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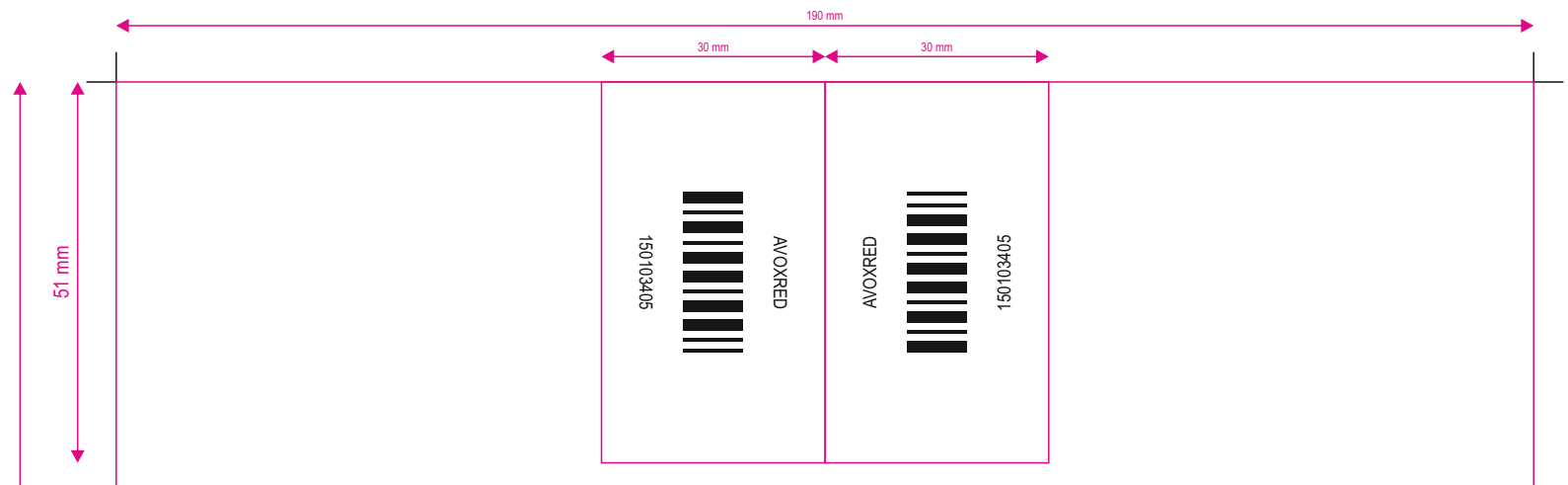

Dr.Reddy's

PRESCRIBING INFORMATION

AVOXRED

Azacitidine powder for suspension for injection 100 mg/vial (SC)

1. Product Name
AVOXRED
Azacitidine powder for suspension for injection 100 mg/vial

2. Name and strength of active ingredient(s)
Azacitidine 100 mg

3. Product description
White to off white lyophilized powder for reconstitution. The reconstituted solution is colorless to either light-yellow or green yellow solution free from visible extraneous matter.

4. Pharmacodynamics/Pharmacokinetics
Pharmacodynamic properties:
Mechanism of action
Azacitidine is believed to exert its antineoplastic effects by multiple mechanisms including cytotoxicity on abnormal haematopoietic cells in the bone marrow and hypomethylation of DNA. The cytotoxic effects of azacitidine may result from multiple mechanisms, including inhibition of DNA, RNA and protein synthesis, incorporation into RNA and DNA, and activation of DNA damage pathways. Non-proliferating cells are relatively insensitive to azacitidine. Incorporation of azacitidine into DNA results in the inactivation of DNA methyltransferases, leading to hypomethylation of DNA. DNA hypomethylation of aberrantly methylated genes involved in normal cell cycle regulation, differentiation and death pathways may result in gene re-expression and restoration of cancer-suppressing functions to cancer cells. The relative importance of DNA hypomethylation versus cytotoxicity or other activities of azacitidine to clinical outcomes has not been established.

