IDHIFA®
(enasidenib) tablets
100mg • 50mg

Bristol Myers Squibb®
Access Support®
Your patient. Our commitment.

A REFERENCE GUIDE TO

Reimbursement and Coding IDHIFA® (enasidenib) tablets

To view authorized distributors/specialty pharmacies for IDHIFA, please click here or visit www.BMSAccessSupport.com.

Please see Important Safety Information on pages 8–9 and U.S. Full Prescribing Information, including **Boxed WARNING**.

Indication

IDHIFA® (enasidenib) is 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.

Select Important Safety Information: **Boxed WARNING**

WARNING: DIFFERENTIATION SYNDROME

Patients treated with IDHIFA have experienced symptoms of differentiation syndrome, which can be fatal if not treated. Symptoms may include fever, dyspnea, acute respiratory distress, pulmonary infiltrates, pleural or pericardial effusions, rapid weight gain or peripheral edema, lymphadenopathy, bone pain, and hepatic, renal, or multi-organ dysfunction. If differentiation syndrome is suspected, initiate corticosteroid therapy and hemodynamic monitoring until symptom resolution.

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For reimbursement assistance, call BMS Access Support® at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSAccessSupport.com.

Bristol Myers Squibb Is Committed to Helping Support Access

This brochure is designed to help appropriate patients get access to our medications by providing helpful reimbursement information for healthcare offices. Healthcare benefits vary significantly; therefore, it is important that healthcare provider offices verify each patient's insurance coverage prior to initiating therapy.

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Healthcare providers should code healthcare claims based upon the service that is rendered, the patient's medical record, the coding requirements of each health insurer, and the best coding practices. The accurate completion of reimbursement- or coverage-related documentation is the responsibility of the healthcare provider and patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

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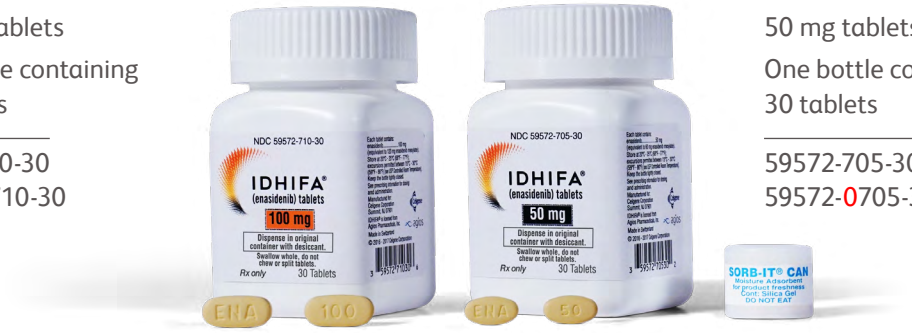
National Drug Code (NDC) Information and Storage for IDHIFA® (enasidenib)

NDCs for IDHIFA[1]

100 mg tablets

One bottle containing 30 tablets

59572-710-30
59572-0710-30



50 mg tablets

One bottle containing 30 tablets

59572-705-30
59572-0705-30

The red zero converts the 10-digit NDC to the 11-digit NDC. Some payers may require each NDC to be listed on the claim. Payer requirements regarding the use of NDCs may vary. Electronic data exchange generally requires use of the 11-digit NDC.

How Supplied[1]

The 50 and 100 mg dosages are supplied in bottles with a desiccant canister.

Storage[1]

Store tablets at 20°C-25°C (68°F-77°F); excursions permitted between 15°C-30°C (59°F-86°F). Keep the bottle tightly closed.

Store in the original bottle (with the desiccant canister) to protect from moisture.

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ICD-10-CM Codes

ICD-10-CM codes are used to identify a patient's diagnosis. On October 1, 2015, the newest version of these codes, ICD-10-CM, was implemented throughout the United States. This version replaces the previous version, ICD-9-CM.[2]

- The ICD-10-CM diagnosis codes contain **categories**, **subcategories**, and **codes**. Characters for categories, subcategories, and codes may be letters or numerals.
- **All categories** are 3 characters
- **Subcategories** are either 4 or 5 characters
- **Codes** may be 3, 4, 5, 6, or 7 characters

The ICD-10-CM codes for the labeled indications for IDHIFA® (enasidenib) tablets are provided below by Bristol Myers Squibb and should be verified with the payer. Some health plan and Medicare insurers may specify which codes are covered under their policies. Please code to the level of specificity documented in the medical record. For additional coding questions, call BMS Access Support® at **1-800-861-0048**, 8 AM to 8 PM ET, Monday–Friday, or visit **www.BMSAccessSupport.com**.

