Prescribing information- Northern Ireland

Zejula (niraparib) 100 mg film-coated tablets Prescribing Information

Please refer to the appropriate Summary of Product Characteristics (SmPC) before prescribing Zejula.

Presentation: Zejula is a grey, oval-shaped (12 mm x 8 mm) film-coated tablet debossed with "100" on one side and "Zejula" on the other side. Each tablet contains niraparib tosylate monohydrate equivalent to 100 mg niraparib and 34.7 mg of lactose monohydrate.

Indication: Monotherapy for the maintenance treatment of adult patients with advanced epithelial (FIGO Stages III and IV) high-grade ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy. Monotherapy for the maintenance treatment of adult patients with platinum sensitive relapsed high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy.

Dosage and administration: For first-line maintenance treatment, the recommended starting dose is 200mg (two 100-mg tablets) taken once daily. For patients who weigh ≥77kg and have baseline platelet count ≥150,000/µL the recommended starting dose is 300 mg (three 100-mg tablets) taken once daily. For recurrent maintenance treatment, the recommended starting dose is 300mg (three 100mg tablets) once daily. Astarting dose of 200mg (two 100-mg tablets) for patients weighing less than 58kg may be considered. No dose adjustment is necessary for elderly patients (≥65 years). Dose reductions may be implemented based on adverse reactions (refer to SmPC). For patients with moderate hepatic impairment the recommended starting dose is 200mg once daily. Use with caution in patients with severe renal (or end stage renal disease undergoing haemodialysis) and severe hepatic impairment. Severe hepatic impairment patients should be carefully monitored. Zejula is for oral use. It is advised to take Zejula tablets without food (at least 1 hour before or 2 hours after a meal) or with a light meal.

Contraindications: Hypersensitivity to the active substance or to any of the excipients and breast-feeding.

Warnings and precautions: Test complete blood counts weekly for the first month, followed by monthly monitoring for the next 10 months of treatment and periodically after this. If a patient develops severe persistent haematologic toxicity including pancytopenia that does not resolve within 28 days following interruption, Zejula should be discontinued. Due to the risk of thrombocytopenia, anticoagulants and medicinal products known to reduce the thrombocyte count should be used with caution. myelodysplastic syndrome/ acute myeloid leukemia (MDS/AML) have been observed in patients treated with Zejula (monotherapy or combination therapy) in clinical trials and postmarketing. In clinical studies, MDS/AML occurred in 1% patients treated with Zejula, with 41% of cases having a fatal outcome. The incidence being higher in patients with relapsed ovarian cancer who had received 2 or more lines of prior platinum chemotherapy and with gBRCAmut patients following 75 months of survival follow-up. For suspected MDS/ AML/ prolonged haematological toxicities, the patient should be referred to a haematologist for further evaluation. If MDS/AML is confirmed, Zejula treatment should be discontinued and the patient treated appropriately. Hypertension, including hypertensive crisis, has been reported with the use of Zejula. Pre-existing hypertension should be adequately controlled before starting Zejula treatment. Blood pressure should be monitored at least weekly for two months, then monthly afterwards for the first year and periodically thereafter during treatment with Zejula. Home blood pressure monitoring may be considered for appropriate patients with instruction to contact their health care provider in case of a rise in blood pressure. Zejula should be discontinued in case of hypertensive crisis or if medically significant hypertension cannot be adequately controlled with antihypertensive therapy. Hypertension should be medically managed with antihypertensive medicinal products as well as adjustment of the Zejula dose (refer to SmPC). There have been reports of Posterior Reversible Encephalopathy Syndrome (PRES) in patients receiving Zejula. PRES is a rare, reversible, neurological disorder which can present with rapidly evolving symptoms including seizures, headache, altered mental status, visual disturbance, or cortical blindness, with or without associated hypertension. A diagnosis of PRES requires confirmation by brain imaging, preferably magnetic resonance imaging (MRI). In case of PRES, it is recommended to discontinue Zejula and to treat specific symptoms including hypertension. The safety of reinitiating Zejula therapy in patients previously experiencing PRES is not known. Patients with galactose intolerance, total lactase deficiency or glucose- galactose malabsorption should not take this medicine. Paediatric safety and efficacy (below 18 years of age) has not yet been established.

