

FDA-Approved Agents for Treatment of MDS: Drug Profiles and Safety Guidelines

	Azacitidine	Decitabine	Lenalidomide
Indication	All 5 FAB subtypes (RA, RARS, RAEB, CMML, RAEB-T)	Int-1/Int-2 /high risk per IPSS, as well as tMDS	Transfusion-dependent MDS, Low-Int-1 MDS with del(5q) with or without additional chromosomal abnormalities
Therapeutic Target and Sensitivity	DNA methyltransferase inhibitor RNA and DNA Proteins and microenvironment No data on use after decitabine failure	DNA methyltransferase inhibitor DNA specific Direct cytotoxic effect May be effective in patients previously treated with azacitidine	Immunomodulatory drug (IMiD) Del(5q)—possible direct cytotoxic effect on clone Without del(5q)—drug may target disease microenvironment Most effective in patients with del(5q) Activity has been demonstrated in non-del(5q) patients
Mode of Use	SC or IV x 7 days every 28 days Outpatient regimen Treat until unacceptable toxicity or disease progression	IV daily for 5 days over 1 hour every 28 days Outpatient regimen Treat until unacceptable toxicity or disease progression	10 mg orally days 1-21 every 28 days Outpatient regimen
Primary End Points Met (IWG)	Improved overall survival (7-day dosing) Hematologic improvement (trilineage) Transfusion independence Cytogenetic response Safety and efficacy	Hematologic improvement Transfusion independence Cytogenetic response Safety and efficacy	Hematologic improvement Transfusion independence Cytogenetic response Efficacy and safety
Median Time to Response	Median time to first response: 2-3 cycles Median time to best response in AZA-001: 92% by 12 cycles Median time from first response to best response: 3-5 cycles	Median time to first response: 2 months Median time to best response: 2 months	Median time to first response: 4-6 weeks (MDS-003) Mean time to first dose modification: 80% of pts—21 days Median duration of drug holiday: 22 days Time between first and second dose modification: (mean) 51 days (34%)
Common Adverse Events and Treatment Considerations	Myelosuppression (most common) Injection-site reactions Nausea and vomiting Constipation Contraindicated in patients with hepatic tumors Use with caution in renal impairment May cause fetal harm	Myelosuppression (most common) Nausea and vomiting Constipation Hyperbilirubinemia Use with caution in renal impairment May cause fetal harm	Myelosuppression (most common) Rash Diarrhea Requires renal dose adjustment Nonteratogenic in animal studies Analog of thalidomide Must be prescribed through Revassist for safety

Kurtin. *JAdPro*, in print September 2011; Kurtin and Demakos. *Clin J Oncol Nurs*. 2010;14:E29-E44 doi:10.1188/10.CJON; Scott and Deeg. *Annu Rev Med*. 2010;53:345-358.

Blum. *Hematology Am Soc Hematol Educ Program*. 2010;2010:314-321.

Renal Dosing for Lenalidomide

1. Lenalidomide is primarily excreted unchanged by the kidney
 - a. Patients with normal renal function ($CL_{cr} \geq 60$ mL/min)—the recommended starting dose is 10 mg/day taken with water
 - b. Dose adjustments are recommended for $CL_{cr} \leq 60$ mL/min—based on National Kidney Foundation criteria
2. Because elderly patients are more likely to have decreased renal function, it may be useful to monitor renal function

Moderate renal impairment ($30 \leq CL_{cr} < 60$ mL/min)	5 mg every 24 hours
Severe renal impairment ($CL_{cr} < 30$ mL/min, not requiring dialysis)	5 mg every 48 hours
End-stage renal disease ($CL_{cr} < 30$ mL/min, not requiring dialysis)	5 mg 3 times/week following each dialysis

3. These recommendations are based on a pharmacokinetic study in patients with renal impairment due to nonmalignant conditions
4. Dosage should be continued or modified based on clinical or laboratory findings

National Kidney Foundation. KDOQI Clinical Practice Guidelines @ <http://www.kidney.org/Professionals/kdoqi>

Revlimid (lenalidomide) prescribing information @ <http://revlimid.com>