Authorized distributors

IDHIFA® (enasidenib) is available for specialty pharmacy dispensing and in-office dispensing by community physicians, hospitals, institutions, Veterans Affairs, and the Department of Defense. The following distributors are authorized to sell IDHIFA® (enasidenib) and are able to service qualified accounts.

Authorized Distributor Network

Physician Offices

Cardinal Health Specialty Pharmaceutical Distribution
Phone: 1-877-453-3972, Monday-Friday, 7:00am-6:00pm CT (24-hour emergency on call)
https://specialtyonline.cardinalhealth.com/

CuraScript Specialty Distribution
Phone: 1-877-599-7748, Monday-Friday, 8:00am-7:00pm ET • https://www.curascriptsd.com

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McKesson Specialty Health
Phone: 1-800-482-6700, Monday-Friday, 7:00am-7:00pm CT • https://mscs.mckesson.com

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Oncology Supply
Phone: 1-800-633-7555, Monday-Friday, 8:00am-7:00pm CT • https://oncologysupply.com

Hospitals and Infusion Centers

ASD Healthcare
Phone: 1-800-746-6273, Monday-Thursday, 7:00am-6:30pm CT; Friday, 7:00am-6:00pm CT
Fax: 1-800-547-9413 • https://www.asdhealthcare.com

Cardinal Health Specialty Pharmaceutical Distribution
Phone: 1-866-677-4844, Monday-Friday, 7:00am-6:00pm CT (24 hour emergency)
Fax: 1-614-553-6301 • https://orderexpress.cardinalhealth.com

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McKesson Plasma and Biologics
Phone: 1-877-625-2566, Monday-Friday 8:00am-6:30pm CT • Fax: 1-888-752-7626 • https://connect.mckesson.com

Puerto Rico Hospitals and Clinics

Cardinal Puerto Rico (Borschow)
Phone: 1-787-625-4200 • cuserv@cardinalhealth.com • Online ordering: https://orderexpress.cardinalhealth.com

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Cesar Castillo Inc
Phone: 1-787-641-5242 (Hospitals) • 1-787-641-5082 (Specialty Pharmacy) • Fax: 1-787-999-1614
Online ordering: https://www.facilfarmaciacci.com/

Please see Important Safety Information on pages 11 and 12 and full Prescribing Information, including Boxed WARNING.

IDHIFA®
(enasidenib) tablets
100mg • 50mg

Product information

Ordering information

National Drug Codes (NDCs)			
10-digit NDC	**11-digit NDC[a]**	**Dosage strength**	**Description**
59572-705-30	59572-0705-30	50-mg tablet	Bottle of 30 pale yellow-to-yellow oval-shaped tablets; each film-coated tablet is debossed “ENA” on one side and “50” on the other side.
59572-710-30	59572-0710-30	100-mg tablet	Bottle of 30 pale yellow-to-yellow capsule-shaped tablets; each film-coated tablet is debossed “ENA” on one side and “100” on the other side.

[a]The red zero converts the 10-digit NDC to the 11-digit NDC. Some payers may require each NDC number 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.

Additional product information

How supplied

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

Storage

- 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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IDHIFA®
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Dosing and administration

Treatment with IDHIFA® begins with a test

Select patients for the treatment of AML with IDHIFA® based on the presence of *IDH2* mutations in the blood or bone marrow.

Recommended dosage

- One 100-mg IDHIFA® tablet daily. *Tablet pictured is not actual size*
- For patients without disease progression or unacceptable toxicity, treat for a minimum of 6 months to allow time for clinical response

Swallow whole with a cup of water. Do not split or crush tablets.

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.

Missed dose

- 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
- Do not take 2 doses at the same time to make up for the missed dose

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.

Important Safety Information

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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Dosing and administration (*cont'd*)

Dosage modifications for toxicities

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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Selected Safety Information: Warnings and Precautions

Differentiation syndrome

14% of patients (29/214) experienced differentiation syndrome.

- 7% (15/214) experienced ≥Grade 3 differentiation syndrome
- 4% required dose interruption

Differentiation syndrome can be fatal if untreated.

Differentiation syndrome is caused by rapid myeloid proliferation and differentiation and is characterized by signs and symptoms such as:

- Fever (36%)
- Dyspnea/hypoxia (68%)
- Need for supplemental oxygen (76%)
- Pulmonary infiltrates (73%)
- Pleural (45%) or pericardial (18%) effusions
- Peripheral edema with rapid weight gain (21%)
- Lymphadenopathy (33%)
- Bone pain (27%)
- Hepatic, renal, or multi-organ dysfunction

There is no diagnostic test for differentiation syndrome.

