Patients with Non-hematologic Toxicity
Following the first cycle of DECIMA™ treatment, if any of the following non-hematologic toxicities are present, DECIMA™ treatment should not be restarted until the toxicity is resolved: 1) serum creatinine ≥2 mg/dL; 2) SGPT, total bilirubin ≥2 times ULN; 3) and active or uncontrolled infection.

Instructions for Intravenous Administration
DECIMA™ is a cytotoxic drug and caution should be exercised when handling and preparing DECIMA™. Procedures for proper handling and disposal of antineoplastic drugs should be applied.
DECIMA™ should be aseptically reconstituted with 10 mL of Sterile Water for Injection (USP); upon reconstitution, each mL
contains approximately 5.0 mg of decitabine at pH 6.7-7.3. Immediately after reconstitution, the solution should be further diluted with 0.9% Sodium Chloride Injection, 5% Dextrose Injection, or Lactated Ringer's Injection to a final drug concentration of 0.1 - 1.0 mg/mL. Unless used within 15 minutes of reconstitution, the diluted solution must be prepared using cold (2°C - 8°C) infusion fluids and stored at 2°C - 8°C (36°F - 46°F) for up to a maximum of 7 hours until administration.
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if there is evidence of particulate matter or discoloration.

CONTRAINDICATIONS
None

ADVERSE REACTION
Clinical Studies Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.
Most Commonly Occurring Adverse Reactions: neutropenia, thrombocytopenia, anemia, fatigue, pyrexia, nausea, cough, petechiae, constipation, diarrhea, and hyperglycemia

Discontinuation: thrombocytopenia, neutropenia, pneumonia, Mycobacterium avium complex infection, cardio-respiratory arrest, increased blood bilirubin, intracranial hemorrhage, abnormal liver function tests.
Dose Delayed: neutropenia, pulmonary edema, atrial fibrillation, central line infection, febrile neutropenia.
Dose Reduced: neutropenia, thrombocytopenia, anemia, lethargy, edema, tachycardia, depression, pharyngitis.

WARNING AND PRECAUTIONS
Neutropenia and Thrombocytopenia
Treatment with DECIMA™ is associated with neutropenia and thrombocytopenia. Complete blood and platelet counts should be performed as needed to monitor response and toxicity, but at a minimum, prior to each dosing cycle. After administration of the recommended dosage for the first cycle, treatment for subsequent cycles should be adjusted. Clinicians should consider the need for early institution of growth factors and/or antimicrobial agents for the prevention or treatment of infections in patients with MDS. Myelosuppression and worsening neutropenia may occur more frequently in the first or second
treatment cycles, and may not necessarily indicate progression of underlying MDS.

Use in Pregnancy
DECIMA™ can cause fetal harm when administered to a pregnant woman. Based on its mechanism of action, DECIMA™ is expected to result in adverse reproductive effects. In preclinical studies in mice and rats, decitabine was teratogenic, fetotoxic, and embryotoxic. There are no adequate and well-controlled studies of DECIMA™ in pregnant women. If this drug is used during pregnancy, or if a patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to the fetus. Women of childbearing potential should be advised to avoid becoming pregnant while taking DECIMA™ .

Use in Women of Childbearing Potential
Women of childbearing potential should be advised to avoid becoming pregnant while receiving DECIMA™ and for 1 month following completion of treatment. Women of childbearing potential should be counseled to use effective contraception during this time.
Based on its mechanism of action, DECIMA™ can cause fetal harm if used during pregnancy.

Use in Men
Men should be advised not to father a child while receiving treatment with DECIMA ™, and for 2 months following completion of treatment . Men with female partners of childbearing potential should use effective contraception during this time. Based on its mechanism of action, DECIMA™ alters DNA synthesis and can cause fetal harm.

OVERDOSE
There is no known antidote for overdosage with DECIMA™. Higher doses are associated with increased myelosuppression including prolonged neutropenia and thrombocytopenia. Standard supportive measures should be taken in the event of an overdose.

STORAGE
Store vials at 25°C (77°F); excursions permitted to 15-30°C (59- 86°F).

PRESENTATION
DECIMA™ is supplied as individually 20ml flint glass vials .

Marketed by:
Getwell Oncology Pvt. Ltd.
(A unit of Getwell)
464, Udyog Vihar, Phase-V, Gurgaon - 122016, Haryana, India

Manufactured by:
Getwell Pharmaceuticals
474, Udyog Vihar, Phase-V, Gurgaon - 122016, Haryana, India

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GETWELL

For the use of Registered Medical Practitioner or Hospital or a Laboratory only.

