DR. REDDY'S LABORATORIES (PTY) LTD.
APPROVED PATIENT INFORMATION LEAFLET:
AZACITIDINE DRL
(lyophilised powder for injection)

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

AZACITIDINE DRL

(lyophilised powder for injection)

azacitidine

Contains sugar (mannitol)

Each vial contains 100 mg mannitol

Read all of this leaflet carefully before you are given AZACITIDINE DRL

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- AZACITIDINE DRL has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours. The injection will be given to you by your medical doctor or by a qualified healthcare professional under her/his supervision.

What is in this leaflet

1. What AZACITIDINE DRL is and what it is used for

AZACITIDINE DRL contains a medicine called azacitidine.

AZACITIDINE DRL is an anti-cancer medicine which belongs to a group of medicines called 'anti-metabolites'. AZACITIDINE DRL prevents cancer cells from growing.

AZACITIDINE DRL is used in adults who are not able to have a stem cell transplantation to treat:

- higher-risk myelodysplastic syndromes (MDS), a group of bone marrow disorders in which the bone marrow does not produce enough healthy blood cells;
- chronic myelomonocytic leukaemia (CMML) a type of cancer of the blood-forming cells of the bone marrow;
- acute myeloid leukaemia (AML), a cancer of the blood cells, characterised by the rapid growth of abnormal white blood cells that accumulate in the bone marrow and interfere with the production of normal blood cells.

2. What you need to know before you are given AZACITIDINE DRL

You should not be administered with AZACITIDINE DRL if:

- you are hypersensitive (allergic) to azacitidine or any of the other ingredients of AZACITIDINE DRL (see What AZACITIDINE DRL contains).
- you have liver cancer.
- do not receive live vaccines while being treated with AZACITIDINE DRL.

- you are pregnant and/or breastfeeding.
- AZACITIDINE DRL is not recommended for use in children and adolescents below the age of 18.

Warnings and precautions

Special care should be taken with AZACITIDINE DRL:

- if you have decreased counts of platelets, red or white blood cells.
- if you have liver problems.
- if you have kidney problems.
- if you have ever had a heart condition or heart attack or any history of lung disease.
- AZACITIDINE DRL may cause a rare infection of the deeper layers of skin and subcutaneous tissues. Tell your doctor if you notice any changes to your skin or if you develop a fever.
- AZACITIDINE DRL may cause a condition that happens when cancer cells die quickly. Dying cells release large amounts of potassium, phosphate, and uric acid into the blood. This can cause heart or kidney problems and lead to kidney failure (tumour lysis syndrome).
  Some of the symptoms are nausea, vomiting, diarrhoea, muscle cramps, numbness, seizures, confusion and weakness. This condition may be life-threatening if it is not managed or treated.
- AZACITIDINE DRL can cause a serious immune reaction called 'differentiation syndrome'.

Blood monitoring

You will have blood tests before you begin treatment with AZACITIDINE DRL 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.

Use in children and adolescents

AZACITIDINE DRL is not to be used to treat children and adolescents below the age of 18.

Use in elderly

Use AZACITIDINE DRL with caution in the elderly, they may be more sensitive to its effects.

Other medicines and AZACITIDINE DRL

Always tell your healthcare professional if you are taking any other medicine.

(This includes complementary or traditional medicines).

Know the medicines you take. Keep a list of them with you to show your doctor and pharmacist each time you get a new medicine.

AZACITIDINE DRL with food and drink

There is no information to suggest that food and drink consumption affects the way that AZACITIDINE DRL works.

Pregnancy, breastfeeding and fertility

- AZACITIDINE DRL may be harmful to the baby, therefore it should not be used if you are pregnant.
- If you are pregnant or breastfeeding, think you may be pregnant or plan to become pregnant consult your doctor, pharmacist or other health care professional for advice before taking

AZACITIDINE DRL.

- Tell your doctor straight away if you become pregnant during treatment.
- If you are a woman who can become pregnant you should use a highly effective method of contraception while using AZACITIDINE DRL and for 6 months after stopping treatment with AZACITIDINE DRL.
- You should not breast-feed when taking AZACITIDINE DRL**,** as it is not known if AZACITIDINE DRL passes into breast milk.
- If you are a male, you should not father a child while receiving treatment with AZACITIDINE DRL. Men should use an effective method of contraception while using AZACITIDINE DRL and for 3 months after stopping treatment with AZACITIDINE DRL. You should seek counselling on sperm storage.
- Female partners of male patients receiving AZACITIDINE DRL should not become pregnant.

Driving and using machines

AZACITIDINE DRL may make you feel tired. If this happens, do not drive or operate any tools and machines.

