**Package leaflet: Information for the user**

**Zavedos® 5 mg and 10 mg Powder for Solution for Injection**
idarubicin hydrochloride

**Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.**
- Keep this leaflet. You may need to read it again.
- If you have any 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 take Zavedos

**Do not take 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 you have an infection which is not under control.
- If your liver or kidneys are not working properly.
- If you have had previous or current history of bone marrow depression caused by previous therapy.
- 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 previously been treated with high doses of idarubicin hydrochloride and/ or other anthracyclines or anthracenediones.
- If you are breast-feeding.

- If you have an intolerance to sugars. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

**Warnings and precautions**
Talk to your doctor, pharmacist or nurse before taking 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.

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

**Children**
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 functions 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, including medicines obtained without a prescription, 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 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 or pharmacist for advice before taking this medicine. Avoid becoming pregnant while you or your partner is being treated with Zavedos. If you are sexually active, you are advised to use effective birth control to prevent pregnancy during treatment, whether you are male or female. Males should continue to use effective contraception up to 3 months after treatment. Zavedos may harm an unborn child, so it is important to tell your doctor if you think you are pregnant**.**

Do not breast-feed whilst receiving Zavedos, as some of the drug may get into your milk and possibly harm your child.

**Driving and using machines**
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.

**Zavedos contains lactose**
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

## 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 "... milligrams per square metre" (mg/m2), given by injection, on 3 days running.
- However, your doctor may alter the dose and number of days treatment depending on your condition and any other treatment you may receive.

**If you use 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.

Intestinal bleeding can occur with high doses of Zavedos. This may need to be observed for patients treated with oral idarubicin.

## 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 taking this medicine. Although they are very rare the symptoms can be severe.

- You may have allergic reactions such as feel dizzy, feverish, short of breath with a tight chest, with or without an itchy rash.
- You have an 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 (severe infections 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, bellyache.
- 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 covering of the heart and 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 (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

**United Kingdom**
Yellow Card Scheme at:www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
**Ireland** HPRA 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 Zavedos

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

Do not use Zavedos after the expiry date, which is stated on the vial after EXP. The expiry date refers to the last date of that month.

Zavedos should be given to you by injection within 24 hours of being made up from the dry powder in the vial. It should be kept in the fridge during this time.

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.
The other ingredient is lactose monohydrate

**What Zavedos looks like and the contents of the pack**

Zavedos is supplied as an orange-red powder in a vial containing either 5 mg or 10 mg of the active substance idarubicin hydrochloride. The vials are packed singly in cartons. Your doctor or nurse will make up the Zavedos with water into an injection.

**Marketing Authorisation Holder and Manufacturer**

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|---|---|
| PL Holder: | Pfizer Limited<br>Ramsgate Road, Sandwich, Kent, CT13 9NJ, UK |
| PA Holder: | Pfizer Healthcare Ireland<br>9 Riverwalk, National Digital Park, Citywest Business Campus, Dublin 24, Ireland. |
| Manufacturer: | Actavis Italy S.p.A.<br>10 Viale Pasteur<br>20014 Nerviano (MI)<br>Italy |

**Company Contact Address:**
If you have any comments on the way this leaflet is written, please contact Medical Information at Pfizer Limited in Walton Oaks, Tadworth, Surrey, Tel :01304 616161.

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