Clexta Innerleaf design (English)

Pantone 185 C & Metallic Coated 8483 C **W- 195 mm X H - 214 mm**

Clexta™
Venetoclax INN

Jenphar Bangladesh | جنفار بنغلاديش

Composition:
Clexta™ 50 Tablet: Each film coated tablet contains Venetoclax INN 50 mg.
Clexta™ 100 Tablet: Each film coated tablet contains Venetoclax INN 100 mg.

Pharmacology:
Venetoclax is a selective and orally bioavailable small-molecule inhibitor of BCL-2, an antiapoptotic protein. Overexpression of BCL-2 has been demonstrated in CLL and AML cells where it mediates tumor cell survival and has been associated with resistance to chemotherapeutics. Venetoclax helps restore the process of apoptosis by binding directly to the BCL-2 protein, displacing pro-apoptotic proteins like BIM, triggering mitochondrial outer membrane permeabilization and the activation of caspases. In nonclinical studies, Venetoclax has demonstrated cytotoxic activity in tumor cells that overexpress BCL-2.

Indications:
- For the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).
- In combination with azacitidine, or decitabine, or low-dose cytarabine for the treatment of newly diagnosed acute myeloid leukemia (AML) in adults 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy.

Dose & administration:
Method of Administration: Venetoclax should be taken orally once daily. Patients should be instructed to take Venetoclax tablet with a meal and water at approximately the same time each day. Venetoclax tablet should be swallowed whole and not chewed, crushed, or broken prior to swallowing.

Recommended Dosage for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: Venetoclax dosing begins with a 5-week ramp-up. The 5-week ramp-up dosing schedule is designed to gradually reduce tumor burden and decrease the risk of TLS. Administer Venetoclax according to the 5-week ramp-up dosing schedule to the recommended dosage of 400 mg orally once daily as shown in table below.

	Starting Dose
Week 1	20 mg
Week 2	50 mg
Week 3	100 mg
Week 4	200 mg
Week 5 and beyond	400 mg

In Combination with Obinutuzumab: Start obinutuzumab administration at 100 mg on cycle 1 day 1, followed by 900 mg on cycle 1 day 2. Administer 1000 mg on days 8 and 15 of cycle 1 and on day 1 of each subsequent 28-day cycle for a total of 6 cycles. Refer to the obinutuzumab prescribing information for additional dosing information. On cycle 1 day 22, start Venetoclax according to the 5-week ramp-up dosing. After completing the ramp-up phase on cycle 2 day 28, continue Venetoclax at a dose of 400 mg orally once daily from cycle 3 day 1 until the last day of cycle 12.

In Combination with Rituximab: Start rituximab administration after the patient has completed the 5-week ramp-up dosing schedule for Venetoclax and has received Venetoclax at the recommended dosage of 400 mg orally once daily for 7 days. Administer rituximab on Day 1 of each 28-day cycle for 6 cycles, at a dose of 375 mg/m^2 intravenously for cycle 1 and 500 mg/m^2 intravenously for cycles 2-6. Continue Venetoclax 400 mg orally once daily for 24 months from cycle 1 day 1 of rituximab.

Monotherapy: The recommended dosage of Venetoclax is 400 mg once daily after completion of the 5-week ramp-up dosing schedule. Continue Venetoclax until disease progression or unacceptable toxicity.

Recommended Dosage for Acute Myeloid Leukemia: The recommended dosage and ramp-up of Venetoclax depends upon the combination agent. Follow the dosing schedule, including the 3-day or 4-day dose ramp-up.

Venetoclax administration on cycle 1 day 1 in combination with:
- Azacitidine 75 mg/m^2 intravenously or subcutaneously once daily on days 1-7 of each 28- day cycle.
- Decitabine 20 mg/m^2 intravenously once daily on days 1-5 of each 28-day cycle.
- Cytarabine 20 mg/m^2 subcutaneously once daily on days 1-10 of each 28-day cycle.

	Venetoclax oral daily dose	
Day 1	100 mg	
Day 2	200 mg	
Day 3	400 mg	
Day 4 & beyond	400 mg orally once daily of each 28 day cycle in combination with azacitidine or decitabine	600 mg orally once daily of each 28- day cycle in combination with low-dose cytarabine

Continue Venetoclax, in combination with azacitidine or decitabine or low-dose cytarabine, until disease progression or unacceptable toxicity.

Contra-indication:
Concomitant use of Venetoclax with strong CYP3A inhibitors at initiation and during the ramp-up phase is contraindicated in patients with CLL/SLL due to the potential for increased risk of tumor lysis syndrome.

