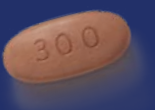
HOW TO DOSE ONUREG®



Recommended dosage:
One 300-mg tablet, orally, once daily with or without food on **Days 1-14** of each 28-day treatment cycle

2 WEEKS ON → **2 WEEKS OFF** → Continue until disease progression or unacceptable toxicity

Patients should take an antiemetic 30 minutes prior to each dose of ONUREG for at least the first 2 cycles[a]

[a]Antiemetic prophylaxis may be omitted after 2 cycles if there has been no nausea and vomiting.[1]

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

INDICATION

ONUREG® (azacitidine) 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.

ONUREG™ (azacitidine) tablets 300 mg • 200 mg

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

GLOBAL

click here links to https://packageinserts.bms.com/pi/pi_onureg.pdf

DOSE MODIFICATIONS MAY HELP MANAGE MYELOSUPPRESSION

Recommended dose modifications for neutropenia

300 mg Days 1-14[a]

Neutrophils <0.5 Gi/L on Day 1 of any cycle

- **Interrupt treatment**
- **Resume treatment at 300 mg** when neutrophils resolve to >0.5 Gi/L

Recommended dose modifications for febrile neutropenia or thrombocytopenia with bleeding

300 mg Days 1-14[a]

1st Occurrence: Neutrophils <1 Gi/L with fever at anytime or Platelets <50 Gi/L with bleeding

- **Interrupt treatment**
- **Resume treatment at 300 mg** when neutrophils resolve to ≥1 Gi/L or platelets resolve to ≥50 Gi/L

300 mg Days 1-14[a]

2 Consecutive Cycles of Occurrence

- **Interrupt treatment**
- **Resume treatment at reduced 200 mg dose** when neutrophils resolve to ≥1 Gi/L or platelets resolve to ≥50 Gi/L

200 mg Days 1-14[a]

Continued Occurrence After Dose Reduction

- **Reduce duration by 7 days**

200 mg Days 1-7[a]

Continued Occurrence After Dose and Schedule Reduction

- **Discontinue treatment**

[a]Each 28-day treatment cycle.

IMPORTANT SAFETY INFORMATION

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.

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

DOSE MODIFICATIONS MAY HELP MANAGE GI AND OTHER ARs

Recommended dose modifications for Grade 3 or 4 nausea, vomiting, diarrhea or other AR

300 mg Days 1-14[a]

1st Occurrence
- **Interrupt treatment** until AR resolves to Grade ≤1
- **Resume treatment at 300 mg**

300 mg Days 1-14[a]

2nd Occurrence
- **Interrupt treatment** until AR resolves to Grade ≤1
- **Resume treatment at reduced 200 mg dose**

200 mg Days 1-14[a]

3rd Occurrence
- **Reduce duration by 7 days**

200 mg Days 1-7[a]

4th Occurrence
- **Discontinue treatment**

[a]Each 28-day treatment cycle.
AR, adverse reaction.

To give your patients the best opportunity to benefit from ONUREG

Manage GI ARs with prophylactic antiemetics and dose modifications

IMPORTANT SAFETY INFORMATION

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.

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

HELPING PATIENTS STAY ON ONUREG®:

Instruct patients of the following when taking ONUREG®:

- Take **antiemetic 30 minutes before each dose** of ONUREG®[a]
- On your treatment days, take doses at the **same time each day** (with or without food) as part of your normal routine
- Swallow tablets whole. Do not cut, crush, or chew ONUREG® tablets[b]
- If you miss a dose or do not take ONUREG® at the usual time:
  - Take the dose as soon as possible on the same day
  - Resume the normal schedule the following day
  - Do not take 2 doses on the same day to make up for a missed dose

- If a dose is vomited, do not take another dose on the same day
  - Resume the normal schedule the following day

Tip: You can recommend that patients **add a reminder on their smartphone**

[a]Antiemetic prophylaxis may be omitted after 2 cycles if there has been no nausea and vomiting.[1]

[b]Instruct patients on the following: If the powder from ONUREG tablets comes in contact with skin, wash the area well right away with soap and water. If the powder comes in contact with mucous membranes (eyes or mouth) flush the area right away with water.[1]

IMPORTANT SAFETY INFORMATION

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.

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

CHECKLIST FOR STARTING PATIENTS ON ONUREG®:

Prescribe an antiemetic
- Educate patient on importance of antiemetic prophylaxis and anti-diarrheal medications during treatment to help manage GI toxicity

Discuss pregnancy risks with appropriate patients
- Recommend testing for pregnancy before starting treatment
- Discuss contraception recommendations for males and females
- Advise against breastfeeding while on ONUREG®

Monitor CBCs for signs of myelosuppression
- Before beginning treatment
- Every other week for the first 2 cycles
- Prior to each cycle after Cycle 2

Monitor ANC on Day 1 of cycle
- Do not administer ONUREG® if <0.5Gi/L

Manage adverse reactions
- Modify dosage or interrupt treatment as recommended
- Provided standard supportive care

Increase monitoring
- After any dose reduction
- In patients with severe renal impairment (CLcr 15-29 mL/min)

ANC, absolute neutrophil count; CBC, complete blood count; CLcr, creatinine clearance; GI, gastrointestinal.

IMPORTANT SAFETY INFORMATION

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/m2 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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ONUREG™
(azacitidine) tablets
300 mg • 200 mg

For additional dosing resources and to learn more about how ONUREG can help your patients, visit https://www.onuregpro.com/dosing-administration

https://www.onuregpro.com/dosing-administration links to https://www.onuregpro.com/dosing-administration

IMPORTANT SAFETY INFORMATION

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%).

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.

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

Reference: 1. ONUREG® [Prescribing Information]. Summit, NJ: Celgene Corporation; 2021.

Bristol Myers Squibb®

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