5. Pharmacokinetic properties:
Absorption
Following subcutaneous administration of a single 75 mg/m2 dose, azacitidine was rapidly absorbed with peak plasma concentrations of 750 ± 403 ng/mL occurring at 0.5 h after dosing (the first sampling point). The absolute bioavailability of azacitidine after subcutaneous relative to intravenous administration (single 75 mg/m2 doses) was approximately 89% based on area under the curve (AUC).
Area under the curve and maximum plasma concentration (C_{max}) of subcutaneous administration of azacitidine were approximately proportional within the 25 to 100 mg/m^{2}dose range.
Distribution
Following intravenous administration, the mean volume of distribution was 76 ± 26 L, and systemic clearance was 147 ± 47 L/h.
Biotransformation
Azacitidine metabolism does not mediated by cytochrome P450 isoenzymes (CYPs), UDP-glucuronosyltransferases (UGTs), sulfotransferases (SULTs), and glutathione transferases (GSTs).
Azacitidine undergoes spontaneous hydrolysis and deamination mediated by cytidine deaminase. In human liver S9 fractions, formation of metabolites was independent of NADPH implying that azacitidine metabolism was not mediated by cytochrome P450 isoenzymes. Azacitidine does not induce CYP 1A2, 2C19, or 3A4 or 3A5. Inhibition of a series of P450 isoenzymes (CYP 1A2, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1 and 3A4) azacitidine up to 100 µM did not produce inhibition. Therefore, CYP enzyme induction or inhibition by azacitidine at clinically achievable plasma concentrations is unlikely.
Elimination
Azacitidine is cleared rapidly from plasma with a mean elimination half-life $t_{1/2}$ after subcutaneous administration of 41 ± 8 minutes. No accumulation occurs after subcutaneous administration of 75 mg/m^2 azacitidine once daily for 7 days. Urinary excretion is the primary route of elimination of azacitidine and/or its metabolites. Following intravenous and subcutaneous administration of ^{14}C-azacitidine, 85 and 50 % of the administered radioactivity was recovered in urine respectively, while < 1 % was recovered in faeces.
Special populations
The effects of hepatic impairment, gender, age, or race on the pharmacokinetics of azacitidine have not been formally studied.
Renal impairment
Azacitidine can be administered to patients with renal impairment without initial dose adjustment provided these patients are monitored for toxicity since azacitidine and/or its metabolites are primarily excreted by the kidney.
Pharmacogenomics
The effect of known cytidine deaminase polymorphisms on azacitidine metabolism has not been formally investigated.

6. Therapeutic Indications
Azacitidine is indicated for the treatment of adult patients who are not eligible for haematopoietic stem cell transplantation (HSCT) with:
- intermediate-2 and high-risk myelodysplastic syndromes (MDS) according to the International Prognostic Scoring System (IPSS),
- chronic myelomonocytic leukaemia (CMML) with 10-29 % marrow blasts without myeloproliferative disorder,
- acute myeloid leukaemia (AML) with 20-30 % blasts and multi-lineage dysplasia, according to World Health Organisation (WHO) classification,