Differentiation syndrome has been observed with and without concomitant hyperleukocytosis and in as early as 1 day and up to 5 months after IDHIFA® initiation.

Please see Important Safety Information on pages 11 and 12 and full Prescribing Information, including Boxed WARNING.

Selected Safety Information: Warnings and Precautions (*cont'd*)

Management of differentiation syndrome

Initiate management	For patients with severe pulmonary symptoms requiring intubation or ventilator support and/or renal dysfunction for more than 48 hours after initiation of corticosteroids
■ If differentiation syndrome is suspected, initiate oral or intravenous corticosteroids (such as dexamethasone 10 mg every 12 hours) and hemodynamic monitoring until improvement ■ Taper corticosteroids only after resolution of symptoms ■ Symptoms may recur with premature discontinuation of corticosteroid treatment ■ Resume IDHIFA® when signs and symptoms improve to Grade 2 or lower	■ **Hospitalization for close observation and monitoring of patients with pulmonary and/or renal manifestations is recommended** ■ Interrupt IDHIFA® until signs and symptoms are no longer severe

Embryo-fetal toxicity

Based on animal embryo-fetal toxicity studies, IDHIFA® can cause embryo-fetal harm when administered to a pregnant woman.

- Advise pregnant women of the potential risk to the fetus
- Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment and for at least 2 months after the last dose of IDHIFA®

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IDHIFA® (enasidenib) tablets 100mg • 50mg

Adverse reactions

- The 30- and 60-day mortality rates observed with IDHIFA® were 4.2% (9/214) and 11.7% (25/214), respectively
- The most common adverse reactions (≥20%) of any grade were nausea, vomiting, diarrhea, elevated bilirubin, and decreased appetite
- 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

The safety profile of IDHIFA® was derived from 214 patients with relapsed/refractory AML in the clinical trial

Adverse reactions reported in ≥10% (any Grade) or ≥3% (Grade 3-5)

Body system Adverse reaction	All grades N = 214 (%)	≥Grade 3 N = 214 (%)
Gastrointestinal disorders[a]		
Nausea	107 (50)	11 (5)
Diarrhea	91 (43)	17 (8)
Vomiting	73 (34)	4 (2)
Metabolism and nutrition disorders		
Decreased appetite	73 (34)	9 (4)
Tumor lysis syndrome[b]	13 (6)	12 (6)
Blood and lymphatic system disorders		
Differentiation syndrome[c]	29 (14)	15 (7)
Noninfectious leukocytosis	26 (12)	12 (6)
Nervous system disorders		
Dysgeusia	25 (12)	0 (0)

[a]Gastrointestinal disorders observed with IDHIFA® treatment can be associated with other commonly reported events such as abdominal pain and weight decreased.
[b]Tumor lysis syndrome observed with IDHIFA® treatment can be associated with commonly reported uric acid increased.
[c]Differentiation syndrome can be associated with other commonly reported events such as respiratory failure, dyspnea, hypoxia, pyrexia, peripheral edema, rash, or renal insufficiency.

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Adverse reactions (*cont'd*)

Most common (≥20%) new or worsening laboratory abnormalities

Parameter[a]	All grades (%)	≥Grade 3 (%)
Total bilirubin increased	81	15
Calcium decreased	74	8
Potassium decreased	41	15
Phosphorus decreased	27	8

[a]Includes abnormalities occurring up to 28 days after last IDHIFA® dose, if new or worsened by at least one grade from baseline, or if baseline was unknown. The denominator varies based on data collected for each parameter (N = 213, except phosphorus [N = 209]).

Elevated bilirubin

IDHIFA® may interfere with bilirubin metabolism through inhibition of UGT1A1.

- 37% of patients (80/214) experienced total bilirubin elevations ≥2x upper limit of normal (ULN) at least one time
- Of those patients who experienced total bilirubin elevations ≥2x ULN, 35% had elevations within the first month of treatment, and 89% had no concomitant elevation of transaminases or other severe adverse events related to liver disorders
- No patients required a dose reduction for hyperbilirubinemia; treatment was interrupted in 3.7% of patients for a median of 6 days
- 3 patients (1.4%) discontinued IDHIFA® permanently due to hyperbilirubinemia

Noninfectious leukocytosis

IDHIFA® can induce myeloid proliferation resulting in a rapid increase in white blood cell count.

