Imetelstat for Anemia in Myelodysplastic Syndrome:
Final Policy Recommendations

August 22, 2024

Policy Recommendations

Introduction

The following policy recommendations reflect the main themes and points made during the Policy Roundtable discussion at the July 14, 2024, CTAF public meeting on the use of Imetelstat for the treatment of Anemia in Myelodysplasic Syndrome. At the meeting, ICER presented the findings of its revised report on these treatments and the CTAF voting council deliberated on key questions related to their comparative clinical effectiveness, potential other benefits and contextual considerations, and long-term value for money at current prices. Following the votes, ICER convened a Policy Roundtable of two patients, two clinical experts, and two payers to discuss how best to apply the evidence and votes to real-world practice and policy. The discussion reflected multiple perspectives and opinions, and therefore, none of the statements below should be taken as a consensus view held by all participants.

A recording of the conversation can be accessed here, and a recording of the voting portion of the meeting can be accessed here. More information on Policy Roundtable participants, including conflict of interest disclosures, can be found in the appendix of this document. ICER's report on these treatments, which includes the same policy recommendations, can be found here.

The roundtable discussion was facilitated by Dr. Steven Pearson, MD, MSc, Special Advisor to ICER. The main themes and recommendations from the discussion are organized by audience and summarized below.

Health Equity

All Stakeholders

All stakeholders have a responsibility and an important role to play in ensuring that effective new treatment options for patients with transfusion-dependent, lower-risk MDS are introduced in a way that will help reduce health inequities.

Safe and effective treatment for anemia in MDS, especially for those with refractory to ESAs, remains a significant unmet healthcare need. Efforts are needed to ensure that new therapies for anemia in MDS such as luspatercept and imetelstat improve the health of patients and families and do not aggravate existing health inequities. Clinical experts and patients noted several limitations in the current health system that lead to access barriers and accentuate disparities for patients from communities of color and those with lower incomes, despite MDS being more common in the non-Hispanic white population. Problems with knowledge about MDS, clinical trial diversity, adequacy

of specialist networks, and costs of treatment and travel for care were highlighted. Several recommendations were made to address these concerns, focusing on specific stakeholders.

Manufacturers should take the following actions:

- **Reduce the price of imetelstat immediately to align with the value of added patient benefits.** Imetelstat has now been approved by the FDA and has been given a list price of approximately $365,000 per year by the manufacturer. However, there are significant uncertainties regarding the long-term efficacy and safety of imetelstat, and ICER's analysis suggested that treatment would achieve common thresholds for cost-effectiveness if priced between $94,800 and $113,000 per year. The manufacturer should reduce its list price and/or meet it with rebates given to payers so that both individual patients and the health system will view the drug as fairly priced, leading to broader access in a way that will help reduce disparities.

- **Take steps necessary to include a more diverse patient population in clinical trials, including an adequate number of patients with diverse ethnic and racial backgrounds, as these patients were under-represented in the iMerge study.**

Payers should take the following actions:

- **Ensure that benefit designs developed in conjunction with employers and other plan sponsors do not create requirements for out-of-pocket spending that create major barriers to appropriate access for vulnerable patients.**

- **Adopt standardized travel benefits for patients who have challenges traveling to a Center of Excellence to receive care or to an infusion center to receive therapy.**
  Patients in rural areas often have challenges coming to medical centers for necessary services that are not available near their homes. Insurance plans variably cover the costs of travel and housing. Additionally, such coverage is commonly tied to specific diagnoses and therapies. Payers should develop standard coverage for travel for needed services to ensure equitable access to therapies like imetelstat which typically will require subspecialist consultation and IV infusions.

Clinicians and clinical specialty societies should take the following actions:

Expand the ability of Centers of Excellence to provide consultation and support for community hematologists.

MDS is relatively uncommon, so many community hematologists will not be up to date on the latest strategies for managing MDS. Patients and their treating hematologists would benefit from

collaborative care through consultation with specialists at a center of excellence. The treatment plan can be designed by the specialist working with the patient and then administered by the community hematologist. Centers of Excellence need to have enough clinicians to meet the demand for consultation and ongoing remote management. Payers need to cover the consultations with Centers of Excellence and ongoing support through telemedicine.

Ensure adequate training of community hematologists about new therapies like imetelstat.

Hematologists in the community may not be fully aware of the subtleties in the management of patients receiving imetelstat. They need to be educated on protocols for administering imetelstat, monitoring patients following the infusion, and how to manage neutropenia, thrombocytopenia and other adverse events commonly seen with imetelstat. Standard protocols for dosing delays or dose reductions should be established and readily available to community hematologists. This can be achieved through updated guidelines for the management of anemia in patients with MDS and through targeted education sessions at national hematology meetings.

