Tabinoz®

Decitabine

Powder for Concentrate for Solution for Infusion

Read this leaflet carefully before you start taking Tabinoz®. This leaflet provides answers to the most common questions. If you have any further questions, ask your doctor or pharmacist. This medicine has been prescribed for your current illness only. Do not take it in similar conditions and do not pass it on to others. The information in this leaflet was last updated on the date listed on the final page. More recent information on the medicine may be available. You should ensure that you speak to your doctor or pharmacist to obtain the most up-to-date scientific information on the medicine.

What is in this leaflet

1. What Tabinoz® is and what it is used for

What Tabinoz® is

Tabinoz® is an anti-cancer medicine. It contains the active substance 'decitabine'.

What Tabinoz® is used for

Tabinoz® is used to treat a type of cancer called 'acute myeloid leukemia' or 'AML'. This is a type of cancer that affects your blood cells. You will be given Tabinoz® when you are first diagnosed with AML. It is used in adults.

How Tabinoz® works

Tabinoz® works by stopping cancer cells from growing. It also kills cancer cells.

Talk to your doctor or nurse if you have any questions about how Tabinoz® works or why this medicine has been prescribed for you.

2. What you need to know before you are given Tabinoz®

Do not use Tabinoz®

– If you are allergic to decitabine or any of the

other ingredients of this medicine (listed in section 6).

- If you are breast-feeding.

If you are not sure if any of the above applies to you, talk to your doctor, pharmacist or nurse before using Tabinoz®.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Tabinoz® if you have

- Low numbers of platelets, red blood cells or white blood cells
- An infection
- Liver disease
- A serious kidney disorder
- A heart disorder

If you are not sure if any of the above applies to you, talk to your doctor, pharmacist or nurse before using Tabinoz®.

Tabinoz® can cause a serious immune reaction called 'differentiation syndrome' (see section 4 'Possible side effects').

Tests or checks

You will have blood tests before you start treatment with Tabinoz® and at the start of each treatment cycle. These tests are to check that:

- You have enough blood cells.
- Your liver and kidneys are working properly.

Talk to your doctor about what your blood test results mean.

Children and adolescents

Tabinoz® is not for use in children or adolescents

under the age of 18.

Other medicines and Tabinoz®

Tell your doctor, nurse or pharmacist if you are using, have recently used or might use any other medicines. This includes medicines obtained without a prescription and herbal medicines. This is because Tabinoz® can affect the way some other medicines work. Also, some other medicines can affect the way Tabinoz® works.

Pregnancy and breast-feeding

- If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine.
- You should not use Tabinoz® if you are pregnant as it may harm your baby. If you are able to become pregnant, your doctor will ask you to take a pregnancy test before you start treatment with Tabinoz®. Tell your doctor immediately if you become pregnant during treatment with Tabinoz®.
- Do not breast-feed if you are using Tabinoz®. This is because it is not known if the medicine passes into the mother's milk.

Male and female fertility and contraception

- Men should not father a child while using Tabinoz®.
- Men should use effective contraception during treatment and for up to 3 months after treatment has stopped.
- Talk to your doctor if you wish to conserve your sperm before starting treatment.
- Women who are able to become pregnant must use effective contraception during treatment

and for 6 months following completion of treatment.

- Talk to your doctor if you wish to freeze your eggs before starting treatment.

Driving and using machines

You may feel tired or weak after using Tabinoz®. If this happens, do not drive or use any tools or machines.

3. How to use Tabinoz®

Tabinoz® will be given to you by a doctor or nurse who is trained in giving this type of medicine.

How much to use

- Your doctor will work out your dose of Tabinoz®. This depends on your height and weight (body surface area).

- The dose is 20 mg/m^2 body surface area.
- You will receive Tabinoz® every day for 5 days, then 3 weeks without the medicine. This is called a 'treatment cycle' and it is repeated every 4 weeks. You will usually receive at least 4 treatment cycles.
- Your doctor may delay your dose and change the total number of cycles, depending on how you respond to the treatment.

How Tabinoz® is given

The solution is given into a vein (as an infusion). This will take one hour.

If you are given more Tabinoz® than you should

This medicine will be given by your doctor or nurse. In the unlikely event that you are given too

much (an overdose), your doctor will check you for side effects and manage them accordingly.

If you forget your appointment to have Tabinoz®

If you miss an appointment, make another one as soon as possible. This is because for this medicine to be as effective as possible, it is important to follow the dosing schedule.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The following side effects may happen with this medicine.

Tell your doctor or nurse immediately if you notice any of the following serious side effects

- Fever: this may be a sign of an infection caused by low levels of white blood cells (very common).
- Chest pain or shortness of breath (with or without fever or cough): these may be signs of an infection of the lung called "pneumonia" (very common) or inflamed lungs (interstitial lung disease (frequency not known)) or cardiomyopathy (heart muscle disease (uncommon)) which can be accompanied with swelling of ankles, hands, legs and feet.
- Bleeding: including blood in the stools. This may be a sign of bleeding in the stomach or gut (common).
- Difficulty with moving, speaking or understanding or seeing, sudden severe

headache, seizure, numbness or weakness in any part of the body. These may be signs of bleeding inside your head (common).

- Difficulty breathing, swelling of the lips, itching or rash. This may be due to an allergic (hypersensitivity) reaction (common).
- Serious immune reaction (differentiation syndrome) that may cause fever, cough, difficulty breathing, rash, decreased urine, hypotension (low blood pressure), swelling of the arms or legs and rapid weight gain (not known).

Tell your doctor or nurse immediately if you notice any of the serious side effects above.