Tumor lysis syndrome

IDHIFA® can induce myeloid proliferation resulting in a rapid reduction in tumor cells, which may pose a risk for tumor lysis syndrome.

Please see Important Safety Information on pages 11 and 12 and full Prescribing Information, including Boxed WARNING.

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Dose adjustments and drug interactions

Dose interruption

- 43% of patients (92/214) required a dose interruption due to an adverse reaction
- The most common adverse reactions leading to interruption were differentiation syndrome (4%) and leukocytosis (3%)

Dose modification/dose reduction

- 5% of patients (10/214) required a dose reduction due to an adverse reaction
- No adverse reaction required dose reduction in more than 2 patients

Therapy discontinuation

- 17% of patients (36/214) permanently discontinued therapy due to an adverse reaction
- The most common adverse reaction leading to permanent discontinuation was leukocytosis (1%)

Effect of IDHIFA® on other drugs

OATP1B1, OATP1B3, and BCRP Substrates

- IDHIFA® is an OATP1B1, OATP1B3, and BCRP inhibitor.
- Coadministration of IDHIFA® increases the exposure of OATP1B1, OATP1B3, and BCRP substrates, which may increase the incidence and severity of adverse reactions of these substrates
- Decrease the dosage of OATP1B1, OATP1B3, and BCRP substrate(s) as recommended in the respective prescribing information, and as clinically indicated

Certain P-glycoprotein (P-gp) Substrates

- IDHIFA® is a P-gp inhibitor
- Coadministration of IDHIFA® increases the exposure of P-gp substrates, which may increase the incidence and severity of adverse reactions of these substrates
- For a P-gp substrate where small concentration changes may lead to serious adverse reactions, decrease the dose or modify the dosing frequency of such a P-gp substrate and monitor for adverse reactions as recommended in the respective prescribing information

You must report side effects to BMS Pharmacovigilance at 1-800-640-7854 (Global Drug Safety & Risk Management) and the FDA at 1-800-FDA-1088.

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Bristol Myers Squibb™

Access Support®

BMS Access Support® Can Provide Patient Access and Reimbursement Assistance

Bristol Myers Squibb is committed to helping patients gain access to their prescribed BMS medications. That's why we offer BMS Access Support. BMS Access Support provides resources to help patients understand their insurance coverage. In addition, we can share information on sources of financial support, including co-pay assistance for eligible commercially insured patients.

How BMS Access Support May Help
Find out how BMS can work with patients and their healthcare providers to help access a prescribed BMS medication.

Financial Support Options
There may be programs and services that could help with the cost of treatment. Learn about what options are available.

Additional Resources
We provide videos, tools, and other resources that may help with your access and reimbursement needs.

Have Questions About Our Program or Possible Financial Support?

If you have questions about coverage for a prescribed BMS medication, BMS Access Support may be able to help. Patients and their healthcare provider can complete an enrollment form to learn about programs that may be of assistance. Visit our website or contact BMS Access Support to learn more.

Call Bristol Myers Squibb Access Support at
1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday

Visit **www.BMSAccessSupport.com**

The accurate completion of reimbursement- or coverage-related documentation is the responsibility of the healthcare provider and the patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

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Important Safety Information

Indication

IDHIFA® (enasidenib) is indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia with an isocitrate dehydrogenase-2 mutation as detected by an FDA-approved test.

Important Safety Information

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 contraception during treatment with IDHIFA and for at least 2 months after the last dose. Advise pregnant women of the potential risk to the fetus.

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Important Safety Information (*cont'd*)

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

DRUG INTERACTIONS

Coadministration of IDHIFA increases the exposure of OATP1B1, OATP1B3, BCRP, and P-glycoprotein (P-gp) substrates, which may increase the incidence and severity of adverse reactions of these substrates. If coadministered, decrease the dosage of the substrate as recommended in the respective prescribing information and as clinically indicated.

LACTATION

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

Please see full Prescribing Information, including Boxed WARNING.

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Learn more about IDHIFA®

Visit **IDHIFApro.com**

Access downloadable patient resources online, including

- BMS Access Support® brochure
- Caregiver brochure
- Patient brochure

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