7. Posology and method of administration:
Azacitidine treatment should be initiated and monitored under the supervision of a physician experienced in the use of chemotherapeutic agents. Patients should be premedicated with anti-emetics for nausea and vomiting.
Posology
The recommended starting dose for the first treatment cycle, for all patients regardless of baseline haematology laboratory values, is 75 mg/m^2 of body surface area, injected subcutaneously, daily for 7 days, followed by a rest period of 21 days (28-day treatment cycle).
It is recommended that patients be treated for a minimum of 6 cycles. Treatment should be continued as long as the patient continues to benefit or until disease progression.
Patients should be monitored for haematologic response/toxicity and renal toxicities; a delay in starting the next cycle or a dose reduction as described below may be necessary.
Laboratory tests
Liver function tests, serum creatinine and serum bicarbonate should be determined prior to initiation of therapy and prior to each treatment cycle. Complete blood counts should be performed prior to initiation of therapy and as needed to monitor response and toxicity, but at a minimum, prior to each treatment cycle.
Dose adjustment due to haematological toxicity
Haematological toxicity is defined as the lowest count reached in a given cycle (nadir) if platelets ≤ 50.0 x 10^9/l and/or absolute neutrophil count (ANC) ≤ 1 x 10^9/l.
Recovery is defined as an increase of cell line(s) where haematological toxicity was observed of at least half of the difference of nadir and the baseline count plus the nadir count (i.e. blood count at recovery ≥ nadir count + (0.5 x [baseline count – nadir count]).
Patients without reduced baseline blood counts (i.e. White Blood Cells (WBC) ≥ 3.0 x 10^9/l and ANC ≥ 1.5 x 10^9/l, and platelets ≥ 75.0 x 10^9/l) prior to the first treatment
If haematological toxicity is observed following Vidaza treatment, the next cycle of the therapy should be delayed until the platelet count and the ANC have recovered. If recovery is achieved within 14 days, no dose adjustment is necessary. However, if recovery has not been achieved within 14 days, the dose should be reduced according to the following table. Following dose modifications, the cycle duration should return to 28 days.

Nadir counts		% Dose in the next cycle, if recovery* is not achieved within 14 days
ANC (x 10^9 /l)	Platelets (x 10^9 /l)	
≤ 1.0	≤ 50.0	50 %
> 1.0	> 50.0	100 %

*Recovery = counts ≥ nadir count + (0.5 x [baseline count – nadir count])
Patients with reduced baseline blood counts (i.e. WBC < 3.0 x 10^9/l or ANC < 1.5 x 10^6/l or platelets < 75.0 x 10^9/l) prior to the first treatment
Following azacitidine treatment, if the decrease in WBC or ANC or platelets from that prior to treatment is ≤ 50 %, or greater than 50 % but with an improvement in any cell line differentiation, the next cycle should not be delayed and no dose adjustment made.
If the decrease in WBC or ANC or platelets is greater than 50 % from that prior to treatment, with no improvement in cell line differentiation, the next cycle of azacitidine therapy should be delayed until the platelet count and the ANC have recovered. If recovery is achieved within 14 days, no dose adjustment is necessary. However, if recovery has not been achieved within 14 days, bone marrow cellularity should be determined. If the bone marrow cellularity is > 50 %, no dose adjustments should be made. If bone marrow cellularity is ≤ 50 %, treatment should be delayed and the dose reduced according to the following table:

Bone marrow cellularity	Dose in the next cycle if recovery is not achieved within 14 days	
	Recovery* ≤ 21 days	Recovery* > 21 days
15-50 %	100 %	50 %
< 15 %	100 %	33 %

*Recovery = counts ≥ nadir count + (0.5 x [baseline count – nadir count])
Following dose modifications, the cycle duration should return to 28 days.
Special populations
Elderly patients
No specific dose adjustments are recommended for the elderly. Because elderly patients are more likely to have decreased renal function, it may be useful to monitor renal function.
Patients with renal impairment
Azacitidine can be administered to patients with renal impairment without initial dose adjustment. If unexplained reductions in serum bicarbonate levels to less than 20 mmol/l occur, the dose should be reduced by 50 % on the next cycle. If unexplained elevations in serum creatinine or blood urea nitrogen (BUN) to ≥ 2-fold above baseline values and above upper limit of normal (ULN) occur, the next cycle should be delayed until values return to normal or baseline and the dose should be reduced by 50 % on the next treatment cycle.
Patients with hepatic impairment
No formal studies have been conducted in patients with hepatic impairment. Patients with severe hepatic organ impairment should be carefully monitored for adverse events. No specific modification to the starting dose is recommended for patients with hepatic impairment prior to starting treatment; subsequent dose modifications should be based on haematology laboratory values. Azacitidine is contraindicated in patients with advanced malignant hepatic tumours.
Paediatric population
The safety and efficacy of Azacitidine in children aged 0-17 years have not yet been established. No data are available.
Method of administration
Reconstituted Azacitidine should be injected subcutaneously into the upper arm, thigh or abdomen. Injection sites should be rotated. New injections should be given at least 2.5 cm from the previous site and never into areas where the site is tender, bruised, red, or hardened.
After reconstitution, the suspension should not be filtered. For instructions on reconstitution of the medicinal product before administration. (see section Special precautions for disposal and other handling)