Join with patient organizations to exercise their joint power to advocate for drug prices that do not exceed a fair value for added clinical benefit.

Patients often have significant co-pays for drugs requiring IV infusions like imetelstat. These costs often fall under Medicare Part B, with the patient required to pay 20% of the cost, and there are no caps on drug costs under Part B like those under Part D coverage via the Inflation Reduction Act. Specialty societies have an opportunity and responsibility to reach out to patient groups to form a united front and advocate for fair insurance access linked to fair prices for drugs. Drug prices that align with analyses of added benefit will often be lower than those initially set by drug makers, and lower prices will lead to fewer restrictions on access to the drugs and less financial burden on patients. In addition, this will enhance more equitable access to effective therapies.

Include connections with reputable sources of information about MDS and referrals for psychological support when establishing initial treatment plans at diagnosis.

Patients consistently reported confusion about their diagnosis and challenges in accessing high-quality information about their disease. In addition, they report significant challenges with anxiety and depression following their diagnosis. Patients suggested that providing links to high-quality information like the NCI's PDQ Information site for patients and contact information for local or national patient support groups would help patients adjust to their diagnosis. In addition, early referral to therapists and/or psychiatrists is essential for the management of the psychosocial stresses of the diagnosis.

<u>Organizations representing patients should take the following actions:</u>

Patient groups should seek relationships with clinical specialty societies to exercise their joint power to advocate for drug prices that do not exceed a fair value for added clinical benefit.

Patients often have significant co-pays for drugs requiring IV infusions like imetelstat. These costs often fall under Medicare Part B, with the patient required to pay 20% of the cost, and there are no caps on drug costs under Part B like those under Part D coverage. Patient groups and specialty organizations have an opportunity and responsibility to advocate for fair insurance access linked to fair prices for drugs. Drug prices that align with analyses of added benefit will often be lower than those initially set by drug makers, and lower prices will lead to fewer restrictions on access to the drugs and less financial burden on patients. In addition, this will enhance more equitable access to effective therapies.

Help raise awareness about MDS

Most patients have never heard of MDS until they receive the diagnosis. The lack of awareness heightens their anxiety and sense of isolation. Greater awareness about MDS in the community will help to reduce the burden on patients and facilitate their ability to talk about their diagnosis and receive much-needed support.

Payers

Recommendation 1

Payers should use the inclusion and exclusion criteria from the Phase 3 trial of imetelstat as the guide to coverage policy and engage clinical experts and diverse patient representatives in considering how to address coverage issues for which there is limited or no evidence at the current time.

Given the limited data from one small, randomized trial and the high cost of imetelstat, it would not be unreasonable for payers to use prior authorization as a component of coverage. Prior authorization criteria should be based on the inclusion and exclusion criteria from the IMerge trial. The process for authorization should be clear and efficient for providers and patients. Options for specific elements of coverage criteria within insurance coverage policy are discussed below.

Coverage Criteria: General

ICER has previously described general criteria for fair coverage policies that should be considered as cornerstones of any drug coverage policy: see Cornerstones of "Fair" Drug Coverage: Appropriate Cost-Sharing and Utilization Management Policies for Pharmaceuticals.

Drug-Specific Coverage Criteria: Imetelstat

The limited data on effectiveness, combined with the significant potential for side effects and the high annual price for imetelstat, will lead payers to develop prior authorization criteria and to consider other limits on utilization.

None of these limits, however, should undermine the tenets of fair access to which all patients have a fundamental right. To explore the appropriate application of evidence to coverage policy, and to reflect the views of patient experts and clinicians on specific ways that payers might appropriately use coverage policy to manage resources prudently, we present the following perspectives on specific elements of cost sharing and coverage criteria for imetelstat.

Outcome-based agreements were briefly discussed, but there was general agreement that there was no role for them with imetelstat as they would be too cumbersome to administer.

Payers should be sensitive to the cumulative effects of cost-sharing on patients and set appropriate caps on the annual out of pocket expenditures for patients.

Step Therapy

Given the high incidence of adverse events with imetelstat, its high cost, and the lack of data demonstrating superiority to luspatercept, it would not be unreasonable for payers to require step therapy through ESAs and luspatercept prior to coverage of imetelstat for the treatment of anemia in patients with MDS.

For imetelsat, the clinical trial did not require patients to fail luspatercept, and there are no head to head trials with luspatercept. However, indirect evidence suggests that imetelstat is not more effective than luspatercept and it is associated with many more grade 3 and 4 hematologic events. The markedly higher cost of imetelstat without clear evidence of clinical benefit over luspatercept will likely drive the adoption of step therapy as a policy lever. Clinical experts participating in the ICER public meeting felt that there were no clear clinical or laboratory predictors of patients who should proceed to receive imetelstat prior to a trial of ESAs and luspatercept. However, payers should be aware that some patients may not be able to tolerate luspatercept therapy due to side effects. Thus, there should be a clear and efficient process for requesting exceptions.

