Olumiant® ▼(baricitinib) PRESCRIBING INFORMATION

Presentation Olumiant 2 mg film-coated tablet contains 2 mg of baricitinib. Olumiant 2 mg tablet is a light pink, 9.0 x 7.5 mm oblong tablets, debossed with "Lilly" on one side and "2" on the other. Olumiant 4 mg film-coated tablet contains 4 mg of baricitinib. Olumiant 4 mg tablet is a medium pink, 8.5 mm round tablets, debossed with "Lilly" on one side and "4" on the other. **Uses** Olumiant is indicated for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drugs. Olumiant may be used as monotherapy or in combination with methotrexate. **Dosage and Administration** Treatment should be initiated by physicians experienced in the diagnosis and treatment of rheumatoid arthritis. Posology The recommended dose of Olumiant is 4 mg once daily. A dose of 2 mg once daily is appropriate for patients such as those aged ≥ 75 years and may be appropriate for patients with a history of chronic or recurrent infections. A dose of 2 mg once daily may also be considered for patients who have achieved sustained control of disease activity with 4 mg once daily and are eligible for dose tapering. Treatment should not be initiated in patients with an absolute lymphocyte count (ALC) less than 0.5 x 10^9 cells/L, an absolute neutrophil count (ANC) less than 1 x 10^9 cells/L, or who have a haemoglobin value less than 8 g/dL. Treatment may be initiated once values have improved above these limits. *Renal impairment:* The recommended dose is 2 mg once daily in patients with creatinine clearance between 30 and 60 mL/min. Olumiant is not recommended for use in patients with creatinine clearance < 30 mL/min (see the SmPC for full information). *Hepatic impairment:* No dose adjustment is required in patients with mild or moderate hepatic impairment. Olumiant is not recommended for use in patients with severe hepatic impairment (see the SmPC for full information). *Co-administration with OAT3 inhibitors:* The recommended dose is 2 mg once daily in patients taking Organic Anion Transporter 3 (OAT3) inhibitors with a strong inhibition potential, such as probenecid (see the SmPC for full information). No clinical pharmacology study has been conducted with OAT3 inhibitors with less inhibition potential. The prodrug leflunomide rapidly converts to teriflunomide which is a weak OAT3 inhibitor and therefore may lead to an increase in baricitinib exposure. Since dedicated interaction studies have not been conducted, caution should be used when leflunomide or teriflunomide are given concomitantly with baricitinib (see the SmPC for full information on Interaction with other medicinal products and other forms of interaction). *Elderly:* Clinical experience in patients ≥ 75 years is very limited and in these patients a starting dose of 2 mg is appropriate. *Paediatric population:* The safety and efficacy of Olumiant in children and adolescents aged 0 to 18 years have not yet been established. No data are available. Method of administration Oral use: Olumiant is to be taken once daily with or without food and may be taken at any time of the day. **Contra-indications** Hypersensitivity to the active substance or to any of the excipients listed in the SmPC. Pregnancy: Women of childbearing potential have to use effective contraception during and for at least 1 week after treatment. If a patient becomes pregnant while taking Olumiant the parents should be informed of the potential risk to the foetus. **Warnings and Special Precautions** Infections: Baricitinib is associated with an increased rate of infections such as upper respiratory tract infections compared to placebo (see the SmPC for full information). In treatment naïve patients, combination with methotrexate resulted in increased frequency of infections compared to baricitinib monotherapy. The risks and benefits of treatment with Olumiant should be carefully considered prior to initiating therapy in patients with active, chronic or recurrent infections (see the SmPC for full information). If an infection develops, the patient should be monitored carefully and Olumiant therapy should be temporarily interrupted if the patient is not responding to standard therapy. Olumiant treatment should not be resumed until the infection resolves. *Tuberculosis:* Patients should be screened for tuberculosis (TB) before starting Olumiant therapy. Olumiant should not be given to patients with active TB. Anti-TB therapy should be considered prior to initiation of Olumiant in patients with previously untreated latent TB. Haematological abnormalities: Absolute Neutrophil Count (ANC) < 1 x 10^9 cells/L, Absolute Lymphocyte Count (ALC) < 0.5 x 10^9 cells/L and haemoglobin < 8 g/ dL were reported in less than 1 % of patients in clinical trials. Treatment should not be initiated, or should be temporarily interrupted, in patients with an ANC < 1 x 10^9 cells/L, ALC < 0.5 x 10^9 cells/L or haemoglobin < 8 g/dL observed during routine patient management (see section 4.2 of the SmPC for further information). The risk of lymphocytosis is increased in elderly patients with