8. Contraindications:
- Hypersensitivity to the active substance or to any of the excipients.
- Advanced malignant hepatic tumours.
- Breast-feeding.

9. Special warnings and precautions for use:
Haematological toxicity
Treatment with azacitidine is associated with anaemia, neutropenia and thrombocytopenia, particularly during the first 2 cycles (See Section undesirable effects). Complete blood counts should be performed as needed to monitor response and toxicity, but at least prior to each treatment cycle. After administration of the recommended dose for the first cycle, the dose for subsequent cycles should be reduced or its administration delayed based on nadir counts and haematological response (See section dosage and administration). Patients should be advised to promptly report febrile episodes. Patients and physicians are also advised to be observant for signs and symptoms of bleeding.
Hepatic impairment
Patients with extensive tumour burden due to metastatic disease have been reported to experience progressive hepatic coma and death during azacitidine treatment, especially in such patients with baseline serum albumin < 30 g/L. Azacitidine is contraindicated in patients with advanced malignant hepatic tumours (See section Contraindication)
Renal impairment
Renal abnormalities ranging from elevated serum creatinine to renal failure and death were reported in patients treated with intravenous azacitidine in combination with other chemotherapeutic agents. In addition, renal tubular acidosis, defined as a fall in serum bicarbonate to < 20 mmol/L in association with an alkaline urine and hypokalaemia (serum potassium < 3 mmol/L) with chronic myelogenous leukaemia (CML) treated with azacitidine and etoposide. If unexplained reductions in serum bicarbonate (< 20 mmol/L) or elevations of serum creatinine or BUN occur, the dose should be reduced or administration delayed (See section dosage and administration).
Patients should be advised to report oliguria and anuria to the health care provider immediately.
Although no clinically relevant differences in the frequency of adverse reactions were noted, patients with renal impairment should be closely monitored for toxicity since azacitidine and/or its metabolites are primarily excreted by the kidney (See section dosage and administration).
Laboratory tests
Liver function tests, serum creatinine and serum bicarbonate should be determined prior to initiation of therapy and prior to each treatment cycle. Complete blood counts should be performed prior to initiation of therapy and as needed to monitor response and toxicity, but at a minimum, prior to each treatment cycle (See section undesirable effects).
Cardiac and pulmonary disease
Patients with a known history of cardiovascular or pulmonary disease showed a significantly increased incidence of cardiac events with azacitidine (See section undesirable effects). It is therefore advised to exercise caution when prescribing azacitidine to these patients. Cardiopulmonary assessment before and during the treatment should be considered.
Necrotising fasciitis
Necrotising fasciitis, including fatal cases, have been reported in patients treated with azacitidine. Azacitidine therapy should be discontinued in patients who develop necrotising fasciitis and appropriate treatment should be promptly initiated.
Tumour lysis syndrome
The patients at risk of tumour lysis syndrome are those with high tumour burden prior to treatment. These patients should be monitored closely and appropriate precautions taken.
Differentiation syndrome
Cases of differentiation syndrome (also known as retinoic acid syndrome) have been reported in patients receiving injectable azacitidine. Differentiation syndrome may be fatal and symptoms and clinical finding include respiratory distress, pulmonary infiltrates, fever, rash, pulmonary oedema, peripheral oedema, rapid weight gain, pleural effusions, pericardial effusions, hypotension and renal dysfunction. Treatment with high-dose IV corticosteroids and haemodynamic monitoring should be considered at first onset of symptoms or signs suggestive of differentiation syndrome. Temporary discontinuation of injectable azacitidine should be considered until resolution of symptoms and if resumed, caution is advised.