AZACITIDINE DRL contains mannitol

AZACITIDINE DRL contains mannitol:

- which is a type of sugar, which may have an effect on the control of your blood sugar if you have diabetes mellitus.

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before using

AZACITIDINE DRL.

- which, on rare occasions, may cause hypersensitivity reactions and may have a laxative effect.

3. How to use AZACITIDINE DRL

Your doctor will decide on the most suitable treatment for you including:

- the correct dose
- how often and for how long you should be treated and
- whether you should also receive other medicines with AZACITIDINE DRL or not.

Your doctor will give you all the necessary information on your treatment plan.

Before giving you AZACITIDINE DRL, 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 AZACITIDINE DRL, depending on your general
condition, height and weight. Your doctor will check your progress and may change your dose if necessary.
AZACITIDINE DRL 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 4 treatment cycles.

AZACITIDINE DRL will be given to you as a subcutaneous injection under the skin or intravenous infusion by a doctor or nurse.
The subcutaneous injection may be given under the skin on your thigh, tummy or upper arm.

The intravenous infusion will be given over a period of 10 to 40 minutes.

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

If you have the impression that the effect of AZACITIDINE DRL is too strong or too weak, tell your doctor or pharmacist.

If you receive more AZACITIDINE DRL than you should

Since a healthcare professional will administer AZACITIDINE DRL to you, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you forget to use AZACITIDINE DRL

Since a healthcare professional will administer AZACITIDINE DRL, it is unlikely that the dose will be missed.

If you stop taking AZACITIDINE DRL

Unless your doctor instructs you to stop treatment, it is important to continue to be given AZACITIDINE DRL**.**

If you stop treatment and your original symptoms come back tell your doctor or pharmacist immediately.

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

4. Possible side effects

AZACITIDINE DRL can have side effects.

Not all side effects reported for AZACITIDINE DRL are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking AZACITIDINE DRL, please consult your doctor, pharmacist or other health care professional for advice.

If any of the following side effects happen, stop taking AZACITIDINE DRL and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling of the hands, feet, ankles, face, mouth, lips, gums, tongue, throat and neck which may cause difficulty in swallowing or breathing', throat tightness, shortness of breath and wheezing, rash, "hives" (raised bumps), blisters or itching.

These are all serious side effects. This may be due to an allergic (hypersensitivity) reaction. You may need urgent medical attention or hospitalisation.

If any of the following side effects happen, tell your doctor immediately or go to the casualty department at your nearest hospital:

- Drowsiness, shaking, jaundice (yellowing of skin and white of eyes), 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.

Other side effects include:

Frequent side effects:

- An infection of the nose and throat or the common cold (nasopharyngitis).
- An infection of the blood caused by bacteria (sepsis). This may be due to low levels of white cells in your blood (neutropenic sepsis).
- Infection of the sinuses, throat, airways or lung (respiratory tract).
- An infection in your urine (urinary tract infection).
- Skin infection (cellulitis).
- Pain in the gut which can result in fever and vomiting due to inflammation of the colon (diverticulitis).
- White coating covering tongue, inner cheeks, and sometimes on the roof of your mouth, gums and tonsils (oral fungal infection).
- Inflammation of the sinuses (sinusitis).
- Sore throat (pharyngitis).

- Runny nose (rhinitis).
- A viral infection causing cold sores (herpes simplex).
- Reduced red blood count (anaemia). You may feel tired and pale.
- Reduced neutrophils (type of white blood cell count (neutropenia)). This may be accompanied by a fever (febrile neutropenia). You are also more likely to get infections.
- A reduced white blood cell count (leukopenia).
- A reduced blood platelet count (thrombocytopenia). You are more prone to bleeding and bruising.
- A reduced red cell, white cell, and platelet count (pancytopenia).
- Bone marrow failure due to the low red and white blood cell and platelet counts.
- Eating disorder (anorexia), loss of appetite, low levels of potassium in the blood (hypokalaemia), increased thirst (dehydration).
- Having trouble sleeping (insomnia), confusion, feeling anxious (anxiety).
- Dizziness, headache, bleeding inside your head (intracranial haemorrhage), fainting (syncope), feeling sleepy (somnolence), feeling tired (lethargy).
- Bleeding in the eye (eye haemorrhage), bleeding of the conjunctiva (conjunctival haemorrhage).
- High or low blood pressure (hypertension or hypotension), low blood pressure that happens when you stand up from sitting or lying down making you feel faint or dizzy (orthostatic hypotension), a solid swelling of clotted blood within the tissues (haematoma).
- Being short of breath (dyspnoea), nose bleeds (epistaxis), water/fluid in the lungs (pleural effusion), being short of breath when you move (dyspnoea exertional), pain in your throat and voice box (pharyngolaryngeal pain).
- Diarrhoea ('runny tummy'), vomiting, constipation, nausea ('feeling sick'), stomach pain, bleeding

in the mouth, stomach and gut (gastrointestinal haemorrhage), bleeding from around your back passage due to piles (haemorrhoidal haemorrhage), inflammation of the mucous membrane of the mouth (stomatitis), bleeding of the gums (gingival bleeding), indigestion (dyspepsia).

