Package leaflet: Information for the user

Zavedos® 1mg/mL Solution for Injection
idarubicin hydrochloride

Read all of this leaflet carefully before you are given 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.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- 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 Zavedos is and what it is used for

Zavedos contains an active ingredient called idarubicin hydrochloride, which belongs to a group of medicines called anthracyclines. Zavedos interferes with ways in which the cells of your body grow and increase in number and is used in the treatment of cancers (chemotherapy).

Zavedos is used in adults and children for the treatment of acute non lymphoblastic leukaemia (ANLL), also referred to as acute myeloid leukaemia (AML).

Zavedos is also used in adults and children as a second line treatment of relapsed acute lymphoblastic leukaemia (ALL).

2. What you need to know before you are given Zavedos

Do not use Zavedos:
- If you have ever had an allergic (hypersensitivity) reaction to
  - idarubicin or any of the other ingredients of this medicine (listed in section 6).
  - other anthracyclines or anthracenediones.
- If your liver or kidneys are not working properly.
- If you have an infection which is not under control.
- If you have had a previous or current history of heart disease.
- If you have had a previous or current history of abnormal heart rhythms.
- If you have had previous or current history of bone marrow depression caused by previous therapy.
- If you have previously been treated with high doses of idarubicin hydrochloride and/ or other anthracyclines or anthracenediones.
- If you are breast-feeding.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before you are given Zavedos if you:
- Suffer from bone marrow depression caused by previous therapy.
- Have suffered from heart trouble in the past or are presently receiving treatment for this.
- You have had a previous or current history of stomach problems (e.g. ulcer) or any problem with your bowels.
- Are taking or have recently taken trastuzumab (a medicine used in the treatment of certain cancers). Trastuzumab can take up to 7 months to be removed from the body. As trastuzumab may affect the heart, you should not use Zavedos for up to 7 months after you have stopped taking trastuzumab. If Zavedos is used before this time, then your heart function should be carefully monitored.

Zavedos may affect male fertility. Talk to your doctor about fertility preservation before starting treatment. Both men and women should use effective contraception (see "Pregnancy, breast-feeding and fertility" section).

If you desire to have children after Zavedos treatment, talk to your doctor about your options.

In these cases, Zavedos might not be a suitable treatment for you, or a reduced dose might have to be used.

Paediatric population
Babies and children are more at risk to heart problems that may be caused by taking Zavedos. Regular checks of the heart for a longer time will be needed.

Regular checks by your doctor during Zavedos treatment
Before starting and during treatment you will need regular checks including blood tests.
Your doctor will be making regular checks of:
- Your blood, to check for low blood cell counts that may need treatment.
- Your heart function, as Zavedos can have effects upon this.
- Your liver and kidneys – again using blood tests – to check that Zavedos is not affecting the way they function in a harmful way.
- Blood uric acid levels – Zavedos may increase uric acid levels in the blood, which might cause gout. Another medicine may be given if your uric acid levels are too high.

You will find more information on some of these effects in section 4.

Other medicines and Zavedos
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, in particular, if you:
- Are given medicines or were previously given medicines such as anthracyclines or anthracenediones that have a similar action to Zavedos. They can make the effects of Zavedos stronger.
- Are using Zavedos with medicines like calcium channel blockers or chemotherapies that have cardiac toxicity.
- Are receiving radiotherapy.
- Are taking oral drugs that prevent blood clots as it will require close monitoring.
- Are taking a medicine called Cyclosporin A.

You should not take live or live-attenuated vaccines (e.g. yellow fever) because of the risk of serious infection after treatment with chemotherapy.

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 Zavedos. Zavedos may harm an unborn baby, so it is important to tell your doctor if you think you are pregnant.

Contraception in women of childbearing potential
You should always use effective birth control (contraception) whilst receiving Zavedos and for at least 6.5 months after the last dose. Talk to your doctor about birth control methods that are right for you and your partner.

Contraception in men
Men should always use effective contraception whilst receiving Zavedos and for at least 3.5 months after the last dose.

Breast-feeding
Do not breast-feed whilst receiving Zavedos and for at least 14 days after the last dose, as some of the drug may get into your milk and possibly harm your child.

Fertility
Both men and women should seek advice on fertility preservation before treatment.

Driving and using machines
It is not known whether Zavedos has an effect on you being able to drive or use any tools or machines. However, special care should be taken if it is essential that you drive or operate machinery while undergoing treatment especially if you are lacking strength or are in a debilitated condition.

3. How Zavedos will be given to you

Zavedos will be given to you by injection into the veins. It should not be given by injection into your spine.
- Your doctor will prescribe the required amount (the dose). The dose is decided by taking into account your condition being treated, your height and weight.
- From your height and weight the doctor will work out your body surface area; this is necessary because the dose is usually calculated as "X milligrams per square metre" (mg/m^2), given by injection, on 3 days running.
- However, your doctor may alter the dose and number of days of treatment depending on your condition and any other treatment you may receive.

If you receive more Zavedos 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. Should this happen, you may need antibiotics or blood transfusions. Mouth ulcers can be treated to make them less uncomfortable as they heal.

Heart damage can occur when high doses of Zavedos are given. This may not be detected for several weeks, so regular tests may be required during this period.