10. Fertility, pregnancy and lactation:
Women of childbearing potential / Contraception in males and females
Women of childbearing potential and men must use effective contraception during and up to 3 months after treatment.
Pregnancy
There are no adequate data on the use of azacitidine in pregnant women. Studies in mice have shown Reproductive toxicity. The potential risk for humans is unknown. Based on results from animal studies and its mechanism of action, azacitidine should not be used during pregnancy, especially during the first trimester, unless clearly necessary. The advantages of treatment should be weighed against the possible risk for the foetus in every individual case.
Breast-feeding
It is not known whether azacitidine or its metabolites are excreted in human milk. Due to the potential serious adverse reactions in the nursing child, breast-feeding is contraindicated during azacitidine therapy.
Fertility
There are no human data on the effect of azacitidine on fertility. In animals, adverse reactions with azacitidine use on male fertility have been documented. Men should be advised not to father a child while receiving treatment and must use effective contraception during and up to 3 months after treatment. Before starting treatment, male patients should be advised to seek counselling on sperm storage.

11. Drug interactions:
Azacitidine metabolism does not appear to be mediated by cytochrome P450 isoenzymes (CYPs), UDP-glucuronosyltransferases (UGTs), sulfotransferases (SULTs), and glutathione transferases (GSTs); clinically significant inhibitory or inductive effects of azacitidine on cytochrome P450 enzymes are unlikely.

12. Effects on ability to drive and use machines
Azacitidine has minor or moderate influence on the ability to drive and use machines. Fatigue has been reported with the use of azacitidine. Therefore, caution is recommended when driving or operating machines.

13. Undesirable Effects
Summary of the safety profile
Adult population with MDS, CMML and AML (20-30% marrow blasts)
Adverse reactions considered to be possibly or probably related to the administration of Vidaza have occurred in 97 % of patients.
The most common serious adverse reactions noted from the pivotal study (AZA PH GL 2003 CL 001) included febrile neutropenia (8.0 %) and anaemia (2.3 %), which were also reported in the supporting studies (CALGB 9221 and CALGB 8921). Other serious adverse reactions from these 3 studies included infections such as neutropenic sepsis (0.8%) and pneumonia (2.5%) (some with fatal outcome), thrombocytopenia (3.5%), hypersensitivity reactions (0.25%) and haemorrhagic events (e.g. cerebral haemorrhage [0.5%], gastrointestinal haemorrhage [0.8%] and intracranial haemorrhage [0.5%])).
The most commonly reported adverse reactions with azacitidine treatment were haematological reactions (71.4 %) including thrombocytopenia, neutropenia and leukopenia (usually Grade 3-4),

600 mm

Open Dimesnsion : 190 x 600 mm
PC : 3435

SS ARTS Graphic Designers

Version No: 00
Date: 04.07.2025
Change History:
New Artwork (04.07.2025)

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gastrointestinal events (60.6 %) including nausea, vomiting (usually Grade 1-2) or injection site reactions (77.1 %; usually Grade 1-2).

Adult population aged 65 years or older with AML with > 30% marrow blasts

The most common serious adverse reactions (≥ 10%) noted from AZA-AML-001 within the azacitidine treatment arm included febrile neutropenia (25.0%), pneumonia (20.3%), and pyrexia (10.6%). Other less frequently reported serious adverse reactions in the azacitidine treatment arm included sepsis (5.1%), anaemia (4.2%), neutropenic sepsis (3.0%), urinary tract infection (3.0%), thrombocytopenia (2.5%), neutropenia (2.1%), cellulitis (2.1%), dizziness (2.1%) and dyspnoea (2.1%).

