ONUREG™ (azacitidine) tablets 300 mg • 200 mg

ONUREG® DOSING GUIDE

INDICATION

ONUREG® is indicated for continued treatment of adult patients with acute myeloid leukemia who achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy and are not able to complete intensive curative therapy.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ONUREG® is contraindicated in patients with known severe hypersensitivity to azacitidine or its components.

WARNINGS AND PRECAUTIONS

Risks of Substitution with Other Azacitidine Products

Due to substantial differences in the pharmacokinetic parameters, the recommended dose and schedule for ONUREG® are different from those for the intravenous or subcutaneous azacitidine products. Treatment of patients using intravenous or subcutaneous azacitidine at the recommended dosage of ONUREG® may result in a fatal adverse reaction. Treatment with ONUREG® at the doses recommended for intravenous or subcutaneous azacitidine may not be effective. Do not substitute ONUREG® for intravenous or subcutaneous azacitidine.

Bristol Myers Squibb™

Please see Important Safety Information throughout and please click here for full Prescribing Information for ONUREG®.

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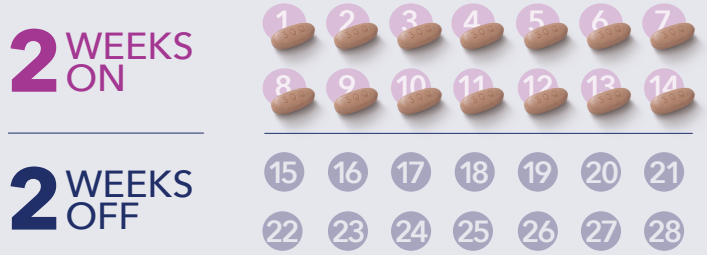
ONUREG® OFFERS CONVENIENT, ONCE-DAILY, ORAL DOSING THAT PATIENTS CAN TAKE AT HOME[1]

The recommended dosage of ONUREG® is one 300-mg tablet orally, once daily with or without food on Days 1-14 of each 28-day treatment cycle

RECOMMENDED DOSAGE



300 MG ON DAYS 1–14
OF EACH 28-DAY TREATMENT CYCLE

Continue ONUREG® until disease progression or unacceptable toxicity

Do not substitute ONUREG® for intravenous or subcutaneous azacitidine. The indications and dosing regimen for ONUREG® differ from that of intravenous or subcutaneous azacitidine

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Myelosuppression

New or worsening Grade 3 or 4 neutropenia and thrombocytopenia occurred in 49% and 22% of patients who received ONUREG®. Febrile neutropenia occurred in 12%. A dose reduction was required for 7% and 2% of patients due to neutropenia and thrombocytopenia. Less than 1% of patients discontinued ONUREG® due to either neutropenia or thrombocytopenia. Monitor complete blood counts and modify the dosage as recommended. Provide standard supportive care, including hematopoietic growth factors, if myelosuppression occurs.

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ONUREG® ADMINISTRATION AND DOSING CONSIDERATIONS[1]

ADMINISTRATION

- Administer an antiemetic 30 minutes prior to each dose of ONUREG® for the first 2 cycles. Antiemetic prophylaxis may be omitted after 2 cycles if there has been no nausea and vomiting
- If the absolute neutrophil count (ANC) is <0.5 Gi/L on Day 1 of a cycle, do not administer ONUREG®. Delay the start of the cycle until the ANC is ≥0.5 Gi/L

Instruct patients on the following:

Take a dose about the same time each day

Do not split, crush, or chew tablets

- If a dose of ONUREG® is missed, or not taken at the usual time, take the dose as soon as possible on the same day, and resume the normal schedule the following day. Do not take 2 doses on the same day
- If a dose is vomited, do not take another dose on the same day. Resume the normal schedule the following day

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DOSAGE MODIFICATIONS FOR ADVERSE REACTIONS[1]

Recommended dosage modifications for ARs: Myelosuppression

Monitor complete blood count every other week for the first 2 cycles of each **28-day treatment cycle** and prior to the start of the next cycle thereafter. Increase monitoring to every other week for the 2 cycles of each **28-day treatment cycle** after any dose reduction for myelosuppression.