- Small red or purple spots caused by bleeding into the skin (petechiae), itching (pruritus), rash, a discoloration of the skin resulting from bleeding underneath, typically caused by bruising (ecchymosis), a rash of purple spots on the skin caused by internal bleeding from small blood vessels (purpura), hair loss (alopecia), "hives"/ itchy rash (urticaria), reddening of the skin(erythema), type of rash (rash macular).
- Joint pains (arthralgia), pain (includes back, bone and pain in extremity), muscle spasms, muscle pain (myalgia).
- Kidney failure (renal failure), blood in the urine (haematuria), increased levels of creatinine (picked up in blood tests).
- Fever (pyrexia), tiredness (fatigue), physical weakness or lack of energy (asthenia), chest pain, injection site reaction including redness, pain or a skin reaction (injection site erythema), injection site pain, bruising, swelling of clotted blood within the tissues (haematoma), hardened mass associated with inflammation (induration), rash, itching (pruritus), swelling (inflammation), discoloration, bleeding at injection site, general feeling of being unwell (malaise), chills, bleeding at the catheter site.
- Decrease in weight.

Less frequent side effects:

- Allergic (hypersensitivity) reactions.
- A group of abnormalities that can occur as a complication during the treatment of cancer e.g., high levels of potassium, phosphorus, calcium, uric acid, blood urea nitrogen (BUN) and other

nitrogen containing compounds (tumour lysis syndrome).

- Group of diseases affecting different parts of the lung (interstitial lung disease).
- Liver failure (hepatic failure), coma caused due to liver failure (progressive hepatic failure).
- A skin disease characterised by the sudden onset of fever, an elevated white blood cell count, and tender, red swellings on the skin (acute febrile neutrophilic dermatosis).
- An accumulation of acid in the body due to a failure of the kidneys to (renal tubular acidosis), "death" of the skin at the injection site (injection site necrosis).

Side effects with and unknown frequency:

- Infection of the deeper layers of skin, which spreads quickly, damaging the skin and tissue, which can be life-threatening (necrotising 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.

If you notice any side effects not on this leaflet, please inform you doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist, or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

By reporting side effects, you can help provide more information on the safety of AZACITIDINE DRL.

5. How to store AZACITIDINE DRL

Unopened vial:

Store at or below 25 °C.

Reconstituted suspension for subcutaneous administration:

When reconstituted with refrigerated (2 °C to 8 °C) water for injections, the reconstituted suspension can be kept in the refrigerator (2 °C to 8 °C) for a maximum of 22 hours.

After removal from refrigerated conditions, the suspension may be allowed to equilibrate to room temperature (25 °C) for up to 30 minutes prior to administration.

Reconstituted suspension for intravenous administration:

When stored at 25 °C, the reconstituted product should be administered within 1 hour.

Discard any unused solution.

Do not dispose medicines in drains or sewerage systems (e.g., toilets).

Return all unused and expired medicines to your pharmacist.

Keep all medicines out of reach and sight of children.

6. Contents of the pack and other information

What AZACITIDINE DRL contains

The active substance is azacitidine.

Each vial contains 100 mg azacitidine.

The reconstituted suspension contains 25 mg/ml azacitidine.

The other ingredients are mannitol, nitrogen and water for injection.

What AZACITIDINE DRL looks like and contents of the pack

AZACITIDINE DRL: white to off-white sterile lyophilised powder.

30 ml USP type I flint tubular glass vial, with a 20 mm dark grey bromobutyl rubber stopper and sealed with 20 mm violet coloured aluminium flip-off tear seal.

Holder of Certificate of Registration

Dr. Reddy's Laboratories (Pty) Ltd.

Block B, 204 Rivonia Road

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2057

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For any information about this medicine, please contact the local representative of the Holder of Certificate of Registration:

Dr. Reddy's Laboratories (Pty) Ltd. Tel: +27 11 324 2100

Other sources of information

Detailed information on this medicine is available on the Dr. Reddy's Laboratories web site:

http://www.drreddys.co.za