

Tinopa®

Thiotepa

Powder for Concentrate for Solution for Infusion

Read this leaflet carefully before you start taking Tinopa®. 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 bottom of the 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. The latest version of this leaflet is available on www.nanoalvand.com.

What is in this leaflet

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

Tinopa® contains the active substance thiotepa, which belongs to a group of medicines called alkylating agents.

Tinopa® is used to prepare patients for bone marrow transplantation. It works by destroying bone marrow cells. This enables the transplantation of new bone marrow cells (hematopoietic progenitor cells), which in turn enable the body to produce healthy blood cells.

Tinopa® can be used in adults and children and adolescents.

2. What you need to know before you take Tinopa®

Do not use Tinopa®

- if you are allergic to thiotepa.
- if you are pregnant or think you may be pregnant.
- if you are breast-feeding.
- if you are receiving yellow fever vaccination, live virus and bacterial vaccines.

Warnings and precautions

Talk to your doctor before using Tinopa® if you have:

- liver or kidney problems.
- heart or lung problems.
- seizures/fits (epilepsy) or have had them in the past (if treated with phenytoin or fosphenytoin).

Because Tinopa® destroys bone marrow cells responsible for producing blood cells, regular blood tests will be taken during treatment to check your blood cell counts.

In order to prevent and manage infections, you will be given anti-infectives.

Tinopa® may cause another type of cancer in the future. Your doctor will discuss this risk with you.

Other medicines and Tinopa®

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

Pregnancy and breast-feeding

Pregnancy

You must tell your doctor if you are pregnant or you think you may be pregnant before you receive Tinopa®. You must not use Tinopa® during pregnancy.

Contraception

Both women and men using Tinopa® must use effective contraceptive methods during treatment. Men should not father a child while treated with Tinopa® and during the year after cessation of treatment.

Breast-feeding

It is not known whether this medicinal product is excreted in breast milk. As a precautionary measure, women must not breast-feed during treatment with Tinopa®.

Fertility

Tinopa® can impair male and female fertility. Male patients should seek for sperm preservation before therapy is started.

Driving and using machines

It is likely that certain adverse reactions of Tinopa® like dizziness, headache and blurred vision could affect your ability to drive and use machines. If you are affected, do not drive or use machines.

3. How to use Tinopa®

Your doctor will calculate the dose according to your body surface or weight and your disease.

How Tinopa® is given

Tinopa® is administered by a qualified healthcare professional as an intravenous infusion (drip in a vein) after dilution of the individual vial. Each infusion will last 2-4 hours.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Tell your doctor if you get any side effects, including those not listed in this leaflet.

The most serious side effects of Tinopa® therapy or the transplant procedure may include:

- decrease in circulating blood cell counts (intended effect of the medicine to prepare you for your transplant infusion)
- infection
- liver disorders including blocking of a liver vein

- the graft attacks your body (graft versus host disease)
- respiratory complications

Your doctor will monitor your blood counts and liver enzymes regularly to detect and manage these events.

Side effects of Tinopa® may occur with certain frequencies, which are defined as follows:

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

- increased susceptibility to infection
- whole-body inflammatory state (sepsis)
- decreased counts of white blood cells, platelets and red blood cells (anemia)
- the transplanted cells attack your body (graft versus host disease)
- dizziness, headache, blurred vision
- uncontrolled shaking of the body (convulsion)
- sensation of tingling, pricking or numbness (paranesthesia)
- partial loss of movement
- cardiac arrest
- nausea, vomiting, diarrhea
- inflammation of the mucosa of the mouth (mucositis)
- irritated stomach, gullet, intestine
- inflammation of the colon
- anorexia, decreased appetite
- high glucose in the blood
- skin rash, itching, shedding
- skin color disorder (do not confuse with jaundice-see below)
- redness of the skin (erythema)
- hair loss
- back and abdominal pain, pain
- muscle and joint pain
- abnormal electrical activity in the heart (arrhythmia)
- inflammation of lung tissue
- enlarged liver
- altered organ function
- blocking of a liver vein (veno-occlusive disease (VOD))
- yellowing of the skin and eyes (jaundice)
- hearing impaired
- lymphatic obstruction
- high blood pressure
- increased liver, renal and digestive enzymes
- abnormal blood electrolytes
- weight gain
- fever, general weakness, chills
- bleeding (hemorrhage)
- nasal bleeding
- general swelling due to fluid retention (edema)
- pain or inflammation at the injection site
- eye infection (conjunctivitis)
- decreased sperm cell count
- vaginal bleeding
- absence of menstrual periods (amenorrhoea)
- memory loss
- delaying in weight and height increase
- bladder dysfunction
- underproduction of testosterone
- insufficient production of thyroid hormone
- deficient activity of the pituitary gland
- confusional state