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.

Tell your doctor immediately if you experience any of the following symptoms after you have been given this medicine. Although they are very rare, the symptoms can be severe.

- Allergic reactions such as feeling dizzy, feverish, breathless with a tight chest, with or without an itchy rash.
- Inflammation of the pericardium (the fibrous sac surrounding the heart), inflammation of the heart muscle, a disease of the electrical system of the heart.
- A condition in which a blood clot that has formed inside a blood vessel or inside the heart.
- Redness of the skin, typically over the cheeks or neck.
- Stomach ulcer (abdominal pain or burning sensation).
- Hand foot syndrome (tingling, redness, flaking, swelling or small sores on the palms of the hands or soles of the feet).
- Anaemia (low red cells) that can leave you feeling tired and lethargic.
- Leukopenia (low white cells) leading to increased chance of infections with symptoms of raised temperature or fever and chills (like flu).
- Thrombocytopenia (low platelets, these help the blood to clot). You may bruise more easily or bleed more than usual if you hurt yourself.
- Tumour lysis syndrome (the breakdown and release of tumour cell contents), a potentially-life threatening condition, in which you may experience decreased or cloudy urination, weakness, irritability and confusion, vomiting, nausea, muscle cramps or joint discomfort, shortness of breath, irregular heartbeat and seizures. These symptoms can be associated with abnormal laboratory test results (high potassium, uric acid and phosphorous levels and low calcium levels in the blood) that can lead to changes in kidney function and acute renal failure.
- Severe infections which can occur after treatment with idarubicin alone or in combination with other medicines, and may be fatal.

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

- Infections.
- Decrease in number of red blood cells, reduced numbers of white blood cells, abnormally low amount of platelets.
- A lack or loss of appetite for food.
- Feeling sick or being sick, the painful inflammation and ulceration of the mucous membranes lining the digestive tract, diarrhoea, stomach ache.
- Hair loss.
- Red colouration of urine.
- Fever (rise in temperature).
- Headache.
- Chills.

Common side effects (may affect up to 1 in 10 people)
- Increase or decrease in heart rate, irregular heart beat/pulse, heart failure, heart attack.
- Inflammation of the vein, swelling (inflammation) of a vein caused by a blood clot.
- Bleeding from the intestines, pain in the stomach or abdomen.
- Liver enzyme elevation.
- Rash, itch.
- Haemorrhages.
- Increased sensitivity of irradiated skin 'radiation recall reaction'.

Uncommon side effects (may affect up to 1 in 100 people)
- Blood infection, bacteria in the blood.
- Cancers of blood such as secondary leukaemia or unfavourable leukaemia (acute myeloid leukaemia (AML) or myelodysplastic syndrome (MDS)).
- Painful joints due to increased uric acid levels in your blood (gouty arthritis).
- ECG changes.
- Shock.
- Inflammation of the oesophagus, inflammation of the colon.
- Darkening of the skin and nails.
- Excessive loss of body fluid.
- Spreading of bacterial infection below the skin surface and tissue damage.
- Heart attack.
- Hives.

Rare side effects (may affect up to 1 in 1,000 people)
- Stroke.

Very rare side effects (may affect up to 1 in 10,000 people)
- Serious allergic reaction.
- Inflammation of the pericardium (the fibrous sac surrounding the heart), defect in the heart's electrical system.
- Minor ulceration of the gastric mucosa.
- Hand foot syndrome.
- Inflammation of heart muscle.
- Thromboembolism.
- Flush.

Additional side effects experienced, (frequency cannot be estimated from the available data)
- Change in certain chemicals in the blood.
- Abnormally low levels of all blood cells produced by the bone marrow.
- Local skin reaction.

Additional side effects in children
Side effects seen in children are similar to those seen for adults. Children have a higher risk for heart problems that could be caused by taking Zavedos.

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. Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Zavedos

Zavedos is for single use only. It should be used immediately after opening and any unused portion should be discarded.

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 vial label and carton after EXP. The expiry date refers to the last date of that month.

Zavedos should be stored in a refrigerator (2°C -8°C) and the vial kept in the outer carton in order to protect from light.
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 Zavedos contains
The active substance is idarubicin hydrochloride. Each mL of solution for injection contains 1 mg idarubicin hydrochloride.

Each vial of 5 mL of solution for injection contains 5 mg of idarubicin hydrochloride.
Each vial of 10 mL of solution for injection contains 10 mg of idarubicin hydrochloride.
Each vial of 20 mL of solution for injection contains 20 mg of idarubicin hydrochloride.

The other ingredients are glycerol, hydrochloric acid and water for injection

What Zavedos looks like and the contents of the pack

Zavedos is supplied as a clear orange-red aqueous solution in glass vials which are closed with a rubber stopper and sealed with an aluminium cap with plastic flip off top. The vials are packed singly in cartons.

Zavedos is available in 5 ml, 10 mL and 20 mL vials. Not all pack sizes may be marketed.

Marketing Authorisation Holder
PA Holder:
Pfizer Healthcare Ireland Unlimited Company
The Watermarque Building
Ringsend Road,
Dublin 4,
D04 K7N3
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Manufacturer:
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