NEUTROPHILS *<0.5 Gi/L*	**DAY 1 OF CYCLE**	**INTERRUPT**	**RESUME** **at 300 mg** *once neutrophils return to 0.5 Gi/L or higher*			
NEUTROPHILS *<1 Gi/L with fever at any time*	**1ST OCCURRENCE**	**INTERRUPT**	**RESUME** **at 300 mg** *once neutrophils return to 1 Gi/L or higher or platelets return to 50 Gi/L or higher*			
PLATELETS *<50 Gi/L with bleeding*	**2 CONSECUTIVE CYCLES OF OCCURRENCE**	**INTERRUPT**	**RESUME** **at reduced dose of 200 mg** *once neutrophils return to 1 Gi/L or higher or platelets return to 50 Gi/L or higher*	**CONTINUED OCCURRENCE**	*If a patient continues to experience the toxicity after dose reduction* **REDUCE** **treatment duration by 7 days**	*If the toxicity reoccurs after dose and schedule reduction* **DISCONTINUE**

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Increased Early Mortality in Patients with Myelodysplastic Syndromes (MDS)

In AZA-MDS-003, 216 patients with red blood cell transfusion-dependent anemia and thrombocytopenia due to MDS were randomized to ONUREG® or placebo. 107 received a median of 5 cycles of ONUREG® 300 mg daily for 21 days of a 28-day cycle. Enrollment was discontinued early due to a higher incidence of early fatal and/or serious adverse reactions in the ONUREG® arm compared with placebo. The most frequent fatal adverse reaction was sepsis. Safety and effectiveness of ONUREG® for MDS have not been established. Treatment of MDS with ONUREG® is not recommended outside of controlled trials.

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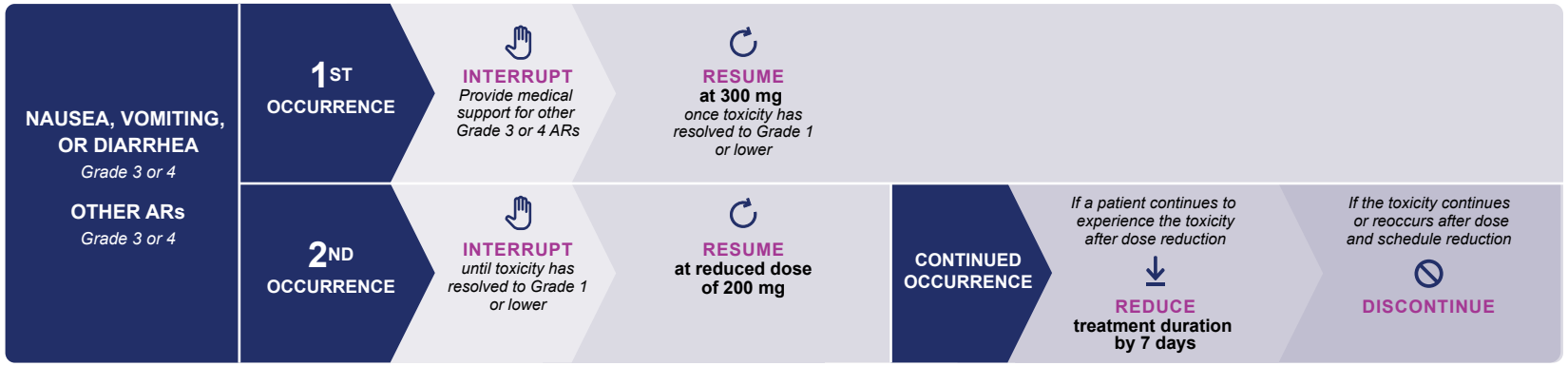
DOSAGE MODIFICATIONS FOR ADVERSE REACTIONS[1] (CONT'D)

Recommended dosage modifications for ARs: GI toxicity or other ARs

Monitor complete blood count every other week for the first 2 cycles of each **28-day treatment cycle** and prior to the start of the next cycle thereafter. Increase monitoring to every other week for the 2 cycles of each **28-day treatment cycle** after any dose reduction for myelosuppression.



IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Embryo-Fetal Toxicity

ONUREG® can cause fetal harm when administered to a pregnant woman. Azacitidine caused fetal death and anomalies in pregnant rats via a single intraperitoneal dose less than the recommended human daily dose of oral azacitidine on a mg/m^2 basis. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with ONUREG® and for at least 6 months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with ONUREG® and for at least 3 months after the last dose.

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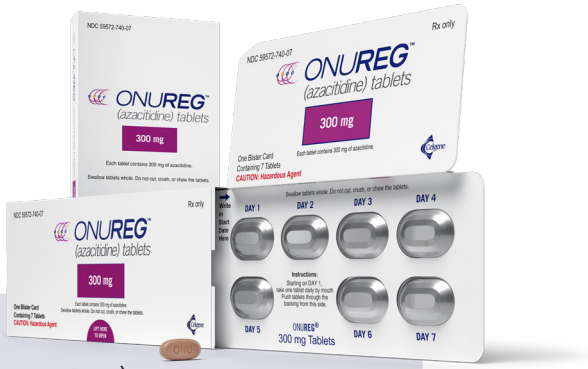
HOW ONUREG® IS SUPPLIED, STORED, AND HANDLED[1]

ONUREG® tablets are available in 2 strengths for once-daily, oral dosing

RECOMMENDED DOSE: 300-MG TABLET	200-MG TABLET
	 (Modified dose if ARs occur)



ONUREG® tablets are supplied in a blister card containing 7 tablets.