ICD-10-CM Codes for IDHIFA® (enasidenib)

ICD-10-CM Codes for IDHIFA[3]	
C92	**Myeloid leukemia**
C92.0	Acute myeloblastic leukemia
C92.00	Acute myeloblastic leukemia, not having achieved remission
C92.01	Acute myeloblastic leukemia, in remission
C92.02	Acute myeloblastic leukemia, in relapse

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Dosage and Administration for IDHIFA® (enasidenib)

Patient Selection[1]

Select patients for the treatment of AML with IDHIFA based on the presence of IDH2 mutations in the blood or bone marrow. Information on FDA-approved tests for the detection of IDH2 mutations in AML is available at http://www.fda.gov/CompanionDiagnostics.

For patients without disease progression or unacceptable toxicity, treat for a minimum of 6 months to allow time for clinical response.

Recommended Dosage[1]

Starting dose: one 100 mg IDHIFA tablet once daily

Swallow tablet whole with a cup (8 ounces) of water. Do not split or crush tablet

Take IDHIFA with or without food at about the same time each day

- Assess blood counts and blood chemistries for leukocytosis and tumor lysis syndrome prior to the initiation of IDHIFA and monitor at a minimum of every 2 weeks for at least the first 3 months during treatment. Manage any abnormalities promptly
- IDHIFA should be taken until disease progression or unacceptable toxicity

Missed Dose[1]

- If dose is vomited, missed, or not taken at the usual time, administer the dose as soon as possible on the same day and return to normal schedule the following day.

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Dosage and Administration for IDHIFA® (enasidenib) (cont.)

Dose Modifications for IDHIFA-Related Toxicities[1]

Adverse Reaction	Recommended Action
Differentiation syndrome	• If differentiation syndrome is suspected, administer systemic corticosteroids and initiate hemodynamic monitoring • Interrupt IDHIFA if severe pulmonary symptoms requiring intubation or ventilator support, and/or renal dysfunction persist for more than 48 hours after initiation of corticosteroids • Resume IDHIFA when signs and symptoms improve to Grade 2[a] or lower
Noninfectious leukocytosis (white blood cell [WBC] count greater than 30 x 10^9/L)	• Initiate treatment with hydroxyurea, as per standard institutional practices • Interrupt IDHIFA if leukocytosis is not improved with hydroxyurea, and then resume IDHIFA at 100 mg daily when WBC is less than 30 x 10^9/L
Elevation of bilirubin greater than 3x upper limit of normal sustained for ≥2 weeks without elevated transaminases or other hepatic disorders	• Reduce IDHIFA dose to 50 mg daily • Resume IDHIFA at 100 mg daily if bilirubin elevation resolves to less than 2x upper limit of normal
Other Grade 3[a] or higher toxicity considered related to treatment, including tumor lysis syndrome	• Interrupt IDHIFA until toxicity resolves to Grade 2[a] or lower • Resume IDHIFA at 50 mg daily; may increase to 100 mg daily if toxicities resolve to Grade 1[a] or lower • If Grade 3[a] or higher toxicity recurs, discontinue IDHIFA

[a] Grade 1 is mild, Grade 2 is moderate, Grade 3 is serious, Grade 4 is life-threatening.

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Important Safety Information for IDHIFA® (enasidenib)

WARNING: DIFFERENTIATION SYNDROME

Patients treated with IDHIFA have experienced symptoms of differentiation syndrome, which can be fatal if not treated. Symptoms may include fever, dyspnea, acute respiratory distress, pulmonary infiltrates, pleural or pericardial effusions, rapid weight gain or peripheral edema, lymphadenopathy, bone pain, and hepatic, renal, or multi-organ dysfunction. If differentiation syndrome is suspected, initiate corticosteroid therapy and hemodynamic monitoring until symptom resolution.

WARNINGS AND PRECAUTIONS

Differentiation Syndrome: See Boxed WARNING. In the clinical trial, 14% of patients treated with IDHIFA experienced differentiation syndrome, which may be life-threatening or fatal if not treated. Differentiation syndrome has been observed with and without concomitant hyperleukocytosis, in as early as 1 day and up to 5 months after IDHIFA initiation. Symptoms in patients treated with IDHIFA included acute respiratory distress represented by dyspnea and/or hypoxia and need for supplemental oxygen; pulmonary infiltrates and pleural effusion; renal impairment; fever; lymphadenopathy; bone pain; peripheral edema with rapid weight gain; and pericardial effusion. Hepatic, renal, and multi-organ dysfunction have also been observed. If differentiation syndrome is suspected, initiate systemic corticosteroids and hemodynamic monitoring until improvement. Taper corticosteroids only after resolution of symptoms. Differentiation syndrome symptoms may recur with premature discontinuation of corticosteroids. If severe pulmonary symptoms requiring intubation or ventilator support and/or renal dysfunction persist for more than 48 hours after initiation of corticosteroids, interrupt IDHIFA until signs and symptoms are no longer severe. Hospitalization for close observation and monitoring of patients with pulmonary and/or renal manifestation is recommended.

