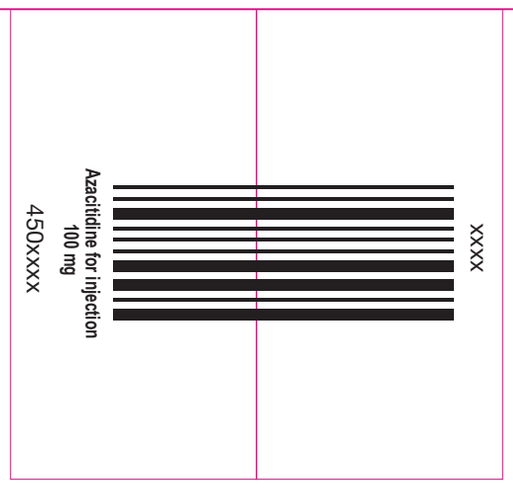

Package leaflet: Information for the user

Azacitidine 25 mg/ml powder for suspension for injection azacitidine

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, pharmacist or nurse.
- 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 Azacitidine is and what it is used for

What Azacitidine is

The name of the product is Azacitidine powder for suspension for injection (called Azacitidine throughout this leaflet). Azacitidine is an anti-cancer agent which belongs to a group of medicines called 'anti-metabolites' and contains the active substance 'azacitidine'.

What Azacitidine is used for

Azacitidine is used in adults who are not able to have a stem cell transplant to treat:

- Higher-risk myelodysplastic syndromes (MDS).
- Chronic myelomonocytic leukaemia (CMML).
- Acute myeloid leukaemia (AML).

These are diseases which affect the bone marrow and can cause problems with normal blood cell production.

How Azacitidine works

Azacitidine works by preventing cancer cells from growing. Azacitidine becomes incorporated into the genetic material of cells (ribonucleic acid (RNA) and deoxyribonucleic acid (DNA)). It is thought to work by altering the way the cell turns genes on and off and also by interfering with the production of new RNA and DNA. These actions are thought to correct problems with the maturation and growth of young blood cells in the bone marrow that cause myelodysplastic disorders, and to kill cancerous cells in leukaemia.

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

2. What you need to know before you use Azacitidine

Do not use Azacitidine if you:

- are allergic to azacitidine or any of the other ingredients of this medicine (listed in section 6).
- have advanced liver cancer.
- are breast-feeding.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Azacitidine if you have:

- decreased counts of platelets, red or white blood cells.
- kidney disease.
- liver disease.
- ever had a heart condition or heart attack or any history of lung disease.

Azacitidine can cause a serious immune reaction called 'differentiation syndrome' (see section 4)

Blood tests

You will have blood tests before you begin treatment with Azacitidine and at the start of each period of treatment (called a 'cycle'). This is to check that you have enough blood cells and that your liver and kidneys are working properly.

Children and adolescents

Azacitidine is not recommended for use in children and adolescents below the age of 18.

Other medicines and Azacitidine

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. This is because Azacitidine may affect the way some other medicines work. Also, some other medicines may affect the way Azacitidine works.

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 using this medicine.

Pregnancy

You should not use Azacitidine during pregnancy as it may be harmful to the baby. If you are a woman who can become pregnant you should use an effective method of contraception while using Azacitidine and for 6 months after stopping treatment with Azacitidine.
Tell your doctor straight away if you become pregnant during treatment.

Breast-feeding

You should not breast-feed when using Azacitidine. It is not known if this medicine passes into human milk.

Fertility

Men should not father a child while receiving treatment with Azacitidine. Men should use an effective method of contraception while using Azacitidine for 3 months after stopping treatment with Azacitidine.
Talk to your doctor if you wish to conserve your sperm before starting this treatment.

Driving and using machines

Do not drive or use any tools or machines if you experience side effects, such as tiredness.

3. How to use Azacitidine

Before giving you Azacitidine, your doctor will give you another medicine to prevent nausea and vomiting at the start of each treatment cycle.

- The recommended dose is 75 mg per m^2 body surface area. Your doctor will decide your dose of this medicine, depending on your general condition, height and weight. Your doctor will check your progress and may change your dose if necessary.
- Azacitidine is given every day for one week, followed by a rest period of 3 weeks. This 'treatment cycle' will be repeated every 4 weeks. You will usually receive at least 6 treatment cycles.

This medicine will be given to you as an injection under the skin (subcutaneously) by a doctor or nurse. It may be given under the skin on your thigh, tummy or upper arm.

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 straight away if you notice any of the following side effects:

- **Drowsiness, shaking, jaundice, abdominal bloating and easy bruising.** These may be symptoms of liver failure and can be life-threatening.
- **Swelling of the legs and feet, back pain, reduced passing of water, increased thirst, rapid pulse, dizziness and nausea, vomiting or reduced appetite and feelings of confusion, restlessness or fatigue.** These may be symptoms of kidney failure and can be life-threatening.
- **A fever**. This could be due to an infection as a result of having low levels of white blood cells, which can be life-threatening.
- **Chest pain or shortness of breath which may be accompanied with a fever.** This may be due to an infection of the lung called "pneumonia", and can be life-threatening.
- **Bleeding**. Such as blood in the stools due to bleeding in the stomach or gut, or such as bleeding inside your head. These may be symptoms of having low levels of platelets in your blood.
- **Difficulty breathing, swelling of the lips, itching or rash.** This may be due to an allergic (hypersensitivity) reaction.