Storing ONUREG® blister cards

Store at 68°F to 77°F (20°C to 25°C)

- Excursions permitted between 59°F to 86°F (15°C to 30°C) (see USP Controlled Room Temperature)
- Store in the original aluminum blisters
- Blister cards will be replacing ONUREG® bottle packaging. Blister cards are provided in 7-count packages to provide flexibility in dispensing the recommended dosage and dosage modifications for adverse reactions

Handling and disposal

ONUREG® is a hazardous drug. Follow applicable special handling and disposal procedures. If powder comes in contact with skin, immediately and thoroughly wash with soap and water. If powder comes in contact with mucous membranes, immediately flush the area with water.

IMPORTANT SAFETY INFORMATION (CONT'D)

ADVERSE REACTIONS

Serious adverse reactions occurred in 15% of patients who received ONUREG®. Serious adverse reactions in ≥2% included pneumonia (8%) and febrile neutropenia (7%). One fatal adverse reaction (sepsis) occurred in a patient who received ONUREG®.

Most common (≥10%) adverse reactions with ONUREG® vs placebo were nausea (65%, 24%), vomiting (60%, 10%), diarrhea (50%, 21%), fatigue/asthenia (44%, 25%), constipation (39%, 24%), pneumonia (27%, 17%), abdominal pain (22%, 13%), arthralgia (14%, 10%), decreased appetite (13%, 6%), febrile neutropenia (12%, 8%), dizziness (11%, 9%), pain in extremity (11%, 5%).

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ONUREG® MAY REQUIRE SPECIAL DISPENSING IF DOSE ADJUSTMENTS ARE MADE

If ONUREG® dosing is decreased to 200-mg 7-day dosing per 28-day cycle (down from 14-day dosing), please use the following dispensing instructions

- If ONUREG® is prescribed at 200 mg for 7-day dosing per 28-day cycle, it is recommended to:
  - **Dispense only the prescribed number of pills** to the patient, using the original blister card
  - **Do not ship more pills than were prescribed,** due to hazardous waste disposal requirements for ONUREG®
  - **Return remaining pills to Celgene** per the ONUREG® 200-mg 7-Tablet Return Program
- Direct patients to take ONUREG® exactly as prescribed by their physician

- For more details on the Celgene ONUREG® 200-mg 7-Tablet Return Program, contact Celgene Customer Care at:
  - **1-888-423-5436**

  or
  - **MG-Onureg200mg7TabletReturn@bms.com**

- **For additional dispensing instructions,** contact BMS Medical Information at 1-800-321-1335

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HOW YOU CAN SUPPORT PATIENTS TAKING ONUREG®

Instruct patients on the following:

ANTI-NAUSEA

Your healthcare provider will prescribe an anti-nausea medication to help prevent nausea and vomiting during treatment with ONUREG®. Take the anti-nausea medicine 30 minutes before each dose of ONUREG®[1]*

FOOD

ONUREG® can be taken with or without food[1]

WHOLE TABLET

Do not split, crush, or chew ONUREG® tablets[1†]

ROUNDTINE/REMINDERS

Take a dose about the same time each day to help patients make their treatment part of their daily routine. You can also recommend that patients add a daily reminder on their smartphone/add to their phone's calendar app[2]

MISSED DOSE

If a dose of ONUREG® is missed, or not taken at the usual time, take the dose as soon as possible on the same day, and resume the normal schedule the following day[1]

NO DOUBLING

Do not take 2 doses on the same day to make up for a missed dose[1]

VOMITING

If a dose is vomited, do not take another dose on the same day. Resume the normal schedule the following day[1]

SUPPORT

See if patients can involve loved ones and/or caregivers to help them take their medication[2]

*Your healthcare provider may decide to stop the anti-nausea medicine after your second cycle of ONUREG®, if you do not have any nausea or vomiting.[1]

†If the powder from ONUREG® tablets comes in contact with your skin, wash the area well right away with soap and water. If the powder from ONUREG® tablets comes in contact with your eyes or mouth (mucous membranes), flush the area right away with water.[1]

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Learn more about ONUREG®

Visit ONUREGpro.com/DosingGuide

to access these and future resources:

How to order and access ONUREG®

ONUREG® patient financial assistance brochure

IMPORTANT SAFETY INFORMATION (CONT'D)

LACTATION

There are no data regarding the presence of azacitidine in human milk or the effects on the breastfed child or milk production. Because of the potential for serious adverse reactions in the breastfed child, advise women not to breastfeed during treatment with ONUREG® and for 1 week after the last dose.

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References: 1. ONUREG® [Prescribing Information]. Summit, NJ: Celgene Corporation; 2020. **2.** Bryant AL, LeBlanc TW, Albrecht T, et al. Oral adherence in adults with acute myeloid leukemia: results of a mixed methods study. *Blood*. 2019;134(suppl 1):2215.

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03/21 US-ONU-21-0026