
PACKAGE LEAFLET: INFORMATION FOR THE PATIENT

Cytarabine “Ebewe” 20mg/ml solution for injection or infusion
Cytarabine “Ebewe” 50mg/ml solution for injection or infusion
Cytarabine “Ebewe” 100mg/ml solution for injection or infusion

Read this entire leaflet carefully before you start taking this medicine.

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

What is in this leaflet:

1. What Cytarabine “Ebewe” is and what it is used for
2. What you need to know before you take Cytarabine Ebewe”
3. How to take Cytarabine Ebewe”
4. Possible side effects
5. How to store Cytarabine Ebewe”
6. Contents of the pack and other information

1. WHAT CYTARABINE IS AND WHAT IT IS USED FOR

Cytarabine “Ebewe” solution for injection or infusion, contains the active substance Cytarabine. The drug Cytarabine is used to treat cancer. It can be used alone but more commonly it is used in combination with other anti-cancer agents.

Cytarabine can be used as monotherapy or in combination with other chemotherapeutics in adults and children with some types of leukaemia (cancer affecting the blood):

- Acute myeloid leukaemia
- Acute non-lymphoblastic leukaemia
- Acute lymphocytic leukaemia
- Erythroleukaemia
- Blast crises of chronic myeloid leukaemia

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE CYTARABINE “Ebewe”

Do not take Cytarabine “Ebewe”:

- If you are hypersensitive (severe allergy) to cytarabine or any of the other ingredients of Cytarabine “Ebewe”.
- If your bone marrow is still recovering from damage caused by other medicines (your doctor will check for this using blood test and will only consider treatment with cytarabine if absolutely necessary).
- If your cancer is not spreading (your doctor will only consider treatment with cytarabine if absolutely necessary)
- If you have anaemia, leucopenia or thrombocytopenia of non-malignant etiology (your doctor will only consider treatment with cytarabine if absolutely necessary)
- If you have degenerative and toxic encephalopathies, especially after the use of methotrexate or radiation treatment

Tell your doctor if you think any of the above applies to you before this medicine is used.

Warnings and precautions:

Talk to your doctor or pharmacist or nurse before taking Cytarabine “Ebewe”

- Cytarabine must only be administered by specialists with experience in chemotherapy of malignant disorders. If the number of cells in your blood (blood cell count) is low (your doctor will check this using blood tests)
- if you have any problems with your liver including jaundice (causes yellowing of the skin) It is important that liver and kidney function tests are carried out regularly to ensure no problems are occurring
- if you have a high number of blast cells or large tumour masses (non-Hodgkin’s lymphomas) prevention of high level of acid in the blood is required through regular monitoring of uric acid levels in blood is recommended (increased uric acid is a result of blood cells breaking down)
- if you have gastrointestinal ulcers, or have recently had an operation you must be kept under close observation
- if you are sexually mature must take contraceptive measures during and until six months after the therapy with Cytarabine
- if you are receiving or have received a live vaccine

No effects have been observed as a result of exposure during handling. Slight irritation of the eye is possible. Repeated or continuous contact with the skin can lead to irritation. After accidental contact, wash the area of skin with copious amounts of water and soap.

Tell your doctor if either of the above applies to you before this medicine is used.
Special care will be taken if cytarabine is to be given to a child

Pregnancy, breast-feeding and fertility

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

During pregnancy, cytarabine may only be administered on strict indication, in which context the benefits of the drug for the mother must be weighed against the possible dangers to the foetus. Animal studies have shown that Cytarabine has embryotoxic and teratogenic effects (see section 5.3).

Men and women must use effective contraceptives during treatment and for six months thereafter.

Breast-feeding

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

It is not known whether Cytarabine is secreted in mother’s milk. As many drugs are secreted in mother’s milk and as Cytarabine can be responsible for serious side effects in the neonate, breastfeeding should be stopped during treatment with Cytarabine.

Driving and using machines:

Cytarabine has no effect on psychomotor performance. Nevertheless, patients receiving chemotherapy have a reduced ability to drive or operate machinery, and should be warned of the risk and advised to avoid this type of activity if this occurs.

Patients who are subject to incidental occurrences of vomiting, dizziness and eye complaints are advised not to drive vehicles or operate machinery.

Cytarabine “Ebewe” contains sodium.

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially ‘sodium-free’. (Please refer to “Section 6. CONTENTS OF THE PACK AND OTHER INFORMATION” for further information on ingredients and excipients)

Other medicines and Cytarabine:

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Cytarabine is often administered in combination with other drugs.