Other side effects include:

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

- Reduced red blood cell count (anaemia). You may feel tired and pale.
- Reduced white blood cell count. This may be accompanied by a fever. You are also more likely to get infections.
- A low blood platelet count (thrombocytopenia). You are more prone to bleeding and bruising.
- Constipation, diarrhoea, nausea, vomiting.
- Pneumonia.
- Chest pain, being short of breath.
- Tiredness (fatigue).
- Injection site reaction including redness, pain or a skin reaction.
- Loss of appetite.
- Joint aches.
- Bruising.
- Rash.
- Red or purple spots under your skin.
- Pain in your belly (abdominal pain).

- Itching.
- Fever.
- Sore nose and throat.
- Dizziness.
- Headache.
- Having trouble sleeping (insomnia).
- Nosebleeds (epistaxis).
- Muscle aches.
- Weakness (asthenia).
- Weight loss.
- Low levels of potassium in your blood.

Common side effects (may affect up to 1 in 10 people):
- Bleeding inside your head.
- An infection of the blood caused by bacteria (sepsis). This may be due to low levels of white cells in your blood.
- Bone marrow failure. This can cause low levels of red and white blood cells and platelets.
- A type of anaemia where your red and white blood cells and platelets are reduced.
- An infection in your urine.
- A viral infection causing cold sores (herpes).
- Bleeding gums, bleeding in the stomach or gut, bleeding from around your back passage due to piles (haemorrhoidal haemorrhage), bleeding in your eye, bleeding under your skin, or into your skin (haematoma).
- Blood in your urine.
- Ulcers of your mouth or tongue.
- Changes to your skin at the injection site. These include swelling, a hard lump, bruising, bleeding into your skin (haematoma), rash, itching and changes in the skin colour.
- Redness of your skin.
- Skin infection (cellulitis).
- An infection of the nose and throat, or sore throat.
- Sore or runny nose or sinuses (sinusitis).
- High or low blood pressure (hypertension or hypotension).
- Being short of breath when you move.
- Pain in your throat and voice box.
- Indigestion.
- Lethargy.
- Feeling generally unwell.
- Anxiety.
- Being confused.
- Hair loss.
- Kidney failure.
- Dehydration.
- White coating covering tongue, inner cheeks, and sometimes on the roof of your mouth, gums and tonsils (oral fungal infection).
- Fainting.
- A fall in blood pressure when standing (orthostatic hypotension) leading to dizziness when moving to a standing or sitting position.
- Sleepiness, drowsiness (somnolence).
- Bleeding due to the use of a catheter line.
- A disease affecting the gut which can result in fever, vomiting and stomach pain (diverticulitis).
- Fluid around the lungs (pleural effusion).
- Shivering (chills).
- Muscle spasms.
- Raised itchy rash on the skin (urticaria).
- Collection of fluid around the heart (pericardial effusion).

Uncommon side effects (may affect up to 1 in 100 people):
- Allergic (hypersensitivity) reaction.
- Shaking.
- Liver failure.
- Large plum-coloured, raised painful patches on the skin with fever.
- Painful skin ulceration (pyoderma gangrenosum).
- Inflammation of the lining around the heart (pericarditis).

Rare side effects (may affect up to 1 in 1,000 people):
- Dry cough.
- Painless swelling in the finger tips (finger clubbing).
- Tumour lysis syndrome - metabolic complications that can occur during treatment of cancer and sometimes even without treatment. These complications are caused by the product of dying cancer cells and may include the following: changes to blood chemistry; high potassium, phosphorus, uric acid, and low calcium consequently leading to changes in kidney function, heartbeat, seizures, and sometimes death.

Not known (frequency cannot be estimated from the available data)
- Infection of the deeper layers of skin, which spreads quickly, damaging the skin and tissue, which can be life-threatening (necrotizing fasciitis).
- Serious immune reaction (differentiation syndrome) that may cause fever, cough, difficulty breathing, rash, decreased urine, low blood pressure (hypotension), swelling of the arms or legs and rapid weight gain.
- Inflammation of blood vessels in the skin which may result in rash (cutaneous vasculitis).

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 the MHRA Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Azacitidine

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 the carton after EXP. The expiry date refers to the last day of that month.
Your doctor, pharmacist or nurse are responsible for storing Azacitidine. They are also responsible for preparing and disposing of any unused Azacitidine correctly.
Unopened vials - This medicinal product does not require any special storage conditions.

<u>When using immediately</u>
Once the suspension has been prepared it should be administered within 60 minutes.

<u>When using later on</u>
If the Azacitidine suspension is prepared using water for injections that has not been refrigerated, the suspension must be placed in the refrigerator (2 °C – 8 °C) immediately after it is prepared and kept refrigerated for up to a maximum of 8 hours.

If the Azacitidine suspension is prepared using water for injections that has been stored in the refrigerator (2 °C – 8 °C), the suspension must be placed in the refrigerator (2 °C – 8 °C) immediately after it is prepared and kept refrigerated for up to a maximum of 22 hours.

The suspension should be allowed up to 30 minutes prior to administration to reach room temperature (20 °C – 25 °C). If large particles are present in the suspension it should be discarded.

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 Azacitidine contains
- The active substance is azacitidine. One vial contains 100 mg azacitidine. After reconstitution with 4 ml of water for injections, the reconstituted suspension contains 25 mg/ml azacitidine.
- The other ingredient is mannitol (E421)

What Azacitidine looks like and contents of the pack
Azacitidine is a white powder for suspension for injection and is supplied in a Type-I clear glass vial sealed with dark grey chloro butyl flurotec coated single slotted rubber stopper or dark grey bromo butyl omniflex coated single slotted lyo rubber stopper and aluminium flip off seal containing 100 mg of azacitidine.

Each pack contains one vial of Azacitidine.

Marketing Authorisation Holder
Zentiva Pharma UK Limited,
12 New Fetter Lane, London EC4A 1JP, United Kingdom.

Manufacturer
APIS Labor GmbH,
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or

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