Prescribing information

Zejula (niraparib) 100 mg hard capsules Prescribing Information

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

Presentation: Zejula is a hard capsule consisting of a white body with "100 mg" printed in black ink and purple cap with "Niraparib" printed in white ink. Each capsule contains niraparib tosylate monohydrate equivalent to 100 mg niraparib, 254.5 mg of lactose monohydrate and 0.0172 mg tartrazine (E102).

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 capsules) taken once daily. Patients who weigh ≥77kg and have baseline platelet count ≥150,000/µL the recommended starting dose is 300 mg (three 100-mg capsules) taken once daily. For recurrent maintenance treatment the recommended starting dose is 300mg (three 100mg capsules) once daily. A starting dose of 200mg (two 100-mg capsules) for patients weighing less than 58kg may be considered. Dose reductions may be implemented based on adverse reactions (refer to SmPC).. No dose reductions in elderly. Use with caution in patients with severe renal and hepatic impairment. For oral use, the capsules should be swallowed whole with water and should not be chewed or crushed. Zejula can be taken without regard to meals.

Contraindications: Hypersensitivity to niraparib 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 28days 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. If MDS and/or AML are confirmed while being prescribed 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, monitored 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 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. 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, the Lapp lactase deficiency or glucose galactose malabsorption should not take this medicine. Tartrazine may cause allergic reactions. Paediatric safety and efficacy has not yet been established.

Interactions: Take niraparib with caution when using in combination with vaccines, immunosuppressant agents or with other cytotoxic medicinal products. 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, respectively. 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, respectively. Increased plasma concentrations of co-administered medicinal products (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 reliable contraception during therapy and for 1 month after receiving the last dose of Zejula. *Lactation*: Not recommended.

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 and dizziness.

Undesirable effects: The most common serious adverse reactions were thrombocytopenia and anaemia. 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): bronchitis, conjunctivitis, dysgeusia hypersensitivity (includes hypersensitivity, drug hypersensitivity, anaphylactoid reaction, drug eruption, angioedema, and urticaria), hypokalemia, anxiety, depression, tachycardia, epistaxis, dry mouth, abdominal distension, mucosal inflammation(including mucositis), stomatitis, photosensitivity, rash, myalgia, oedema peripheral. Uncommon(≥1/1000 to <1/100): urinary tract infections, bronchitis, febrile neutropenia, pancytopenia, hypersensitivity, decreased appetite, insomnia, anxiety, depression, confusional state, headache, dyspnoea, epistaxis, pneumonitis, diarrhoea, constipation, mucosal inflammation stomatitis, dry mouth, photosensitivity, rash, back pain, arthralgia, myalgia. 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: 84 x 1 £6,750 and 56 x 1 £4,500 hard capsules.

MA Number: EU/1/17/1235/001, EU/1/17/1235/002

MA Holder: GlaxoSmithKline (Ireland) Limited. 2 Riverwalk, *Citywest Business Campus, Dublin 24, Ireland. Full SmPC available from GSK Limited or from www.medicines.org.uk.*

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Adverse events should be reported.
Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to GSK Limited on +44 (0) 800 221 441

Once-daily oral Zejula® niraparib capsules 100 mg