Warning and precaution:
Tumor Lysis Syndrome (TLS): Anticipate TLS; assess risk in all patients. Premedicate with anti-hyperuricemics and ensure adequate hydration. Employ more intensive measures (intravenous hydration, frequent monitoring, hospitalization) as overall risk increases.
Neutropenia: Monitor blood counts. Interrupt dosing and resume at same or reduced dose. Consider supportive care measures.
Infections: Monitor for signs and symptoms of infection and treat promptly. Withhold for Grade 3 and 4 infection until resolution and resume at same or reduced dose.
Immunization: Do not administer live attenuated vaccines prior to, during, or after treatment with Venetoclax until B-cell recovery.
Embryo-Fetal Toxicity: May cause embryo-fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception. Treatment of patients with multiple myeloma with Venetoclax in combination with bortezomib plus dexamethasone is not recommended outside of controlled clinical trials.

Adverse effects:
In CLL/SLL: The most common adverse reactions (≥20%) for Venetoclax when given in combination with obinutuzumab or rituximab or as monotherapy are neutropenia, thrombocytopenia, anemia, diarrhea, nausea, upper respiratory tract infection, cough, musculoskeletal pain, fatigue, and edema.
In AML: The most common adverse reactions (≥30%) in combination with azacitidine or decitabine or low-dose cytarabine are nausea, diarrhea, thrombocytopenia, constipation, neutropenia, febrile neutropenia, fatigue, vomiting, edema, pyrexia, pneumonia, dyspnea, hemorrhage, anemia, rash, abdominal pain, sepsis, musculoskeletal pain, dizziness, cough, oropharyngeal pain, and hypotension.

Use in specific populations
Pregnancy: Based on findings in animals and its mechanism of action, Venetoclax may cause embryo-fetal harm when administered to a pregnant woman. There are no available data on Venetoclax use in pregnant women to inform a drug-associated risk. Advise pregnant women of the potential risk to a fetus.
Lactation: There are no data on the presence of Venetoclax in human milk or the effects on the breastfed child or milk production. Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment with Venetoclax and for 1 week after the last dose.
Females and Males of Reproductive Potential: Venetoclax may cause fetal harm when administered to pregnant women.
Pediatric Use: The safety and effectiveness of Venetoclax have not been established in pediatric patients.
Geriatric Use: No clinically meaningful differences in safety and effectiveness were observed between older and younger patients in the combination and monotherapy studies.
Renal Impairment: Due to the increased risk of TLS, patients with reduced renal function (CLcr <80 mL/min, calculated by Cockcroft-Gault formula) require more intensive prophylaxis and monitoring to reduce the risk of TLS when initiating treatment with Venetoclax. No dose adjustment is recommended for patients with mild, moderate or severe renal impairment (CLcr ≥15 mL/min).
Hepatic Impairment: No dose adjustment is recommended for patients with mild (Child-Pugh A) or moderate (ChildPugh B) hepatic impairment. Reduce the dose of Venetoclax for patients with severe hepatic impairment (Child-Pugh C); monitor these patients more frequently for adverse reactions.

Drug interaction:
- *Strong or moderate CYP3A inhibitors or P-gp inhibitors:* It may increase Venetoclax toxicities, including the risk of TLS. Adjust dosage of Venetoclax. Avoid grapefruit products, seville oranges, and starfruit during treatment with Venetoclax, as they contain inhibitors of CYP3A.
- *Strong or moderate CYP3A inducers:* It may decrease Venetoclax efficacy. Avoid concomitant use of Venetoclax with strong CYP3A inducers or moderate CYP3A inducers.
- *Warfarin:* It may increase the risk of bleeding. Monitor international normalized ratio (INR) more frequently in patients using warfarin concomitantly with Venetoclax.
- *P-gp substrates:* Avoid concomitant use of Venetoclax with a P-gp substrate. If a concomitant use is unavoidable, separate dosing of the P-gp substrate at least 6 hours before Venetoclax.

Overdose:
There is no specific antidote for Venetoclax. For patients who experience overdose, closely monitor and provide appropriate supportive treatment; during ramp-up phase interrupt Venetoclax and monitor carefully for signs and symptoms of TLS along with other toxicities. Based on venetoclax large volume of distribution and extensive protein binding, dialysis is unlikely to result in significant removal of venetoclax.

Storage:
Store in a cool & dry place below 30^0 C, protect from light & moisture. Keep out of the reach of children.

Packing:
Clexta™ 50 Tablet: Each box contains 30 tablets and one packet silica gel in a sealed HDPE container.
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Manufactured for
Jenphar Bangladesh Ltd.
Sreepur, Gazipur, Bangladesh.
by Techno Drugs Ltd.
Satirpara, Narsingdi, Bangladesh