Paribac

Niraparib Tosylate Monohydrate INN

Composition:
Paribac 100 Capsule: Each capsule contains Niraparib Tosylate Monohydrate INN equivalent to Niraparib 100 mg.

Pharmacology:
Niraparib is an inhibitor of poly(ADP-ribose) polymerase (PARP) enzymes, PARP-1 and PARP-2, which plays a role in DNA repair. In vitro studies have shown that Niraparib-induced cytotoxicity may involve inhibition of PARP enzymatic activity and increased formation of PARP-DNA complexes resulting in DNA damage, apoptosis and cell death. Increased Niraparib-induced cytotoxicity was observed in tumor cell lines with or without deficiencies in BRCA1/2.

Indications:
Paribac is a poly (ADP -ribose) polymerase (PARP) inhibitor indicated:
• for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy.
• for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.
• for the treatment of adult patients with advanced ovarian, fallopian tube or primary peritoneal cancer who have been treated with 3 or more prior chemotherapy regimens and whose cancer is associated with homologous recombination deficiency (HRD) positive status defined by
either:
• a deleterious or suspected deleterious BRCA mutation or
• genomic instability and who have progressed more than 6 months after response to the last platinum-based chemotherapy.

Dosage and administration:
First-Line Maintenance Treatment of Advanced Ovarian Cancer:
• For patients weighing <77 kg (<170 lbs) or with a platelet count of <150,000/mcL, the recommended dosage is 200 mg (two 100-mg capsules) taken orally once daily.
• For patients weighing ≥77 kg (≥170 lbs) and who have a platelet count ≥150,000/mcL, the recommended dosage is 300 mg (three 100-mg capsules) taken orally once daily.
Maintenance Treatment of Recurrent Ovarian Cancer:
The recommended dosage of Ovaxa is 300 mg (three 100-mg capsules) taken orally once daily.
Treatment of Advanced Ovarian Cancer after 3 or more chemotherapies:
The recommended dosage of Ovaxa is 300 mg (three 100-mg capsules) taken orally once daily.

Contra-indications
None.

Warnings & precautions:
• Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): MDS/AML occurred in patients exposed to Niraparib and some cases were fatal. Monitor patients for hematological toxicity and discontinue if MDS/AML is confirmed.
• Bone Marrow Suppression: Test complete blood counts weekly for the first month, monthly for the next 11 months and periodically thereafter for clinically significant changes.
• Hypertension and Cardiovascular Effects: Monitor blood pressure and heart rate at least weekly for the first 2 months, then monthly for the first year and periodically thereafter during treatment with Niraparib. Manage with antihypertensive medications and adjustment of the dose of
Niraparib, if necessary.
• Posterior Reversible Encephalopathy Syndrome (PRES): PRES has occurred in patients treated with Niraparib. Discontinue Niraparib if PRES is confirmed.
• Embryo-Fetal Toxicity: Niraparib can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception.
• Allergic Reactions to FD&C Yellow No. 5 (Tartrazine): Contains FD&C Yellow No. 5 (tartrazine) as a color additive, which may caus allergic-type reactions (including bronchial asthma) in certain susceptible patients.

Adverse reactions:
Most common adverse reactions (incidence ≥10%) in patients who received Niraparib were nausea, thrombocytopenia, anemia, fatigue, constipation, musculoskeletal pain, abdominal pain, vomiting, neutropenia, decreased appetite, leukopenia, insomnia, headache, dyspnea, rash, diarrhea, hypertension, cough, dizziness, acute kidney injury, urinary tract infection, and hypomagnesemia.

Use in special populations:
Pregnancy: Based on its mechanism of action, Niraparib can cause fetal harm when administered to pregnant women. There are no data regarding the use of Niraparib in pregnant women to inform the drug-associated risk.
Lactation: No data are available regarding the presence of Niraparib or its metabolites in human milk or on its effects on the breastfed infant or milk production.
Females and Males of Reproductive Potential:
Females: Advise females of reproductive potential to use effective contraception during treatment with Niraparib and for at least for 6 months following the last dose.
Males: Niraparib may impair fertility in males of reproductive potential.
Pediatric use: Safety and effectiveness of Niraparib have not been established in pediatric patients.
Geriatric Use: No overall differences in safety and effectiveness of Niraparib were observed between these patients and younger patients but greater sensitivity of some older individuals.
Renal Impairment: No dose adjustment is necessary for patients with mild (CLcr:60 to 89 mL/min) to moderate (CLcr:30 to 59 mL/min) renal impairment.
Hepatic impairment: For patients with moderate hepatic impairment, reduce the starting dosage of niraparib to 200 mg once daily.Niraparib exposure increased in patients with moderate hepatic impairment. For patients with mild hepatic impairment no dose adjustment is needed. The recommended dose of Ovaxa has not been established for patients with severe hepatic impairment.

Overdose:
There is no specific treatment in the event of Niraparib overdose and symptoms of overdose are not established.

Drug interaction:
No clinical drug interaction studies have been performed with Niraparib.

Storage
Do not store above 25^{0}C. Protect from light. Keep out of the reach of children.

Packaging:
Paribac 100 Capsule: Each HDPE container of Paribac 100 contains 30 capsules, a silica gel desiccant and polyester coil with a child resistant closure.

Manufactured by:
ZISKA PHARMA **Ziska Pharmaceuticals Ltd.**
Kaliakoir, Gazipur, Bangladesh

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