Interactions: Take niraparib with caution when using in combination with vaccines, immunosuppressant agents or with other cytotoxic medicinal products.

Caution is recommended when niraparib is combined with active substances, the metabolism of which is CYP3A4 dependent and, notably, those having a narrow therapeutic range (e.g. ciclosporin, tacrolimus, alfentanil, ergotamine, pimozide, quetiapine and halofantrine). Caution is recommended when niraparib is combined with active substances, the metabolism of which is CYP1A2-dependent and, notably, those having a narrow therapeutic range (e.g. clozapine, theophylline and ropinirole). In vitro, niraparib inhibits P-gp and BCRP. Caution is therefore recommended when niraparib is combined with substrates of BCRP (e.g. irinotecan, rosuvastatin, simvastatin, atorvastatin and methotrexate). Niraparib is an inhibitor of MATE1 and -2. Increased plasma concentrations of co-administered medicinal products that are substrates of these transporters (e.g. metformin) cannot be excluded.

Fertility, pregnancy and lactation: *Fertility*: No clinical data on fertility. *Pregnancy*: Do not use during pregnancy or in women of childbearing potential not willing to use highly effective contraception during therapy and for 6 months after receiving the last dose of Zejula. A pregnancy test should be performed on all women of childbearing potential prior to treatment. Lactation: contraindicated during administration of Zejula and for 1 month after receiving the last dose.

Effects on ability to drive and use machines: Zejula has moderate influence on the ability to drive and use machines. Advise patients that Zejula may cause asthenia, fatigue, dizziness or difficulties concentrating. Patients who experience these symptoms should observe caution when driving or using machines.

Undesirable effects: The most common serious adverse reactions were thrombocytopenia and anaemia. All CTCAE (Common Terminology Criteria for Adverse Events) grade adverse reactions: Very common (≥1/10): urinary tract infection, thrombocytopenia, anaemia, neutropenia, leukopenia, decreased appetite, insomnia, headache, dizziness, palpitations, hypertension, dyspnoea, cough, nasopharyngitis, nausea, constipation, vomiting, abdominal pain, diarrhoea, dyspepsia, back pain, arthralgia, fatigue, asthenia. Common (≥1/100 to <1/10): myelodysplastic syndrome/ acute myeloid leukaemia, bronchitis, conjunctivitis, dysgeusia, hypersensitivity (includes hypersensitivity, drug hypersensitivity, anaphylactoid reaction, drug eruption, angioedema, and urticaria), hypokalemia, anxiety, depression, cognitive impairment (includes memory and concentration impairment), tachycardia, epistaxis, dry mouth, abdominal distension, mucosal inflammation, stomatitis, photosensitivity, rash, myalgia, peripheral oedema,increase in gamma-glutamyl transferase, increase in AST, increase in blood creatine, increase in ALT, increase in blood alkaline phosphatase and decrease in weight. Uncommon (CTCAE Grade 3-4 ≥1/1000 to <1/100) : Urinary tract infections, bronchitis, pancytopenia, febrile neutopenia, hypersensitivity, decreased appetite, insominia, anxiety, depression, confusional state, headache, dyspnoea, epistaxis, pneumonitis, diarrhoea, constipation, mucosal inflammation, stomatitis, dry mouth, photosensitivity, rash, back pain, arthralgia, myalgia, AST increase, blood alkaline phosphatase increase.. Rare (≥1/10,000 to <1/1,000): Posterior Reversible Encephalopathy Syndrome (PRES), Hypertensive crisis. Refer to the SmPC for a full list of adverse events.

Overdose: Refer to SmPC. **Legal Category:** POM.

Pack size: 56 film-coated tablets £4,500.

MA Number: EU/1/17/1235/004, EU/1/17/1235/006

MA Holder: GlaxoSmithKline (Ireland) Limited. 12 Riverwalk, *Citywest Business Campus, Dublin 24, Ireland. Full SmPC available from GSK Limited or from www.medicines.org.uk.*

Date of preparation: November 2023

PI Job Bag Number: PI-12420

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to GSK Limited on (0) 800 221 441 or UKSafety@gsk.com