doctor or pharmacist if you are taking or have recently taken any other medicines including medicines obtained without prescription.

- digoxin or beta-acetyldigoxin tablets (used to treat certain heart conditions)
- gentamicin (an antibiotic used to treat bacterial infections)
- 5-fluorocytosine (a medicine used to treat fungal infections)
- given medicines containing cyclophosphamide, vincristine and prednisone which are used in cancer treatment programmes.
- any other medicine which may suppress your immune system (such as azathioprine or mercaptopurine).

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 or pharmacist for advice before taking this medicine.

Pregnancy

Avoid becoming pregnant while you or your partner is being treated with cytarabine. 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 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 because this medicine may be harmful to infants being breast-fed.

Fertility

Cytarabine may lead to suppression of menstrual cycles in females and lead to amenorrhea and may suppress sperm production in male patients. Male patients undergoing cytarabine treatment should use a reliable contraceptive method.

Driving and using machines

Cytarabine 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 machines.

Cytarabine Solution for Injection/ Infusion contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per 5 ml, that is to say essentially 'sodium free'.

3. HOW TO USE CYTARABINE SOLUTION FOR INJECTION/INFUSION

Cytarabine solution for injection/infusion will be given to you under the direction of specialists in hospital. Your doctor will decide what dose to given and the number of days treatment you will receive depending on your condition.

This medicine may be given by solution for injection/infusion (using a syringe) under the skin (subcutaneous) or into a vein (intravenous) or into a muscle (intramuscular) or into the spine (intrathecal).

Dosage
Based on your condition, your doctor will decide the dose of cytarabine, 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.

If you take more Cytarabine solution for injection/infusion than you should

High doses can worsen side effects like sores in the mouth or may decrease the number of white blood cells and platelets (these help the blood to clot) in the blood, damage to nerves, severe lung disorders, heart problems and may even cause death. 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 product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Cytarabine solution for injection/infusion can cause side effects, although not everybody gets them.

The side effects of cytarabine are dependent on the dose. The digestive tract is most commonly affected, but also the blood. The side effects on the digestive tract are less if cytarabine is given by infusion.

If any of the following happen, you may need urgent medical attention. Tell your doctor immediately, if you notice any of following:

- sudden signs of allergy such as rash, itching or hives on the skin, swelling of the face, lips mouth or throat, shortness of breath or wheezing
- a combination of symptoms such as fever or low body temperature, rapid breathing, elevated heart rate, confusion and oedema which may be signs of blood poisoning
- infection or inflammation at the site of solution for injection/infusion
- spinal cord injury resulting in paralysis of two or more limbs
- weakness or numbness of the limbs, sexual dysfunction, fits and loss of consciousness which may be signs of damage to the brain or nerves
- unusual muscle pain or tenderness

- sore, watery or burning eyes with bleeding, vision disturbance, sensitivity to light
- complete loss of vision
- sudden sharp chest pain spreading into the shoulders and neck
- severe abdominal pain with vomiting, diarrhoea, constipation or blood in the stool
- sudden weight loss or jaundice (yellow skin and eyes), changes to the colour of urine or stoolspersistent cough with fever, chills and shortness of breath, caused by an infection of the lungs
- increase in other signs of infection such as sore throat or mouth ulcers, which may be caused by a reduction in white blood cells
- pale skin and tiredness or increased bleeding or bruising, which may be caused by a reduction in other types of blood cells
- difficulty passing urine or emptying the bladder

Other possible side effects include:

Common: may affect up to 1 in 10 people

- fever
- abnormal blood cells (megaloblastosis)
- loss of appetite
- swallowing difficulties
- pain in the gut (abdominal pain)
- nausea (feeling sick)
- being sick (vomiting)
- reduced consciousness (at high doses),
- speaking difficulties (at high doses),
- abnormal eye movements (nystagmus at high dose),
- diarrhoea,
- inflammation or ulceration in the mouth or anus
- reversible effects on the liver such as increased enzyme levels
- reversible effects to the skin such as reddening (erythema), blistering, rash, hives, blood vessel inflammation (vasculitis), hair loss
- kidney problems that may be identified by a blood or urine test
- abnormal high blood uric acid levels (hyperuricaemia)