While it is possible to tailor step therapy in a clinically responsible fashion, it is often administered with documentation burdens and inadequate procedures for exceptions that make step therapy a source of great frustration and the cause of poor outcomes for some patients due to the discontinuation of medicine/missed doses. Payers must ensure that their step therapy protocols are administered in a way that avoids these common problems that can cause delays and unnecessary barriers to appropriate care.

Clinical Coverage Criteria

- **Age:** Age 18 years or older.
- **Clinical eligibility**: Patients with low or intermediate-risk MDS who are dependent on RBC transfusions (≥4 units over 8 weeks) and are relapsed, refractory to, or ineligible for ESAs.
- **Exclusion criteria**: History of stem cell transplantation; prior treatment with lenalidomide or a hypomethylating agent; del(5q) subtype.
- **Dose:** 7.1 mg/kg IV infusion every four weeks with dose reductions or delays as appropriate based on adverse events such as neutropenia or thrombocytopenia.
- **Duration of coverage and renewal criteria**: Initial coverage will likely be for a period of 4 to 6 months, which is long enough to assess response to therapy. Clinical experts and payers felt that it would be appropriate to require attestation for continuation of therapy. In the iMerge trial, patients who had prolonged periods of transfusion independence responded within the first 4 months. Clinical experts suggested that a 4 to 6 month period prior to renewal would be appropriate.
- **Provider restrictions**: Clinical experts agreed that it is reasonable to restrict prescriptions for imetelstat to hematologists. Specialty clinicians are better suited to identify patients who are most likely to benefit, provide sufficient information for patients to make a well-informed decision, and monitor for response and side effects, and to make appropriate adjustments to the treatment interval and dose of imetelstat.

Recommendation 2

Site of Service Policies
Payers should establish site-of-service policies that cover home infusion or care at other low-cost sites when feasible.

Clinical experts did not suggest that there were risks of administration of imetelstat that would make it necessary to administer it in specialized clinical settings. Given the reduced cost and increased convenience for patients when infusions are delivered at home rather than at hospital-

based infusion centers, payers should establish site-of-service policies that cover home infusion or care at other low-cost sites when feasible. Benefit design should enable patients to have lower cost sharing when lower-cost settings are used, and rapid, transparent procedures for exceptions should be universal.

Manufacturers

Recommendation 1

Manufacturers should set prices that will foster affordability and good access for all patients by aligning prices with the patient-centered therapeutic value of their treatments. In the setting of these new interventions for MDS, while there is considerable hope associated with the promise of the therapies, there also remains substantial uncertainty regarding their longer-term safety and effectiveness. Manufacturer pricing should also reflect these considerations in moderating launch pricing.

Drug prices that are set well beyond the cost-effective range not only cause financial toxicity for patients and families using the treatments but also contribute to general healthcare cost growth that pushes families out of the insurance pool and causes others to ration their own care in ways that can be harmful.

Manufacturers should, therefore, price novel treatments in accordance with the demonstrated benefits to patients. In settings of substantial uncertainty, initial pricing should err on the side of being more affordable. This would allow more patients access, generating additional data on the real-world effectiveness of novel treatments that could be used in future assessment updates. With the accumulation of evidence of substantial patient benefit, manufacturers should be allowed to increase pricing in accordance with benefit.

Imetelstat is priced well beyond its currently known clinical value. The manufacturer should reduce the price to promote equitable access and reduce financial toxicity for patients.

Researchers/Regulators

Recommendation 1

Explore biomarkers that will help predict response to treatments for MDS

Only approximately 10% of patients remained transfusion-independent for a year or more, and 60% never achieved transfusion independence for even 8 weeks. Researchers should try to identify biomarkers that identify patients who are likely to have a significant clinical response to imetelstat and those who are unlikely to respond. Financial incentives suggest that the manufacturers are unlikely to fund these studies, so Federal agencies and potential payers using the coverage with evidence mechanism should fund this research.

Recommendation 2

Measure the impact of treatment on caregiver burden

The potential impact of effective therapy for anemia in MDS on caregiver burden was identified as an important potential benefit, but this is not explicitly measured in most clinical trials. Patient organizations have an important opportunity to pair with researchers in developing measures of caregiver burden and advocating to pharmaceutical companies and the FDA to include them in future trials of therapies like imetelstat.