Common side effects (may affect up to 1 in 10 people)

- anxiety, confusion
- abnormal bulging outward of one of the arteries in the brain (intracranial aneurysm)
- creatinine elevated
- allergic reactions
- occlusion of a blood vessel (embolism)
- heart rhythm disorder
- heart inability
- cardiovascular inability
- oxygen deficiency
- fluid accumulation in the lungs (pulmonary edema)
- pulmonary bleeding
- respiratory arrest
- blood in the urine (hematuria) and moderate renal insufficiency
- inflammation of the urinary bladder
- discomfort in urination and decrease in urine output (dysuria and oliguria)
- increase in the amount of nitrogen components in the blood stream (BUN increase)
- cataract
- inability of the liver
- cerebral hemorrhage
- cough
- constipation and upset stomach
- obstruction of the bowel

- perforation of stomach
- changes in muscle tone
- gross lack of coordination of muscle movements
- bruises due to a low platelet count
- menopausal symptoms
- cancer (second primary malignancies)
- abnormal brain function
- male and female infertility
- Uncommon side effects (may affect up to 1 in 100 people)**
- inflammation and exfoliation of the skin (erythrodermic psoriasis)
- delirium, nervousness, hallucination, agitation
- gastrointestinal ulcer
- inflammation of the muscular tissue of the heart (myocarditis)
- abnormal heart condition (cardiomyopathy)

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

- increased blood pressure in the arteries (blood vessels) of the lungs (pulmonary arterial hypertension)
- severe skin damage (e.g. severe lesions, bullae, etc.) potentially involving the full body surface which can be even life-threatening
- damage to a component of the brain (the so-called white matter) which can be even life-threatening (leukoencephalopathy)

5. How to store Tinopa®

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date.
- Store in a refrigerator (2°C to 8°C). Do not freeze.
- After reconstitution the product is stable for 8 hours when stored at 2°C to 8°C. After dilution the product is stable for 24 hours when stored at 2°C to 8°C and for 4 hours when stored below 30°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.
- Cytotoxic agent. Must be transported, stored and used according to guidelines for handling of cytotoxic compounds.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Tinopa® contains

The active substance is thiotepa. One vial contains 100 mg thiotepa. After reconstitution, each ml contains 10 mg thiotepa (10 mg/ml). Tinopa® does not contain any other ingredients.

What Tinopa® looks like and contents of the pack

Tinopa® is a white crystalline powder supplied in a glass vial containing 100 mg thiotepa. Each vial packed in a box with a leaflet.

For medical or healthcare professionals only

Reconstitution

Tinopa® must be reconstituted with 10 ml of sterile water for injection.

Using a syringe fitted with a needle, aseptically withdraw 10 ml of sterile water for injection.

Inject the content of the syringe into the vial through the rubber stopper.

Remove the syringe and the needle and mix manually by repeated inversions.

Only colorless solutions, without any particulate matter, must be used. Reconstituted solutions may occasionally show opalescence; such solutions can still be administered.

Further dilution in the infusion bag

The reconstituted solution is hypotonic and must be further diluted prior to administration with 500 ml sodium chloride 9 mg/ml (%0.9) solution for injection (1000 ml if the dose is higher than 500 mg) or with an appropriate volume of sodium chloride 9 mg/ml (%0.9) in order to obtain a final thiotepa concentration between 0.5 and 1 mg/ml.

Administration

Tinopa® infusion solution should be inspected visually for particulate matter prior to administration. Solutions containing a precipitate should be discarded.

The infusion solution must be administered to patients using an infusion set equipped with a 0.2 µm in-line filter. Filtering does not alter solution potency.

Tinopa® should be aseptically administered as a 2-4 hours infusion under room temperature (about 30°C) and normal light conditions.

Prior to and following each infusion, the indwelling catheter line should be flushed with approximately 5 ml sodium chloride 9 mg/ml (%0.9) solution for injection.

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