Decitabine/Cedazuridine (Inqovi®)

BY ALEXANDRA LOVELL, PHARMD, BCOP

What is decitabine/cedazuridine (Inqovi®)?

Inqovi® is a combination tablet comprised of decitabine and cedazuridine. Decitabine/cedazuridine is the only available oral hypomethylating agent approved for the treatment of myelodysplastic syndrome (MDS) and chronic myelomonocytic leukemia (CMML).

How does decitabine/cedazuridine work?

Decitabine is a nucleoside metabolic inhibitor that results in hypomethylation of DNA and cell differentiation leading to apoptosis. Cedazuridine is a cytidine deaminase inhibitor. Cytidine deaminase is an enzyme highly expressed within the gastrointestinal (GI) tract and liver that catalyzes the degradation of cytidine and its analogs, including decitabine. Cedazuridine is included in the combination tablet to prevent degradation of decitabine and improve oral bioavailability.

What is this approved for?

Decitabine/cedazuridine was granted approval by the FDA for use in adults with untreated or previously treated MDS and CMML.

What is the basis for this approval?

Decitabine/cedazuridine was studied in a Phase II multicenter, open-label, randomized, crossover trial comparing systemic exposure, demethylation activity, and safety between intravenous decitabine and oral decitabine/cedazuridine (*Blood* 2020;136(6):674-683). Patients were randomized to receive decitabine 20 mg/m^2 IV for 5 days or decitabine 35 mg/cedazuridine 100 mg for 5 days in cycle 1 followed by a crossover to the other treatment in cycle 2. All patients received decitabine/cedazuridine starting cycle 3. Each cycle was 28 days. Median follow-up was 24.3 months and patients received a median of 7 cycles of treatment. Dose reductions were required in 40 percent of patients and cycles were delayed in 51 percent of patients. Mean systemic decitabine exposure and demethylation activity was similar between groups. Clinical response was seen in 60 percent of patients with decitabine/cedazuridine with 21 percent achieving complete response (CR). Fifty percent of patients became red blood cell and platelet transfusion independent. Median overall survival was 18.3 months. Adverse events were similar between groups.

How do you administer this drug?

Decitabine/cedazuridine is available as a combination tablet containing 35 mg of decitabine and 100 mg of cedazuridine. It is administered orally on days 1 through 5 of each 28-day cycle until progression or unacceptable toxicity. Tablets should be swallowed whole and should be taken on an empty stomach. Do not consume food within 2 hours before or 2 hours after each dose.

Are there any pre-medications needed?

Decitabine/cedazuridine has low emetic risk. No routine pre-medications are recommended; however, antiemetics prior to each dose may be considered to minimize nausea and vomiting.

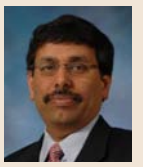
What are the common side effects associated with decitabine/cedazuridine (> or =20%)?

The most common adverse events were myelosuppression, fatigue, constipation, hemorrhage, myalgia, mucositis, arthralgia, nausea, dyspnea, diarrhea, rash, dizziness, febrile neutropenia, edema, headache, cough, decreased appetite, upper respiratory tract infection, pneumonia, and elevated transaminases.

What are the uncommon side effects associated with decitabine/cedazuridine (less than 20%)?

Pyrexia, abdominal pain, vomiting, neuropathy, cellulitis, sepsis, renal impairment, hypotension, arrhythmias, and embryo-fetal toxicity were also seen in studies.





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Are there any important drug interactions I should be aware of?

Cedazuridine inhibits cytidine deaminase. Drugs that are metabolized by cytidine deaminase should be avoided to avoid the risk of increased exposure and toxicity.

How do I adjust the dose in the setting of renal or hepatic insufficiency?

No dose adjustments are needed in patients with mild hepatic dysfunction or those with mild or moderate renal dysfunction. Decitabine/cedazuridine has not been studied in those with moderate or severe hepatic dysfunction, severe renal impairment, or end-stage renal disease. If hepatic or renal toxicity develops during treatment, delay the start of the next cycle until toxicity resolves.

What should my patients know about decitabine/cedazuridine?

- Fatal and severe myelosuppression can occur with decitabine/cedazuridine. Patients should be advised to report any infectious signs and symptoms to their healthcare provider. Growth factor support, antimicrobials for prophylaxis or treatment, or dose reductions may be necessary.
- Pregnancy should be avoided due to the risk for embryo-fetal toxicity. Effective contraception should be used during treatment and at least 3 months for men and 6 months for women following the last dose of decitabine/cedazuridine. Breastfeeding should be avoided during treatment and at least 2 weeks after the last dose.

What else should I know about decitabine/cedazuridine?

Although most responses were seen by cycle 3, complete or partial response may take longer than 4 cycles to achieve. A minimum of 4 cycles should be given to evaluate for response. Decitabine/cedazuridine should not be substituted for intravenous decitabine within a cycle.

What useful links are available regarding decitabine/cedazuridine?

Drug Information: https://bit.ly/3omI82j
FDA Approval: https://bit.ly/3nj0NLc

Any ongoing clinical trials related to decitabine/cedazuridine?

Decitabine/cedazuridine is being studied in combination with venetoclax and other therapies for MDS and CMML. It is also being studied for treatment of acute myeloid leukemia. More information is available about these trials at clinicaltrials.gov. OT