Uncommon: may affect up to 1 in 100 people

- sore throat
- headache
- inflammation and ulcers of the gullet
- brown/black spots on the skin (lentigo),
- ulceration of the skin,
- numbness of arms and legs
- itching
- shortness of breath
- joint and muscle pain

Very rare: may affect up to 1 in 10,000 people

- blisters or eruption of the skin
- irregular heart beat (arrhythmia)

Not known: frequency cannot be estimated from the available data:

- dizziness
- painful swelling in the arms or legs
- freckling of the skin
- rash
- chest pain
- burning pain of palms and soles
- slower than usual heart rate or heart beat

Other side effects:

The cytarabine syndrome may occur 6-12 hours after start of treatment. The symptoms include:
- fever
- bone and muscle pain
- sore eyes (conjunctivitis)
- generally feeling unwell
- occasional chest pain
- rash
- nausea (feeling sick)

The following symptoms may develop after intrathecal treatment (injection into the space around the spinal cord) with cytarabine:

- inflammation of the membrane surrounding brain and spinal cord which may include symptoms such as severe headache, numbness or tingling sensation of the hands and legs etc.

Your doctor may prescribe corticosteroids (anti-inflammatory medicines such as hydrocortisone, prednisolone, dexamethasone) to prevent or treat these symptoms. If they are effective, treatment with cytarabine may be continued.

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
- problems of coordination & balance
- confusion
- sleepiness
- shaking

These side effects may occur more often:
- in elderly patients (>55 years of age)
- in patients with impaired liver and kidney function
- after previous cancer treatment to the brain and spinal cord for instance radiotherapy or injection of cytostatic
- with alcohol abuse

The risk of nervous system damages increases if the cytarabine treatment

- is given at high doses or at short intervals
- is combined with other treatments that are toxic to the nerves system (such as radiotherapy or methotrexate)

Cytarabine therapy may also cause lack of menstrual periods in females and lack of production of sperms in males.

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 (see contact details below). By reporting side effects you can help provide more information on the safety of this medicine.

Ireland
HPRA Pharmacovigilance
Website: www.hpra.ie

5. HOW TO STORE CYTARABINE SOLUTION FOR INJECTION/INFUSION

Keep out of sight and reach of children

Do not use Cytarabine solution for injection/infusion if you notice the solution is not clear, colourless and free from visible particles.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer use. These measures will help protect the environment.

Expiry
This medicine must not be used after the expiry date which is stated on the vial and carton after 'EXP'. Where only a month and year is stated, the expiry date refers to the last day of that month.

Storage
Do not store above 25°C. Do not refrigerate or freeze.

Chemical and physical in-use stability has demonstrated at 0.04 mg/ml, 0.1 mg/ml, 1.0 mg/ml and 4.0 mg/ml concentration. The product is stable for 8 days at below 25ºC.

From a microbiological point of view, unless the method of dilution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Cytarabine solution for injection/infusion contains

The active substance is cytarabine. Each one millilitre (1 ml) of solution contains 20 milligrams (mg) of cytarabine.

The other ingredients are sodium chloride, sodium hydroxide (for pH adjustment), hydrochloric acid concentrate (for pH adjustment) and Water for Injections. See section 2 'Cytarabine solution for injection/infusion contain sodium'.

What Cytarabine solution for injection/infusion looks like and contents of the pack

Cytarabine solution for injection/infusion is a clear, colourless solution and free from visible particles.

2 ml: Clear glass vial with a butyl rubber stopper and aluminium flip off blue seal.
5 ml: Clear glass vial with a butyl rubber stopper and aluminium flip off red seal.

Glass vial is wrapped with superficial plastic sheathing along with Non-PVC base.

Pack sizes:
2 ml : 1 vial, 5 vials and 25 vials
5 ml : 1 vial, 5 vials and 25 vials

Not all packs may be marketed.

