Dear NCCN Myelodysplastic Syndromes Guidelines Panel:

On behalf of Celgene Corporation, we respectfully request that the NCCN Guidelines Panel for Myelodysplastic Syndromes (MDS) review the enclosed recently published Phase III data on the use of REVLIMID® (lenalidomide) in International Prognostic Scoring System (IPSS) Low or Intermediate-1 Risk MDS patients with red blood cell transfusion-dependent (RBC-TD) symptomatic anemia, without deletion 5q (del(5q)) abnormality. The submission of this publication is in follow-up to a previous submission dated December 22, 2014 (enclosed for your reference).

**Specific Changes:** Recommend the use of lenalidomide in patients with IPSS low/intermediate-1 risk MDS with symptomatic anemia without del(5q) and are ineligible for or refractory to ESAs as a preferred treatment option, with a Category 1 rating. In addition, we request an update to the discussion section to include a description of these Phase III data, recently published in the Journal of Clinical Oncology.

**FDA Clearance:** REVLIMID is not approved for the treatment of non-del(5q) MDS. REVLIMID is indicated for the treatment of patients with transfusion-dependent anemia due to low- or intermediate-1 risk myelodysplastic syndromes (MDS) associated with a deletion 5q abnormality with or without additional cytogenetic abnormalities (Celgene Corporation, 2015).

Please see the enclosed REVLIMID Prescribing Information for additional indications.

**Rationale:**
The MDS-005 study was an international, multicenter, randomized, double-blind Phase III trial comparing the efficacy and safety of lenalidomide to placebo in RBC-TD patients with IPSS low or intermediate-1 risk non-del(5q) MDS -ineligible for or refractory to ESAs (Santini et al., 2016). Two hundred thirty nine patients were randomized 2:1 to receive either lenalidomide (n=160) 10 mg orally...
daily (5 mg daily for patients with creatinine clearance 40-60 mL/min) or placebo (n=79) (both on 28-day cycles). Median age of the patients was 71 years (range, 43-87 years) and baseline characteristics were similar. The primary endpoint of RBC transfusion independence (RBC-TI) for ≥8 weeks was achieved by significantly more patients treated with lenalidomide (26.9%) versus placebo (2.5%) (P<0.001); RBC-TI for ≥24 weeks was observed in 17.5% vs. 0%, respectively. Ninety percent of patients responded within 4 cycles of treatment and the median duration of RBC-TI ≥8 weeks was 30.9 weeks (95% confidence interval [CI], 20.7, 59.1).

In a univariate analysis, response was significantly higher in patients with baseline EPO ≤500 mU/mL than in patients with EPO >500 mU/mL (34% vs. 15.5%; P=.015). Median OS has not yet been reached; data are not mature enough to permit a definitive analysis. Collection of long term (≥5 years) follow-up data for OS is ongoing. The incidence of AML progression was 1.91 (95% CI, 0.80, 4.59) and 2.46 (95% CI, 0.79, 7.64) per 100 person-years for lenalidomide vs. placebo patients, respectively.

Grade 3/4 hematologic and non-hematologic treatment-emergent adverse events (TEAEs; ≥5%) in the lenalidomide vs. placebo arms, respectively, included: neutropenia (61.9% vs. 12.7%), thrombocytopenia (35.6% vs. 3.8%), infection (14.4% vs. 3.8%), hepatic disorder (5% vs. 2.5%) and cardiac arrhythmia (1.3% vs. 5.1%).

A copy of the 2016 publication is enclosed for your review (Santini et al., 2016).

Your consideration of this submission is greatly appreciated.

Sincerely,

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Sr. Manager, Global Medical Information

Mary Sugrue, MD, PhD
Executive Director, US Medical Affairs Disease Lead-MDS, AML

Cited References: