# Enasidenib (IDHIFA)
# Criteria for Use
# May 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 enasidenib.

- ☐ 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
  - 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-2 (IDH2) mutation
- ☐ ECOG performance status 0-2

For women of childbearing potential

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

  *Note: This may include men with female partners of childbearing potential if specified that adequate contraception should be practiced in males receiving certain medications*

## Dosage and Administration

- The recommended starting dose of enasidenib is 100 mg taken orally once daily with or without food until disease progression or unacceptable toxicity.
- For patients without disease progression or unacceptable toxicity, treat for a minimum of 6 months to allow time for clinical response. Of responding patients within the clinical trial setting, 85% did so within 6 months.
- Please refer to Product Information for dosing modification based on adverse events

## Monitoring

- Blood counts and blood chemistries for leukocytosis and tumor lysis syndrome prior to the initiation of enasidenib and monitor at a minimum of every 2 weeks for at least the first 3 months during treatment.
- Liver function tests including bilirubin level, should be evaluated at least monthly, or when clinically indicated.
- 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 10 days and up to 5 months after therapy initiation.

## Issues for Consideration

- **FDA-approved indication**. Enasidenib is an isocitrate dehydrogenase-2 inhibitor indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with an isocitrate dehydrogenase-2 (IDH2) mutation as detected by an FDA-approved test.
- **Off-label uses in other hematologic malignancies with IDH2-positive mutations**. At the current time, outcomes have been reported in the R/R-AML population. Outcome data in other IDH2-positive hematologic malignancies are awaited. Use local adjudication processes to address drug requests outside of the FDA-approved indication.
- **Differentiation syndrome.** Boxed warning highlights the risk of differentiation syndrome, which was reported in 14% of patients treated with enasidenib in clinical trials. Differentiation syndrome has been observed as early as 10 days and up to 5 months after enasidenib initiation. If suspected, initiate oral or IV corticosteroids with hemodynamic monitoring until improvement. Refer to Prescribing Information or drug monograph for further details.

## 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

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