Marketing authorisation holder and manufacturer

Marketing Authorisation Holder
Accord Healthcare Ireland Ltd.
Euro House
Euro Business Park
Little Island
Cork T45 K857
Ireland

Manufacturer:
Accord Healthcare Limited,
Sage House, 319 Pinner Road,
Harrow, HA1 4HF
United Kingdom

and

Laboratori Fundació Dau
Pol. Ind. Consorci Zona Franca,
c/ C, 12-14 Barcelona, 08040,
Spain

and

Accord Healthcare Polska Sp.z o.o.,
ul. Lutomierska 50,95-200 Pabianice, Poland

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

Name of member state	Name of the medicinal product
Austria	Cytarabin Accord 20 mg/ml Injektions-/ Infusionslösung
Germany	Cytarabine Accord 20 mg/ml Lösung für Injektion / Infusion
Denmark	Cytarabine Accord 20 mg/ml
Spain	Cytarabine 20 mg/mL Solución para inyección/infusión
Finland	Cytarabine Accord Healthcare 20 mg/ml injektio-/infuusioneste, liuos
France	Cytarabine Accord 20 mg/ml solution injectable/pour perfusion
Ireland	Cytarabine 20 mg/ml solution for injection/ infusion
Malta	Cytarabine 20 mg/ml solution for injection/ infusion
Norway	Cytarabine Accord
Poland	Cytarabina Accord
Romania	Citarabină Accord 20 mg/ml soluție injectabilă/perfuzabilă
Sweden	Cytarabine Accord 20 mg/ml Injektions-/infusionsvätska, lösning
Slovenia	Citarabin Accord 20 mg/ml raztopina za injiciranje/infundiranje
United Kingdom	Cytarabine 20 mg/ml solution for injection/ infusion

This leaflet was last revised in 01/2020.

The following information is intended for medical or healthcare professionals only:

Further to the information included in section 3, practical information on the preparation/handling of the medicinal product is provided here.

Incompatibilities

Solutions of cytarabine have been reported to be incompatible with various drugs, i.e. carbenicillin sodium, cephalothin sodium, fluorouracil, gentamicin sulphate, heparin sodium, hydrocortisone sodium succinate, insulin-regular, methylprednisolone sodium succinate, nafacillin sodium, oxacillin sodium, penicillin G sodium (benzylpenicillin), methotrexate, predinisolone succinate.

However, the incompatibility depends on several factors (e.g. concentrations of the drug, specific diluents used, resulting pH, temperature). Specialised references should be consulted for specific compatibility information.

This medicinal product must not be mixed with other medicinal product except recommended dilution fluids.

Use and cytotoxic handling guidelines

For single use only. Any unused solution should be discarded.

Cytarabine solution for injection/infusion is intended for intravenous, intramuscular, subcutaneous or intrathecal use.

The diluted solution should be clear, colourless and free from visible particles.

Parenteral drugs should be inspected visually for particulate matter and discolouration, prior to administration, whenever solution and container permit.

If the solution appears discoloured or contains visible particles, it should be discarded.

Cytarabine solution for injection/infusion is a ready to use solution but it can be diluted with sterilised Water for Injections, 5% Dextrose Injection or 0.9% Sodium Chloride injection.

Chemical and physical in-use stability has demonstrated at 0.04 mg/ml, 0.1 mg/ml, 1.0 mg/ml and 4.0 mg/ml concentration. The product is stable for 8 days at below 25ºC.

From a microbiological point of view, unless the method of dilution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

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.

In the event of contact with the skin or eyes, the affected area should be washed with copious amounts of water or normal saline. A bland cream may be used to treat the transient stinging of skin. Medical advice should be sought if the eyes are affected.

In the event of spillage, operators should put on gloves and mop up the spilled material with a sponge kept in the area for that purpose. Rinse the area twice with water. Put all solutions and sponges into a plastic bag and seal it.

Disposal

To destroy, place in high risk (for cytotoxic) waste disposal bag and incinerate at 1100°C. 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 pill area should be cleaned with copious amounts of water. Place the contaminated material in a leak proof disposal bag for cytotoxic and incinerate at 1100°C.

Any unused product or waste material should be disposed of in accordance with local requirements.