The most commonly reported (≥ 30%) adverse reactions with azacitidine treatment were gastrointestinal events, including constipation (41.9%), nausea (39.8%), and diarrhoea (36.9%), (usually Grade 1-2), general disorders and administration site conditions including pyrexia (37.7%; usually Grade 1-2) and haematological events, including febrile neutropenia (32.2%) and neutropenia (30.1%), (usually Grade 3-4).

Tabulated list of adverse reactions

Table 1 below contains adverse reactions associated with azacitidine treatment obtained from the main clinical studies in MDS and AML and post marketing surveillance.

Frequencies are defined as: very common (≥ 1/10), common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness. Adverse reactions are presented in the table below according to the highest frequency observed in any of the main clinical studies.

Table 1: ADRs reported in patients with MDS or AML treated with azacitidine (clinical studies and post- marketing)

System Organ Class	Very common	Common	Uncommon	Rare	Not Known
Infections and infestations	pneumonia* (including bacterial, viral and fungal), nasopharyngitis	sepsis* (including bacterial, viral and fungal), neutropenic sepsis*, respiratory tract infection (includes upper and bronchitis), urinary tract infection, cellulitis, diverticulitis, oral fungal infection, sinusitis, pharyngitis, rhinitis, herpes simplex, skin infection			necrotising fasciitis*
Neoplasms benign, malignant and unspecified (including cysts and polyps)					Differentiation syndrome*
Blood and lymphatic system disorders	febrile neutropenia*, neutropenia, leukopenia, thrombocytopenia, anaemia	pancytopenia*, bonemarrow failure			
Immune system disorders			hypersensitivity reactions		
Metabolism and nutrition disorders	anorexia, decreased appetite, hypokalemia	dehydration		tumour lysis syndrome	
Psychiatric disorders	insomnia	confusional state, anxiety			
Nervous system disorders	dizziness, headache	intracranial haemorrhage*, syncope, somnolence, lethargy			
Eye disorders		eye haemorrhage, conjunctival haemorrhage			
Vascular disorders		hypotension*, hypotension, hypertension, haematoma orthostatic			
Respiratory, thoracic and mediastinal disorders	dyspnoea, epistaxis	pleural effusion, dyspnoea exertional, pharyngolaryngea l pain		interstitial lung disease	
Gastrointestinal disorders	diarrhoea, vomiting, constipation, nausea, abdominal pain (includes upper and abdominal discomfort)	gastrointestinal haemorrhage* (includes mouth haemorrhage), haemorrhoidal haemorrhage, stomatitis, gingival bleeding, dyspepsia			
Hepatobiliary disorders			hepatic failure*, progressive hepatic coma		
Skin and subcutaneous tissue disorders	petechiae, pruritus (includes generalized), rash, ecchymosis	purpura, alopecia, urticaria, erythema, rash macular	acute febrile neutrophilic dermatosis, pyoderma gangrenosum		
Musculoskeletal, and connective tissue disorders	arthralgia, musculoskeletal pain (includes back, bone and pain in extremity)	muscle spasms, myalgia			
Renal and urinary disorders		renal failure*, haematuria, elevated serum creatinine	renal tubular acidosis		
General disorders and administration site conditions	pyrexia*, fatigue, asthenia, chest pain, injection site erythema, injection site pain, injection site reaction (unspecified)	bruising, haematoma, induration, rash, pruritus, inflammation, discoloration, nodule and haemorrhage (at injection site), malaise, chills, catheter site hemorrhage		injection site necrosis (at injection site)	
Investigations	weight decreased				

* = rarely fatal cases have been reported

Description of selected adverse reactions

Haematologic adverse reactions

The most commonly reported (≥ 10%) haematological adverse reactions associated with azacitidine treatment include anaemia, thrombocytopenia, neutropenia, febrile neutropenia and leukopenia, and were usually Grade 3 or 4. There is a greater risk of these events occurring during the first 2 cycles, after which they occur with less frequency in patients with restoration of haematological function. Most haematological adverse reactions were managed by routine monitoring of complete blood counts and delaying azacitidine administration in the next cycle, prophylactic antibiotics and/or growth factor support (e.g. G-CSF) for neutropenia and transfusions for anaemia or thrombocytopenia as required.

