INDICATION AND IMPORTANT SAFETY INFORMATION FOR DACOGEN® (decitabine) for injection

INDICATION:

DACOGEN is indicated for treatment of patients with myelodysplastic syndromes (MDS) including Previously treated and untreated De novo and secondary All French-American-British (FAB) subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, and chronic myelomonocytic leukemia) Intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System (IPSS) groups

IMPORTANT SAFETY INFORMATION:

- **Neutropenia and Thrombocytopenia:** Treatment with DACOGEN 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 if indicated by dose adjustment guidelines. 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:** DACOGEN may cause fetal harm when administered to a pregnant woman. There are no adequate and well-controlled studies of DACOGEN 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 DACOGEN
- **Use in Women of Childbearing Potential:** Women of childbearing potential should be advised to avoid becoming pregnant while receiving treatment with DACOGEN and for 1 month following completion of treatment. Women of childbearing potential should be counseled to use effective contraception during this time.
- **Use in Men:** Men should be advised not to father a child while receiving treatment with DACOGEN and for 2 months following completion of treatment. DACOGEN may cause fetal harm. Men with female partners of childbearing potential should use effective contraception during this time.

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.

Following the first cycle of DACOGEN treatment, if any of the following non-hematologic toxicities are present, DACOGEN 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.

Most Commonly Occurring Adverse Reactions: neutropenia, thrombocytopenia, anemia, fatigue, pyrexia, nausea, cough, petechiae, constipation, diarrhea, and hyperglycemia.

Clinically Important Adverse Reactions: In the phase 3 clinical trial, the highest incidence of Grade 3 or Grade 4 adverse events in the DACOGEN arm was neutropenia (87%), thrombocytopenia (85%), febrile neutropenia (23%), and leukopenia (22%). Bone marrow suppression was the most frequent cause of dose reduction, delay, and discontinuation. Six patients had fatal events associated with their underlying disease and myelosuppression (anemia, neutropenia, and thrombocytopenia) that were considered at least possibly related to drug treatment. For DACOGEN-treated patients, 8 of 83 permanently discontinued therapy for adverse events; compared to 1 of 81 patients in the supportive care arm.

In the single-arm study, the highest incidence of Grade 3 or Grade 4 adverse events was neutropenia (37%), thrombocytopenia (24%), and anemia (22%). Seventy-eight percent of patients had dose delays, the median duration of this delay was 7 days. Hematologic toxicities and infections were the most frequent causes of dose delays and discontinuation. Eight patients had fatal events due to infection and/or bleeding that were considered at least possibly related to drug treatment.

USE IN SPECIFIC POPULATIONS: *Nursing Mothers:* Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions from DACOGEN in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. *Renal and Hepatic Impairment:* Because there are no data, DACOGEN should be used with caution in patients with renal or hepatic dysfunction.

To report SUSPECTED ADVERSE REACTIONS, contact Otsuka America Pharmaceutical, Inc. at 1-800-438-9927 or FDA at 1-800-FDA1088 (www.fda.gov/medwatch).

Please see FULL PRESCRIBING INFORMATION**.**