Venclexta

(venetoclax)

New Product Slideshow

MPR

Introduction

- **Brand name:** Venclexta
- **Generic name:** Venetoclax
- **Pharmacological class:** BCL-2 inhibitor
- **Strength and Formulation:** 10mg, 50mg, 100mg; tablets
- **Manufacturer:** AbbVie
- **How supplied:** Starting Pack—1 (four weekly blisters); Wallets 10mg—14; 50mg—7; Tabs 100mg—120
- **Legal Classification:** Rx

VENCLEXTA


Rx only
VENCLEXTA™
(venetoclax) tablets
10 mg
14 Tablets
WEEK 1
Record Start Date
QUESTIONS? Call 844-782-7883
abbvie
Genentech
1
2
3
4
OPEN
VENCLEXTA™
(venetoclax) tablets
10 mg, 50 mg, and 100 mg
Each tablet contains 10 mg venetoclax
Each tablet contains 50 mg venetoclax
Each tablet contains 100 mg venetoclax
(No. TEST)
VENCLEXTA™
venetoclax tablets
10 mg, 50 mg, and 100 mg
Rx Only
FOR DEMONSTR

Indications

- **Chronic lymphocytic leukemia (CLL)** in patients with 17p deletion, as detected by an FDA-approved test, who have received at least 1 prior therapy

Dosage & Administration

- Swallow whole
- Take with food and water
- Initially 20mg once daily for Week 1, then 50mg once daily for Week 2, then 100mg once daily for Week 3, then 200mg once daily for Week 4, then 400mg once daily for Week 5 and beyond until disease progression or unacceptable toxicity
- Risk assessment/prophylaxis for tumor lysis syndrome or dose modifications for toxicities: see full labeling

Considerations for Special Populations

- **Pregnancy:** Avoid
- **Nursing mothers:** Not recommended
- **Pediatric:** Not established
- **Geriatric:** No overall differences in safety and efficacy
- **Hepatic impairment:** Moderate to severe impairment: monitor closely
- **Renal impairment:** Severe impairment or dialysis: no dose recommended

Warnings/Precautions

- Risk of **tumor lysis syndrome** (esp. with high tumor burden, comorbidities, CrCl <80mL/min); perform tumor burden assessment, radiographic evaluation, blood chemistry; correct pre-existing abnormalities prior to initiation
- Premedicate with anti-hyperuricemics and ensure adequate hydration
- Monitor CBCs and for signs of **infection**; interrupt or reduce dose if severe neutropenia occurs

Warnings/Precautions

- Embryo-fetal toxicity
- Females of reproductive potential: should undergo pregnancy testing prior to initiation
- Use effective contraception during and for ≥1 month after final dose

Interactions

- See Contraindications
- Concomitant **strong CYP3A inhibitors** after ramp-up phase (eg, ketoconazole, conivaptan, clarithromycin, indinavir, itraconazole, lopinavir, ritonavir, telaprevir, posaconazole, voriconazole); avoid use or reduce venetoclax dose by ≥75%

Interactions

- Avoid concomitant **moderate CYP3A inhibitors** (eg, erythromycin, ciprofloxacin, diltiazem, dronedarone, fluconazole, verapamil) **or P-gp inhibitors** (eg, amiodarone, azithromycin, captopril, carvedilol, cyclosporine, felodipine, quercetin, quinidine, ranolazine, rifampin, ticagrelor); consider alternatives; if inhibitor necessary, reduce venetoclax dose by ≥50% and monitor closely

Interactions

- Resume at prior venetoclax dose 2–3 days after discontinuing the inhibitor
- Avoid concomitant **strong CYP3A inducers** (eg, carbamazepine, phenytoin, rifampin, St. John's Wort) or **moderate CYP3A inducers** (eg, bosentan, efavirenz, etravirine, modafinil, nafcillin); consider alternatives
- Avoid live attenuated vaccines until B-cell recovery

Interactions

- Avoid grapefruit, Seville oranges, and starfruit during treatment
- Monitor INR with concomitant warfarin
- Avoid **P-gp substrates with narrow therapeutic index** (eg, digoxin, everolimus, sirolimus); if necessary, take ≥6hrs before venetoclax

Adverse Reactions

- Neutropenia
- Diarrhea
- Nausea
- Anemia
- Upper respiratory tract infection
- Thrombocytopenia
- Fatigue

Mechanism of Action

- Venetoclax is a selective and orally bioavailable small-molecule inhibitor of BCL-2
- It helps restore the process of apoptosis by binding directly to the BCL-2 protein, displacing pro-apoptotic proteins, triggering mitochondrial outer membrane permeabilization and the activation of caspases
- In non-clinical studies, venetoclax demonstrated cytotoxic activity in tumor cells that overexpress BCL-2

Pharmacokinetics

- **Distribution:** Highly bound to plasma protein
- **Metabolism:** CYP3A4/5 (major)
- **Elimination:** Fecal

Clinical Trials

- The efficacy of Venclexta was established in an open-label, single-arm, multicenter trial (n=106) in patients with CLL with 17p deletion who had received at least 1 prior therapy
- Patients received Venclexta via a weekly ramp-up schedule starting at 20mg and ramping to 50mg, 100mg, 200mg, and finally 400mg once daily until disease progression or unacceptable toxicity

Clinical Trials

- The efficacy of Venclexta was evaluated by **overall response rate (ORR)** as assessed by an Independent Review Committee (IRC) using the updated NCI-WG guidelines
- The median time on treatment at the time of evaluation was 12.1 months

Clinical Trials

- **ORR** was seen in 80.2% of patients (95% CI: 71.3, 87.3) treated with Venclexta
- Complete remission was seen in 5.7% of patients and complete remission with incomplete marrow recovery was seen in 1.9% of patients
- Nodular partial remission was seen in 2.8% of patients
- Partial remission was seen in 69.8% of patients

Clinical Trials

- The median time to first response was 0.8 months (range 0.1–8.1 months)
- For patients who achieved complete remission or complete remission with incomplete bone marrow recovery, 3% were minimal residual disease (MRD) negative in the peripheral blood and bone marrow
- For more clinical data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

  http://www.empr.com/venclexta/drug/34571/