Other side effects of Tabinoz® include

Very common (may affect more than 1 in 10 people):

- Urine infection
- Other infection in any part of the body, caused by bacteria, virus or fungi
- Bleeding or bruising more easily, these may be signs of a drop in the number of blood platelets (thrombocytopenia)
- Feeling tired or looking pale, these may be signs of a drop in the number of red blood cells (anemia)
- High level of sugar in the blood
- Headache
- Nose bleeds
- Diarrhea

- Vomiting
- Nausea
- Fever
- Abnormal liver function

Common (may affect up to 1 in 10 people):

- An infection of the blood caused by bacteria, this may be a sign of a low level of white blood cells
- Sore or runny nose, sore sinuses
- Mouth or tongue ulcers
- High level of bilirubin in the blood

Uncommon (may affect up to 1 in 100 people):

- A drop in the number of red blood cells, white blood cells and platelets (pancytopenia)
- Heart muscle disease

- Red, raised painful patches on the skin, fever, and an increase in white blood cells, these may be signs of 'Acute Febrile Neutrophilic Dermatosis' or 'Sweet's Syndrome'

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

- Inflamed gut (enterocolitis, colitis and cecitis), with symptoms of abdominal pain, bloating, or diarrhea. Enterocolitis may lead to septic complications and may be associated with fatal outcome.

5. How to store Tabinoz®

Your doctor, nurse or pharmacist is responsible for storing Tabinoz®.

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

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

Store in the original package in order to protect from light.

Store below 30°C.

Cytotoxic agent. Must be transported, stored and used according to guidelines for handling of cytotoxic compounds.

After reconstitution, the concentrate must be further diluted within 15 minutes using cold infusion fluids. Your doctor, nurse or pharmacist is responsible for disposing of any unused Tabinoz® correctly.

6. Contents of the box and other information

What Tabinoz® contains

- The active substance is decitabine. Each vial contains 50 mg decitabine. After reconstitution with 10 ml of water for injections, each ml of concentrate contains 5 mg of decitabine.
- The other ingredients are potassium dihydrogen phosphate, sodium hydroxide, sodium hydroxide and/or hydrochloric acid (for pH-adjustment).

Contents of the container

Tabinoz® is a powder for concentrate for solution for infusion. It is supplied in a glass vial containing 50 mg decitabine. Each box contains 1 vial.

7. Posology and method of administration

Decitabine administration must be initiated under

the supervision of physicians experienced in the use of chemotherapeutic medicinal products.

Posology

In a treatment cycle, decitabine is administered at a dose of 20 mg/m^2 body surface area by intravenous infusion over one hour repeated daily for 5 consecutive days (i.e., a total of 5 doses per treatment cycle). The total daily dose must not exceed 20 mg/m^2 and the total dose per treatment cycle must not exceed 100 mg/m^2. If a dose is missed, treatment should be resumed as soon as possible. The cycle should be repeated every 4 weeks depending on the patient's clinical response and observed toxicity. It is recommended that patients be treated for a minimum of 4 cycles; however, a complete or partial remission may take longer than 4 cycles to be obtained.

Treatment may be continued as long as the patient shows response, continues to benefit or exhibits stable disease, i.e., in the absence of overt progression.

If after 4 cycles, the patient's hematological values (e.g., platelet counts or absolute neutrophil count), have not returned to pre-treatment levels or if disease progression occurs (peripheral blast counts are increasing or bone marrow blast counts are worsening), the patient may be considered to be a non-responder and alternative therapeutic options to decitabine should be considered.

Pre-medication for the prevention of nausea and vomiting is not routinely recommended but may be administered if required.

Management of myelosuppression and associated complications

Myelosuppression and adverse events related to myelosuppression (thrombocytopenia, anemia, neutropenia, and febrile neutropenia) are common in both treated and untreated patients with AML. Complications of myelosuppression include infections and bleeding. Treatment may be delayed at the discretion of the treating physician, if the patient experiences myelosuppression-associated complications, such as those described below:

- Febrile neutropenia (temperature ≥ 38.5°C and absolute neutrophil count < 1,000/µl)
- Active viral, bacterial or fungal infection (i.e., requiring intravenous anti-infectives or extensive supportive care)
- Hemorrhage (gastrointestinal, genito-urinary, pulmonary with platelets < 25,000/µl or any central nervous system hemorrhage)

Treatment with decitabine may be resumed once these conditions have improved or have been stabilized with adequate treatment (anti-infective therapy, transfusions, or growth factors).

In clinical studies, approximately one-third of patients receiving decitabine required a dose delay. Dose reduction is not recommended.

Pediatric population

Decitabine should not be used in children with AML aged < 18 years, because efficacy was not established.

Hepatic impairment

Studies in patients with hepatic impairment have not been conducted. The need for dose adjustment in patients with hepatic impairment

has not been evaluated. If worsening hepatic function occurs, patients should be carefully monitored.

Renal impairment

Studies in patients with renal impairment have not been conducted. The need for dose adjustment in patients with renal impairment has not been evaluated.

Method of administration

Decitabine is administered by intravenous infusion. A central venous catheter is not required.

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Marketing Authorization Holder and Manufacturer:

Nano Fanavaran Darouei Alvand (NanoAlvand)

No. 1462, Pharmaceutical Incubation Center, Avicenna Tech. Park of Tehran University of Medical Sciences, North Kargar Ave., Tehran, Iran.

P.O. Box: 1439955991

Tel: +9821-88020579

Fax: +9821-88020597

E-mail: info@nanoalvand.com

URL: www.nanoalvand.com

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