Embryo-Fetal Toxicity: Based on animal embryo-fetal toxicity studies, IDHIFA can cause embryo-fetal harm when administered to a pregnant woman. Advise females of reproductive potential and males with female partners of reproductive potential to use effective non-hormonal contraception during treatment with IDHIFA and for 2 months after the last dose. Advise pregnant women, of the potential risk to the fetus.

ADVERSE REACTIONS

- The most common adverse reactions (≥20%) included total bilirubin increased (81%), calcium decreased (74%), nausea (50%), diarrhea (43%), potassium decreased (41%), vomiting (34%), decreased appetite (34%), and phosphorus decreased (27%)
- The most frequently reported ≥Grade 3 adverse reactions (≥5%) included total bilirubin increased (15%), potassium decreased (15%), phosphorus decreased (8%), calcium decreased (8%), diarrhea (8%), differentiation syndrome (7%), non-infectious leukocytosis (6%), tumor lysis syndrome (6%), and nausea (5%)
- Serious adverse reactions were reported in 77.1% of patients. The most frequent serious adverse reactions (≥2%) were leukocytosis (10%), diarrhea (6%), nausea (5%), vomiting (3%), decreased appetite (3%), tumor lysis syndrome (5%), and differentiation syndrome (8%). Differentiation syndrome events characterized as serious included pyrexia, renal failure acute, hypoxia, respiratory failure, and multi-organ failure

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Important Safety Information for IDHIFA® (enasidenib) (cont.)

DRUG INTERACTIONS

Certain CYP1A2 CYP2C19 Substrates

Avoid concomitant use with IDHIFA unless otherwise recommended in the Prescribing Information for CYP1A2, CYP2C19 substrates where minimal concentration changes may lead to serious adverse reactions.

Consider reducing the frequency of caffeine intake from various food and beverages in a 24-hour period while taking IDHIFA because IDHIFA may increase the effect of caffeine in patients who are sensitive to it.

Enasidenib is a CYP1A2, CYP2C19 inhibitor. Concomitant use of IDHIFA increases the exposure of CYP1A2, CYP2C19 substrates, which may increase the risk of adverse reactions related to the substrates.

Certain CYP3A Substrates

Avoid concomitant use with IDHIFA unless otherwise recommended in the Prescribing Information for CYP3A substrates where minimal concentration changes may lead to reduced efficacy.

Do not administer IDHIFA with anti-fungal agents that are substrates of CYP3A due to expected loss of antifungal efficacy.

Co-administration of IDHIFA may decrease the concentrations of hormonal contraceptives. Consider alternative methods of contraception in patients receiving IDHIFA.

Enasidenib is a CYP3A inducer. Concomitant use of IDHIFA decreases the exposure of CYP3A substrates, which may reduce the efficacy of the substrates.

Certain OATP1B1, OATP1B3, and BCRP Substrates

Avoid coadministration of IDHIFA with OATP1B1, OATP1B3, and BCRP substrates, for which minimal concentration changes may lead to serious toxicities. If coadministration cannot be avoided, decrease the OATP1B1, OATP1B3, and BCRP substrates dosage(s) in accordance with the respective Prescribing Information.

Enasidenib is an OATP1B1, OATP1B3, and BCRP transporter inhibitor. Concomitant use of IDHIFA increases the exposure of OATP1B1, OATP1B3, and BCRP, which may increase the risk of adverse reactions related to these substrates.

Certain P-glycoprotein (P-gp) Substrates

When coadministered with IDHIFA, follow recommended P-gp substrates Prescribing Information and monitor more frequently for adverse reactions related to these substrates.

Enasidenib is a P-gp transporter inhibitor. Concomitant use of IDHIFA increases the exposure of P-gp substrates, which may increase the risk of adverse reactions related to the substrates.

LACTATION

Because of the potential for adverse reactions in the breastfed child, advise women not to breastfeed during treatment with IDHIFA and for 2 months after the last dose.

Please see U.S. Full Prescribing Information, including **Boxed WARNING**.

For reimbursement assistance, call BMS Access Support® at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSAccessSupport.com.

References

1. IDHIFA® (enasidenib). Prescribing Information. Celgene Corp.
2. eHealth University, Centers for Medicare & Medicaid Services. The ICD-10- transition: an introduction. Updated August 2014. Accessed May 6, 2021. https://www.cms.gov/Medicare/Coding/ICD10/Downloads/ICD10Introduction20140819.pdf.
3. Centers for Medicare & Medicaid Services. ICD-10-CM tabular list of diseases and injuries. Accessed May 6, 2021. https://www.cms.gov/medicare/icd-10/2021-icd-10-cm.

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Access Support®

Looking for support? We're here for you.

Coverage assistance, educational resources, and financial support options may be available through **BMS Access Support®**

Call a Patient Access Specialist at **1-800-861-0048**, 8 AM to 8 PM ET, Monday–Friday

Visit **www.BMSAccessSupport.com**

Scheduling a meeting with a BMS Access and Reimbursement Manager on the BMS Access Support website

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