Decitabine Lyophilized Powder for Injection 50mg

DECIMA™

Rx only

WARNING

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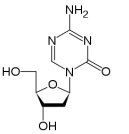
Treatment with DECIMA™ is associated with neutropenia and thrombocytopenia. Complete blood and platelet counts should be performed as needed to monitor response and toxicity, but at a minimum, prior to each dosing cycle. After administration of the recommended dosage for the first cycle, treatment for subsequent cycles should be adjusted [see Dosage and Administration (2.1, 2.2)]. Clinicians should consider the need for early institution of growth factors and/or antimicrobial agents for the prevention or treatment of infections in patients with MDS. Myelosuppression and worsening neutropenia may occur more frequently in the first or second

DESCRIPTION
Decitabine is a hypomethylating agent. It hypomethylates DNA by inhibiting DNA methyltransferase. It functions in a similar manner to azacitidine, although decitabine can only be incorporated into DNA strands while azacitidine can be incorporated into both DNA and RNA chains.

CHEMICAL STRUCTURE



COMPOSITION

Each vial contains:

Decitabine	50mg
Monobasic Potassium Phosphate USP	68 mg
Sodium Hydroxide IP	11.6 mg

CLINICAL PHARMACOLOGY
Decitabine is believed to exert its antineoplastic effects after phosphorylation and direct incorporation into DNA and inhibition of DNA methyltransferase, causing hypomethylation of DNA and cellular differentiation or apoptosis. Decitabine inhibits DNA methylation in vitro, which is achieved at concentrations that do not cause major suppression of DNA synthesis. Decitabine-induced hypomethylation in neoplastic cells may restore normal function to genes that are critical for the control of cellular differentiation and proliferation. In rapidly dividing cells, the cytotoxicity of decitabine may also be attributed to the formation of covalent adducts between DNA methyltransferase and decitabine incorporated into DNA. Nonproliferating cells are relatively insensitive to decitabine.

INDICATION
DECIMA™ is indicated for treatment of Patients with Myelodysplastic syndromes (MDS) including previously treated and untreated, de novo and secondary MDS of all French-American-British subtypes(refractory anaemia, refectory anaemia with ringed sinderoblasts, refractory anaemia with excess blasts, refractory anemia with excess blast in transformation, and chronic myelomonocytic leukemia) and intermediate-2, and high risk International Prognostic scoring system group.

DOSAGE AND ADMINISTRATION
There are two regimens for DECIMA™ administration. With either regimen it is recommended that patients be treated for a minimum of 4 cycles; however, a complete or partial response may take longer than 4 cycles. Complete blood counts and platelet counts should be performed as needed to monitor response and toxicity, but at a minimum, prior to each cycle. Liver chemistries and serum creatinine should be obtained prior to initiation of treatment.

Treatment Regimen – Option 1
DECIMA™ is administered at a dose of 15 mg/m^2 by continuous intravenous infusion over 3 hours repeated every 8 hours for 3 days. This cycle should be repeated every 6 weeks. Patients may be premedicated with standard anti-emetic therapy. If hematologic recovery (ANC ≥1,000/μL and platelets ≥50,000/μL) from a previous DECIMA™ treatment cycle requires more than 6 weeks, then the next cycle of DECIMA™ therapy should be delayed and dosing temporarily reduced by following this algorithm:
Recovery requiring more than 6, but less than 8 weeks - DECIMA™ dosing to be delayed for up to 2 weeks and the dose temporarily reduced to 11 mg/m^2 every 8 hours (33 mg/m^2/day, 99 mg/m^2/cycle) upon restarting therapy.
Recovery requiring more than 8, but less than 10 weeks - Patient should be assessed for disease progression (by bone marrow aspirates); in the absence of progression, the DECIMA™ dose should be delayed up to 2 more weeks and the dose reduced to 11 mg/m^2 every 8 hours (33 mg/m^2/day, 99 mg/m^2/cycle) upon restarting therapy, then maintained or increased in subsequent cycles as clinically indicated.

Treatment Regimen – Option 2
DECIMA™ is administered at a dose of 20 mg/m^2 by continuous intravenous infusion over 1 hour repeated daily for 5 days. This cycle should be repeated every 4 weeks. Patients may be premedicated with standard anti-emetic therapy. If myelosuppression is present, subsequent treatment cycles of DECIMA™ should be delayed until there is hematologic recovery (ANC ≥ 1,000/μL platelets ≥50,000/μL)