- The absorption of digoxin may be reduced if digoxin is combined with chemotherapeutics (including Cytarabine). The plasma levels of digoxin must therefore be monitored. Cytarabine can counteract the effect of gentamicin against *Klebsiella pneumoniae*.
- The concomitant administration of cytarabine with other cytotoxic drugs can potentiate toxicity, especially bone marrow toxicity.
- Combination of fluorocytosine with Cytarabine can lead to a reduced effectiveness of fluorocytosine.

3. HOW TO TAKE CYTARABINE “Ebewe”

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure. As this drug can only be administered intravenously (IV) or subcutaneously (SC), this drug will be administered by medical personnel; do not take it yourself. If you notice any unusual signs, symptoms or sensations please notify your doctor or nurse immediately.

If you take more Cytarabine “Ebewe” than you should:

If overdose occurs or you feel marked side effects tell your doctor immediately.

In the event of an overdose, therapy must be stopped, followed by treatment of the subsequent bone marrow depression, including total blood or platelet transfusion and antibiotics, as required.

In the event of intrathecal overdose, the cerebrospinal fluid must immediately be replaced with isotonic salt solution.

Cytarabine can be removed by means of haemodialysis.

If you forget to take Cytarabine “Ebewe”:

Do not take a double dose to make up for forgotten individual doses.

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

If you stop taking Cytarabine

Keep taking this medicine until your doctor tells you to stop. Do not stop taking it just because you feel better. If you stop taking this medicine, your condition may re-occur or get worse. If you experience symptoms on stopping treatment, contact your doctor.

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

4. POSSIBLE SIDE EFFECTS

Like all medicines, Cytarabine can have side effects, although not everybody gets them.

Side effects of Cytarabine are dose dependent. The most common are gastrointestinal side effects, and Cytarabine is toxic to the bone marrow (myelosuppression) and causes haematological side effects.

Cytarabine Syndrome (immunoallergic effect): this is characterised by fever, joint pain, bone pain, occasionally chest pain, skin rash, pink eye, nausea and feeling unwell.

Very common: may affect more than 1 in 10 people

- For 50mg & 100mg : Fever, thrombophlebitis at the injection site,
- Cytarabine (Ara-C) syndrome: fever, muscle pain, bone pain, incidental chest pain, break out rash, eye infection and feeling sick may occur 6-12 hours after the start of the therapy. Skin bleeding, hair loss. Corticosteroids can be used as prevention and to treat symptoms.. If these are effective, the therapy with Cytarabine can be continued. Bone marrow activity can be slowed, this can be severe and last some time.
- Reversible effects on the liver with increased enzyme levels

Common may affect up to 1 in 10 people

- a decrease in amount of red blood cells, chronic decrease in red blood cells, decrease in a number of white blood cells, decrease in the number of blood cells required for clotting, bleeding. reversible pink eye, (light sensitivity, stinging, visual disorders, increased flow of tears), inflammation of the eye painful inflammation and ulceration of the mucous membranes lining the digestive tract and stomach, lack of interest in food, difficulty in swallowing food, headache, dizziness, inflammation of nerves abdominal pain, feeling sick, vomiting, diarrhoea, oral/anal inflammation or ulceration, reversible effects on the liver function and yellowing of skin and eyes
- In the event of high dosages, cerebellar or cerebral toxicity with decreased consciousness level, dysarthria, nystagmus, seizure (when given intrathecally), neuritis, fever, thrombophlebitis at the injection site,
- reversible side effects to the skin, such as redness of the skin, skin blistering. itching, inflammation of blood cells, hair-loss, painful redness and blistering on the palms of the hands and soles of the feet (high dose therapy), pigmentation of the skin, bacterial infection of the skin at the injection site, skin breakdown, swelling, burning pain on the palms of the hands and soles of the feet.
- For 50 & 100mg only Kidney function disorders, urinary retention. hyperuricaemia.
- Anorexia
- Abnormally high levels of uric acid in the blood, pain
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Uncommon may affect up to 1 in 100 people

- Swelling due to allergy reaction; anaphylaxis, the restriction of air ways which can cause death, one case of anaphylaxis has been reported, which resulted in a heart attack. This occurred immediately after intravenous administration of Cytarabine. Sepsis a serious life threatening infection, suppression of the immune system; an impairment in motor or sensory function of the lower regions of the body following injection at the spinal cord.
- Fluid build-up on the lungs, difficulty breathing, sore throat, lung disease. acute respiratory distress syndrome inflammation and open sores in the lining of the oesophagus; gas in bowel wall, death in tissue cells, pneumonia, skin ulceration
- Kidney function disorders, not peeing enough
- Joint pain

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

- Breakdown of muscle has been reported after cytarabine therapy.
- Killing of white brain matter, paralysis of the lower limbs or paralysis of the upper and lower body have been reported after intrathecal treatment (i.e injection into the spinal space).
- Abnormal heart rhythm, Heart disease has been reported after cytarabine therapy.

