PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

PrONUREG®

azacitidine tablets

Tablets, 200 mg, 300 mg azacitidine, Oral

Antineoplastic / Pyrimidine Analogue

Celgene Inc., a Bristol-Myers Squibb company
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Date of Initial Approval:
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Submission Control No: 240668

RECENT MAJOR LABEL CHANGES

Not Applicable.

TABLE OF CONTENTS

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

ONUREG® (azacitidine tablets) is a nucleoside metabolic inhibitor indicated for:

- maintenance therapy in adult patients with acute myeloid leukemia (AML) who achieved complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following induction therapy with or without consolidation treatment, and who are not eligible for hematopoietic stem cell transplantation (HSCT).

Limitations of Use:

- ONUREG® is not interchangeable with, and should not be substituted with or for, azacitidine for injection. See **DOSAGE AND ADMINISTRATION, Administration** and **WARNINGS AND PRECAUTIONS, General**.
- The safety and effectiveness of ONUREG for treatment of myelodysplastic syndromes have not been established. Treatment of patients with myelodysplastic syndromes with ONUREG is not recommended outside of controlled trials. See **WARNINGS AND PRECAUTIONS, General**.

1.1 Pediatrics

Pediatrics (**< 18 years of age)**: No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

1.2 Geriatrics

Geriatrics (≥ 65 years of age): No dosage adjustment is required for ONUREG® based on age, see **ACTION AND CLINICAL PHARMACOLOGY, Pharmacokinetics.**

2 CONTRAINDICATIONS

ONUREG® is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see **DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.**

ONUREG® is contraindicated in patients with advanced malignant hepatic tumors.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- Health Canada has not authorized an indication for pediatric use, see **INDICATIONS**.
- No specific dose adjustments are recommended for elderly patients (≥ 65 years of age), see **INDICATIONS**.
- 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.

- ONUREG® can be administered to patients with renal impairment without initial dose adjustment, see **DOSAGE AND ADMINISTRATION, Recommended Dose and Dosage Adjustment** and **CLINICAL PHARMACOLOGY, Pharmacokinetics**.

4.2 Recommended Dose and Dosage Adjustment

Recommended Starting Dosage:

The recommended starting dose of ONUREG® is 300 mg orally once daily on Day 1 through Day 14 of repeated 28-day treatment cycles.

If the absolute neutrophil count (ANC) is less than 500/mcL on Day 1 of a cycle, do not administer ONUREG®. Delay the start of the cycle until the ANC is 500/mcL or more.

ONUREG® maintenance therapy should be initiated after achievement of a CR/CRi following completion of induction and consolidation therapy or following induction if consolidation therapy is not planned.

Dose Modifications During Treatment:

Dose Adjustment for Renal Impairment: No dose adjustment is required for patients with mild to moderate renal impairment.

ONUREG® can be administered to patients with severe renal impairment without initial dose adjustment. Monitor patients with severe renal impairment (creatinine clearance [CLcr] 15 to 29 mL/min calculated by Cockcroft-Gault formula) more frequently for adverse reactions and modify the ONUREG dosage for adverse reactions, see **WARNINGS AND PRECAUTIONS, Monitoring and Laboratory Tests**.

Dose Adjustment for Hepatic Impairment: ONUREG® has not been studied in patients with pre-existing severe hepatic impairment (total bilirubin > 3 × ULN).

A recommended dosage of ONUREG® has not been established for patients with moderate hepatic impairment (total bilirubin > 1.5 to 3 × ULN).

No dose adjustment of ONUREG® is recommended for patients with mild hepatic impairment (total bilirubin ≤ ULN and AST > ULN, or total bilirubin 1 to 1.5 × ULN and any AST).

Dose Adjustment for Adverse Reactions: Dose modification guidelines for hematologic and non-hematologic adverse reactions are recommended based on clinical and laboratory findings if toxicities are judged related to ONUREG® (see Table 1).

Table 1: Dose Adjustment for Hematological and Nonhematological Adverse Reactions

Adverse Reaction	Recommended Action
Grade 4 Neutropenia	First Occurrence

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