Infections

Myelosuppression may lead to neutropenia and an increased risk of infection. Serious adverse reactions such as sepsis, including neutropenic sepsis, and pneumonia were reported in patients receiving azacitidine, some with a fatal outcome. Infections may be managed with the use of anti-infectives plus growth factor support (e.g. G-CSF) for neutropenia.

Bleeding

Bleeding may occur with patients receiving azacitidine. Serious adverse reactions such as gastrointestinal haemorrhage and intracranial haemorrhage have been reported. Patients should be monitored for signs and symptoms of bleeding, particularly those with pre-existing or treatment-related thrombocytopenia.

Hypersensitivity

Serious hypersensitivity reactions have been reported in patients receiving azacitidine. In case of an anaphylactic-like reaction, treatment with azacitidine should be immediately discontinued and appropriate symptomatic treatment initiated.

Skin and subcutaneous tissue adverse reactions

The majority of skin and subcutaneous adverse reactions were associated with the injection site. None of these adverse reactions led to discontinuation of azacitidine, or reduction of azacitidine dose in the pivotal studies. The majority of adverse reactions occurred during the first 2 cycles and tended to decrease with subsequent cycles. Subcutaneous adverse reactions such as injection site rash/inflammation/pruritus, rash, erythema and skin lesion may require management with concomitant medicinal products, such as antihistamines, corticosteroids and non-steroidal anti-inflammatory medicinal products (NSAIDs). These cutaneous reactions have to be distinguished from soft tissue infections, sometimes occurring at injection site. Soft tissue infections, including cellulitis and necrotising fasciitis in rare cases leading to death, have been reported with azacitidine in the post marketing setting.

Gastrointestinal adverse reactions

The most commonly reported gastrointestinal adverse reactions associated with azacitidine treatment included constipation, diarrhoea, nausea and vomiting. These adverse reactions were managed symptomatically with anti-emetics for nausea and vomiting; anti-diarrhoeals for diarrhoea, and laxatives and/or stool softeners for constipation.

Renal adverse reactions

Renal abnormalities, ranging from elevated serum creatinine and haematuria to renal tubular acidosis, renal failure and death were reported in patients treated with azacitidine.

Hepatic adverse reactions

Patients with extensive tumour burden due to metastatic disease have been reported to experience hepatic failure, progressive hepatic coma and death during azacitidine treatment.

Cardiac events

Data from a clinical trial allowing enrolment of patients with known history of cardiovascular or pulmonary disease showed a statistically significant increase in cardiac events in patients with newly diagnosed AML treated with azacitidine.

Elderly population

There is limited safety information available with azacitidine in patients ≥85 years (with 14 [5.9%] patients ≥85 years.

14. Overdosage

A patient experienced diarrhoea, nausea, and vomiting after receiving a single intravenous dose of approximately 290 mg/m^2, almost 4 times the recommended starting dose during clinical use.
In the event of overdose, the patient should be monitored with appropriate blood counts and should receive supportive treatment, as necessary. There is no known specific antidote for azacitidine overdose.

15. Special precautions for disposal and other handling).

Recommendations for safe handling

Azacitidine is a cytotoxic drug and, as with other potentially toxic compounds, caution should be exercised when handling and preparing Azacitidine suspensions.
If reconstituted Azacitidine comes into contact with the skin, immediately and thoroughly wash with soap and water. If it comes into contact with mucous membranes, flush thoroughly with water.
The Azacitidine vial is single-use and does not contain any preservatives. Unused portions of each vial should be discarded properly. Do not save any unused portions for later administration.