Recommendation 3

Expand research on telomerase inhibition

Given that imetelstat is the first telomerase inhibitor approved by the FDA, this should spur additional research to find telomerase inhibitors that are less toxic and more effective. The development of an oral form would remove the burden of coming to an infusion center for IV therapy every 4 weeks. Finally, studies exploring the expansion of telomerase inhibitors to high-risk MDS or in combination with other therapies for anemia in MDS may identify additional roles these therapies can play.

Recommendation 4

Expand research on the underlying biology of MDS

More research needs to be done on the underlying pathophysiology of MDS, which may lead to more effective and less toxic targeted therapies. The goal is either to cure MDS or to turn it into a chronic disease with minimal impact on the patient's quality of life.

Appendix

Appendix Tables 1 through 3 contain conflict of interest (COI) disclosures for all participants at the July 19, 2024, Public meeting of CTAF.

Appendix Table 1. ICER Staff and Consultants and COI Disclosures

ICER Staff and Consultants	
Josh Carlson, PhD, MPH, Professor, Department of Pharmacy, University of Washington	**Sarah Emond, MPP,** President and CEO, ICER
Shahariar Mohammed Fahim, PhD, Research Lead, ICER	**Grace Ham, MSc,** Program and Events Coordinator, ICER
Belén Herce-Hagiwara, BA, Research Assistant, ICER	**Linda Luu, MSc**, Research Assistant, Department of Pharmacy, University of Washington
Dan Ollendorf, PhD, MPH, Chief Scientific Officer and Director of HTA Methods and Engagement, ICER	**Steven Pearson, MD, MSc,** Special Advisor, ICER
Becca Piltch, MPP, Program Manager, ICER	**Marina Richardson, PhD, MSc,** Senior Health Economist, ICER

*No conflicts of interest to disclose, defined as individual health care stock ownership (including anyone in the member's household) in any company with a product under study, including comparators, at the meeting in excess of $10,000 during the previous year, or any health care consultancy income from the manufacturer of the product or comparators being evaluated.

Appendix Table 2. CTAF Panel Member Participants and COI Disclosures

Participating Members of CTAF*	
Ralph Brindis, MD, MPH, Clinical Professor of Medicine, UCSF	**Felicia Cohn, PhD, HEC-C**, Bioethics Director, Kaiser Permanente Orange County
Robert Collyar, Patient Advocate, Patient Advocates in Research	**Rena Fox MD,** Professor of Medicine, UCSF
Paul Heidenreich MD, MS, Professor of Medicine, Stanford University	**Jeffrey Hoch, MA, PhD**, Professor, University of California, Davis
Annette Langer-Gould, MD, PhD, Regional Lead for Translational Neuroscience, Southern California Permanente Medical Group/Kaiser Permanente	**Sei Lee, MD MAS,** Professor of Medicine, UCSF
Joy Melnikow, MD, MPH, Professor emeritus, University of California Davis	**Lisa Murphy, MD, DPhil,** Professor of Medicine, UCSF
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Rita F Redberg, MD, MSc, Professor, UCSF	**Joanna Smith, LCSW, MPH,** Healthcare Liaison, Independent
Tony Sowry, MA, National Patient Advocate Foundation	

*No conflicts of interest to disclose, defined as individual health care stock ownership (including anyone in the member's household) in any company with a product under study, including comparators, at the meeting in excess of $10,000 during the previous year, or any health care consultancy income from the manufacturer of the product or comparators being evaluated.

Appendix Table 3. Policy Roundtable Participants and COI Disclosures

Policy Roundtable Participant	Conflict of Interest
Joan Durnell-Powell, MDS Patient Advocate, AA&MDS International Foundation	No conflicts to disclose.
Timothy Graubert, MD, Director, Hematologic Malignancy Program, Massachusetts General Hospital, Harvard Medical School	Dr. Graubert has a family member who is a full-time employee of Alexion Pharmaceuticals and has equity in AstraZeneca, Biogen, and Blueprint.
Leslie Fish, PharmD, SVP Pharmacy, IPD Analytics	Dr. Fish is a full-time employee at IPD Analytics.
Andreas Klein, MD, Chief, ad interim, Division of Hematology/Oncology and Director, Transplant and Cellular Therapies Program, Tufts Medical Center	Dr. Klein is employed by an academic medical center physician organization.
Daneen Sekoni, MHSA, Vice President, Policy and Advocacy, Cancer Support Community	The Cancer Support Community has received more than 25% of overall funding from health care companies and has received direct service/policy/psychosocial research support from BMS and Geron.
Emily Tsiao, PharmD, BCPS, Medical Policies Clinical Pharmacist, Premera Blue Cross	Dr. Tsiao is a full-time employee at Premera Blue Cross.