Package leaflet: Information for the user

Zavedos® 5mg and 10mg Hard Capsules
(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 further questions, ask your doctor or pharmacist.
- 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 or pharmacist. 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
2. What you need to know before you take Zavedos
3. How to take Zavedos
4. Possible side effects
5. How to store Zavedos
6. Contents of the pack and other information

1. What Zavedos is and what it is used for

- Zavedos Hard capsules 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 for the treatment of a type of leukaemia called acute non-lymphocytic leukaemia (ANLL) also referred to as acute myelogenous leukaemia (AML).

2. What you need to know before you take Zavedos

Do not use Zavedos capsules:
- If you are allergic to Idarubicin hydrochloride or other similar anthracycline medicines or any of the other ingredients of this medicine (listed in Section 6).
- 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 had a previous or current history of stomach problems (e.g. ulcer) or any problem with your bowels.
- If you have previously been treated with high doses idarubicin hydrochloride and/ or other anthracyclines or anthracenediones.
- If you are breast feeding.

Warnings and precautions
Talk to your doctor if you are currently taking or have recently taken Trastuzumab (a medicine used in the treatment of certain cancers). Trastuzumab can remain in the body for up to 7 months. 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. Your doctor will assess your health and discuss the risk and benefits of your treatment carefully before prescribing Zavedos capsules to you.

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 you doctor about your options.

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:

- medicines such as anthracyclines or anthracenediones that have a similar action to Zavedos. They can make the effects of Zavedos stronger.

- medicine like calcium channel blockers or chemotherapies that have cardiac toxicity.

- radiotherapy.

- oral medicines that prevent blood clots as it will require close monitoring.

- 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.

Zavedos with food and drink
Zavedos capsules may be taken with a light meal.

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.

<u>Contraception in women of childbearing potential</u>
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.

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

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.

3. How to take Zavedos

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Zavedos capsules are taken by mouth.
- 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 (in square metres); this is necessary because the dose is usually calculated as "…milligrams per square metre" (mg/m^2).
- The dose will be given daily for three days.
- However, your doctor may alter the dose and number of days depending on your condition and any other treatment you may receive.
- The capsules should be swallowed whole with some water and should not be sucked, bitten or chewed.

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 – again using blood tests – to check that Zavedos is not affecting the way it 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 'Possible Side Effects'.

If you take more Zavedos than you should
The single-dose packaging is designed to minimise the risk of overdose.
Intestinal bleeding can occur with high doses of Zavedos. This may need to be observed for patients treated with oral idarubicin.

However if you take more Zavedos than you should, then seek medical attention.

If you forget to take Zavedos

If you forget to take Zavedos take it as soon as you can. Take your next dose at the right time. Do not take a double dose to make up for a forgotten dose.

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

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).

Very common (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 coloration of urine.
- Fever (rise in temperature).
- Headache.
- Chills.

Common (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 (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)).
- Increased serum uric acid levels.
- 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 (may affect up to 1 in 1,000 people)

- Stroke.

Very rare (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.

Not known (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.

Reporting of side effects
If you get any side effects, talk to your doctor 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

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

Do not use Zavedos after the expiry date, which is stated on the carton and bottle. The expiry date refers to the last day of that month.

Do not store above 25°C. Keep the bottle tightly closed in order to protect from moisture.

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 ingredients are microcrystalline cellulose and glyceryl palmito-stearate.
Capsule shell: red iron oxide (E172), titanium dioxide (E171) and gelatin.
Printing ink: shellac, propylene glycol, black iron oxide (E172), strong ammonia solution and potassium hydroxide.

What Zavedos looks like and the contents of the pack
Zavedos capsules contain 5mg or 10mg of the active substance idarubicin hydrochloride and are packaged in amber glass bottles.

5 mg capsules:	Opaque, red cap and red body containing an orange powder
10mg capsules:	Opaque, red cap and white body containing an orange powder

The capsules are packed in amber glass bottles.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:	Pfizer Healthcare Ireland 9 Riverwalk National Digital Park City west Business campus Dublin 24 Ireland
Manufacturer:	Actavis Italy S.p.A. 10 Viale Pasteur 20014 Nerviano (MI) Italy

Company contact address:
For further information on your medicine contact Medical Information at the following address: Pfizer Healthcare Ireland, 9 Riverwalk, National Digital Park, Citywest Business Campus, Dublin 24, Ireland.
Telephone 1800 633 363

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