Instructions for Subcutaneous Administration

Azacitidine should be reconstituted aseptically with 4 mL sterile water for injection. The diluent should be injected slowly into the vial. Vigorously shake or roll the vial until a uniform suspension is achieved. The suspension will be cloudy. The resulting suspension will contain azacitidine 25 mg/mL. Do not filter the suspension after reconstitution. Doing so could remove the active substance.

Preparation for Immediate Subcutaneous Administration:

Doses greater than 4 mL should be divided equally into 2 syringes. The product may be held at room temperature for up to 1 hour, but must be administered within 1 hour after reconstitution.

Preparation for Delayed Subcutaneous Administration:

The reconstituted product may be kept in the vial or drawn into a syringe. Doses greater than 4 mL should be divided equally into 2 syringes. The product must be refrigerated immediately. When Azacitidine is reconstituted using water for injection that has not been refrigerated, the reconstituted product may be held under refrigerated conditions (2ºC - 8ºC, 36ºF - 46ºF) for up to 8 hours. When Azacitidine is reconstituted using refrigerated (2ºC - 8ºC, 36ºF - 46ºF) water for injection, the reconstituted product may be stored under refrigerated conditions (2ºC - 8ºC, 36ºF - 46ºF) for up to 22 hours. After removal from refrigerated conditions, the suspension may be allowed to equilibrate to room temperature for up to 30 minutes prior to administration.

Subcutaneous Administration

To provide a homogeneous suspension, the contents of the dosing syringe must be re-suspended immediately prior to administration. To re-suspend, vigorously roll the syringe between the palms until a uniform, cloudy suspension is achieved.
Azacitidine suspension is administered subcutaneously. Doses greater than 4 mL should be divided equally into 2 syringes and injected into 2 separate sites. Rotate sites for each injection (thigh, abdomen, or upper arm). New injections should be given at least 2.5 cm from an old site and never into areas where the site is tender, bruised, red, or hard.
After reconstitution, the suspension should not be filtered.

Suspension Stability: Azacitidine reconstituted with non-refrigerated water for injection for subcutaneous administration may be stored for up to 1 hour at 25°C (77°F) or for up to 8 hours between 2°C and 8°C (36°F and 46°F); when reconstituted with refrigerated (2ºC -8ºC, 36ºF -46ºF) water for injection, it may be stored for 22 hours between 2°C and 8°C (36°F and 46°F).

16. Storage condition

Store below 30 °C
Shelf Life
Unopened Vial: 24 months
After reconstitution:
Azacitidine for Injection, 100 mg/vial reconstituted with non-refrigerated water for injection for subcutaneous administration may be stored for up to 1 hour at 25°C (77°F) or for up to 8 hours between 2°C and 8°C (36°F and 46°F); when reconstituted with refrigerated (2ºC - 8ºC, 36ºF - 46ºF) water for injection, it may be stored for 22 hours between 2°C and 8°C (36°F and46°F).
Azacitidine for Injection, 100 mg/vial reconstituted either with 0.9% Sodium Chloride Injection or Lactated Ringer's Injection for intravenous administration may be stored for up to 1 hour at 25°C (77°F).

17. Dosage forms and packaging available

Powder for suspension for injection
The product is packed in Type I glass vial stoppered with bromobutyl rubber stopper and sealed with flip-off seal. Filled vial is packed with basecap and sleeve, further kept in a carton box with Pack Insert.

18. Name and Address of Manufacturer

Dr. Reddy's Laboratories Limited,
Formulation Unit -VII, Plot No. P1 to P9,
Phase-III,VSEZ, Duvvada,
Visakhapatnam District 530046,
Andhra Pradesh, India.

Product Registration Holder

Dr. Reddy`s Laboratories Malaysia Sdn. Bhd.
UNIT NO. SO-29-07 AND SO-29-08, MENARA 1,
STRATA OFFICE, NO. 3, JALAN BANGSAR, KL ECO CITY,
59200 KUALA LUMPUR
MALAYSIA

19. Date of Revision of Package Insert

July 2025