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- Skin lesions.
 - The chance of CNS toxicity increases if cytarabine is administered intrathecally, the intrathecally cytarabine treatment is combined with other treatments which are toxic to the CNS, such as radiation, high dose therapy, or intrathecal methotrexate, or if the cytarabine treatment is intrathecally administered with short intervals or in doses above 30 mg/m².
 - Severe spinal cord toxicity is predominantly associated with intrathecal administration, but isolated cases have also been reported with high intravenous doses during combination chemotherapeutic regimens. Other isolated neuro toxicities have been reported.
 - Blindness has been reported after intrathecal treatment.
 - Inflammation of the pancreas, when intravenous doses are given quickly, patients may become nauseated and may vomit for several hours afterwards. The problem tends to be less severe when cytarabine is infused.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the HPRC Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie

5. HOW TO STORE CYTARABINE “Ebewe”

Keep this medicine out of the sight and reach of children
Store in the original packaging. Do not store above 25°C. Do not refrigerate or freeze.

Expiry Date

The reference to the expiry date must correspond to the wording used on the label i.e. Do not use this medicine after the expiry date which is stated on the label after ‘EXP’.

Storage life after reconstitution

Chemical and physical stability after dilution with 0.9% (m/f) sodium chloride solution and 5% (m/f) glucose solution has been demonstrated for 4 days at 2-8°C and for 24 hours when stored at a temperature below 25°C.

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 reconstitution/dilution has taken place in controlled and validated aseptic conditions.

Do not use this medicine if you notice any visible signs of deterioration or damage.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Cytarabine “Ebewe” contains:

The active substance is Cytarabine and each vial contains 100 mg, 500 mg, 1,000 mg, 2,000 mg, 5,000 or 10,000 mg of Cytarabine.

The other ingredients are sodium chloride (only for Cytarabine 20mg/ml), sodium lactate, and lactic acid water for injections

What Cytarabine looks like and contents of the pack

Cytarabine is a clear colourless sterile solution for injection or infusion

Vial sizes: 5ml,
20mg- vial sizes: 5ml
50mg- vial sizes: 10ml, 20ml, 40ml
100mg - Vial sizes: 5ml, 50ml, 100ml
1 vial per carton
Not all pack sizes may be marketed

Marketing Authorisation Holder

Fannin Limited,
Fannin House,
South County Business Park,
Dublin 18.

Manufacturer:

Ebewe Pharma Ges.m.b.H. Nfg. KG
A-4866 Unterach, Austria

For any information about this medicinal product, please contact your doctor, your pharmacist or the local representative of the Marketing Authorisation Holder.

This leaflet was last approved on XXXXX

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

Instructions for use and handling and disposal

Cytarabine must be diluted for infusion with 0.9% sodium chloride solution or 5% glucose solution. Compatibility with 0.9% sodium chloride solution and 5% glucose solution has been studied in concentrations of 0.2-3.2 mg/ml in PVC infusion bags, PE infusion vials and perfusion syringes. For intrathecal administration, 0.9% sodium chloride without preservative must be used as diluent. If Cytarabine comes into contact with the skin, the exposed area must be rinsed with copious amounts of water, and then washed thoroughly with water and soap. If the solution comes in contact with the eyes, rinse the eyes extremely carefully with copious amounts of water, then contact an eye specialist immediately.

Pregnant employees should be excluded from working with this drug.

After use, bottles and injection materials, including gloves, must be destroyed in accordance with the rules for cytotoxic drugs.

Spilled or leaked product can be inactivated with 5% sodium hypochlorite solution. All cleaning materials must be cleared away as indicated above.

Extravasation

1. Stop injection/infusion immediately
2. Replace infusion lead or syringe with 5ml disposable syringe and aspirate slowly as much as possible of the extravasated drug; CARE! Do not exert pressure on extravasation area
3. Remove i.v. access while aspirating
4. Regular control (aftercare)

Incompatibilities

Cytarabine is physically incompatible with various drugs, i.e., heparin, insulin, methotrexate, 5-fluorouracil, nafcillin, oxacillin, carbenicillin sodium, cephalothin sodium, gentamicin sulphate, hydrocortisone sodium succinate, penicillin G sodium, benzylpenicillin and methylprednisolone sodium succinate.

However the incompatibility depends on several factors (eg concentrations for 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 products except those mentioned in section 6.6 of the Summary of Product Characteristics.