# Ivosidenib Criteria

## Criteria for Use
November 2018

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD USE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at the [PBM INTERnet](#) or [PBM INTRAnet](#) site for further information.

## Exclusion Criteria

If the answer to ANY item below is met, then the patient should NOT receive ivosidenib.

- ☐ Pregnancy (i.e. known pregnancy or positive pregnancy test) and/or actively breastfeeding
- ☐ Inability to swallow whole tablets

## Inclusion Criteria

The answers to all of the following must be fulfilled in order to meet criteria.

- ☐ Diagnosis of relapsed/refractory acute myeloid leukemia (see Issues for Consideration)
  
  Defined as relapsed disease after 2 previous inductions OR
  Relapsed disease after 1 induction and not suitable for intensive chemotherapy

- ☐ Presence of an isocitrate dehydrogenase-1 (IDH-1) mutation

- ☐ ECOG performance status 0-2

- ☐ Goals of care and role of Palliative Care consult have been discussed and documented

For women of childbearing potential

- ☐ Pregnancy should be excluded prior to receiving ivosidenib and the patient provided contraceptive counseling on potential risks vs. benefits of taking ivosidenib if patient were to become pregnant.

- ☐ Advise women not to breastfeed during treatment with ivosidenib and for at least 1 month after the last dose.

## Dosage and Administration

- The recommended starting dose of ivosidenib is 500 mg taken orally with or without food until disease progression or unacceptable toxicity. Avoid dosing around a high-fat meal.

- For patients without disease progression or unacceptable toxicity, treat for a minimum of 6 months to allow time for clinical response. Of responding patients who achieved a best response of CR or CRh, all achieved their first response within 6 months.

- Please refer to Product Information for dosing modification based upon adverse reactions.
**Monitoring**

- Blood counts and blood chemistries for leukocytosis and tumor lysis syndrome prior to the initiation of ivosidenib, at least once weekly for the first month, once every other week for the second month and once monthly for the duration of therapy.
- Monitor blood creatine phosphokinase weekly for the first month of therapy
- Monitor ECGs and electrolytes at least once weekly for the first 3 weeks of therapy, then at least once monthly for the duration of therapy
- Pregnancy test (in women with childbearing potential) at baseline.
- Signs and symptoms of differentiation syndrome (fever, cough, dyspnea, bone pain, rapid weight gain, edema, lymphadenopathy) and tumor lysis syndrome. Differentiation syndrome has been noted as early as 1 day and up to 3 months after therapy initiation.
- Monitor for new onset of motor and/or sensory neuropathy such as uni- or bilateral weakness, sensory alterations, paresthesias or difficulty breathing.

**Issues for Consideration**

- **FDA-approved indication.** Ivosidenib is an isocitrate dehydrogenase-1 inhibitor indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with an isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test.
- **Off-label uses in other AML or hematologic malignancy settings with IDH1-positive mutations.**
  - Enroll patient in a clinical trial
  - Consider submitting tissue and an e-consult to the VA Precision Oncology Program
  - Adjudicate locally to address drug requests outside of the FDA-approved indication
- **Differentiation syndrome.** Boxed warning highlights the risk of differentiation syndrome, which was reported in 19% of patients with relapsed or refractory AML, treated with ivosidenib in clinical trials. Differentiation syndrome has been observed as early as 1 day and up to 3 months after ivosidenib initiation. If suspected, initiate oral or IV corticosteroids with hemodynamic monitoring until improvement. Refer to Prescribing Information or drug monograph for further details.
- **QTc Interval Prolongation.** Ivosidenib can cause QTc prolongation. Inquire about concomitant non-prescription, as well as prescription medications, as well as other comorbidities to assess further risk. Educate and ensure appropriate monitoring of ECG and electrolytes.
- **Guillain-Barre syndrome.** Patients should be made aware of signs or symptoms.
- **Drug Interactions.** Multiple interactions can affect the efficacy/toxicity of ivosidenib and others.

**Renewal Criteria**

- Documented benefit (defined as no disease progression or RBC and/or platelet transfusion independence)
- And ECOG performance status has not declined to a level unacceptable to maintain quality of life