rheumatoid arthritis. Rare cases of lymphoproliferative disorders have been reported. Viral reactivation: Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster, herpes simplex), were reported in clinical studies (see the SmPC for full information). Herpes zoster was reported more commonly in patients ≥ 65 years of age who had previously been treated with both biologic and conventional DMARDs. If a patient develops herpes zoster, Olumiant treatment should be temporarily interrupted until the episode resolves. Vaccination: Use with live, attenuated vaccines during, or immediately prior to, Olumiant therapy is not recommended. Prior to initiating Olumiant, it is recommended that all patients be brought up to date with all immunisations in agreement with current immunisation guidelines. Lipids: Dose dependent increases in blood lipid parameters were reported in patients treated with baricitinib compared to placebo (see the SmPC for full information). Elevations in LDL cholesterol decreased to pre-treatment levels in response to statin therapy. Lipid parameters should be assessed approximately 12 weeks following initiation of Olumiant therapy and thereafter patients should be managed according to international clinical guidelines for hyperlipidaemia. The effect of these lipid parameter elevations on cardiovascular morbidity and mortality has not been determined. Hepatic transaminase elevations: Increases in alanine transaminase (ALT) and aspartate transaminase (AST) to ≥ 5 and ≥ 10 x upper limit of normal (ULN) were reported in less than 1 % of patients in clinical trials. In treatment-naïve patients, combination with methotrexate resulted in increased frequency of hepatic transaminase elevations compared with baricitinib monotherapy (see the SmPC for full information). If increases in ALT or AST are observed during routine patient management and drug-induced liver injury is suspected, Olumiant should be temporarily interrupted until this diagnosis is excluded. Malignancy: The risk of malignancies including lymphoma is increased in patients with rheumatoid arthritis. Immunomodulatory medicinal products may increase the risk of malignancies including lymphoma. The clinical data are insufficient to assess the potential incidence of malignancies following exposure to baricitinib. Venous Thromboembolism: Events of deep venous thrombosis (DVT) and pulmonary embolism (PE) have been reported in patients receiving baricitinib. Olumiant should be used with caution in patients with risk factors for DVT/PE, such as older age, obesity, a medical history of DVT/PE, or patients undergoing surgery and immobilisation. If clinical features of DVT/PE occur, Olumiant treatment should be temporarily interrupted and patients should be evaluated promptly, followed by appropriate treatment. Laboratory monitoring: Please refer to the SmPC for laboratory measures and monitoring guidance. Immunosuppressive medicinal products: Combination with biologic DMARDs or other Janus kinase (JAK) inhibitors is not recommended, as a risk of additive immunosuppression cannot be excluded. Data concerning use of baricitinib with potent immunosuppressive medicinal products (e.g., azathioprine, tacrolimus, ciclosporin) are limited and caution should be exercised when using such combinations (see the SmPC for full information). **Interactions** See the SmPC for full information on interaction with immunosuppressive medicinal products, potential for other medicinal products to affect the pharmacokinetics of baricitinib, and potential for baricitinib to affect the pharmacokinetics of other medicinal products. **Fertility, Pregnancy, and Lactation** *Pregnancy:* There are no adequate data from the use of baricitinib in pregnant women. Studies in animals have shown reproductive toxicity (see the SmPC for full information). Baricitinib was teratogenic in rats and rabbits Olumiant is contraindicated during pregnancy. *Breast-feeding:* It is unknown whether baricitinib/metabolites are excreted in human milk. Available pharmacodynamic/toxicological data in animals have shown excretion of baricitinib in milk. A decision must be made whether to discontinue breast-feeding or to discontinue Olumiant therapy. *Fertility:* The effect of baricitinib on human fertility has not been evaluated. Studies in animals suggest that treatment with baricitinib has the potential to decrease female fertility while on treatment, but there was no effect on male spermatogenesis. **Effects on ability to drive and use machines** Olumiant has no or negligible influence on the ability to drive and use machines. **Undesirable Effects** *Summary of the safety profile:* The most commonly reported adverse drug reactions occurring in ≥ 2 % of patients treated with Olumiant monotherapy or in combination with conventional synthetic DMARDs were increased LDL cholesterol (33.6 %), upper respiratory tract infections (14.7 %) and nausea (2.8 %). Infections reported with Olumiant treatment included Herpes zoster. *Very common (≥ 1/10):* Upper respiratory tract infection, Hypercholesterolaemia, *Common (≥ 1/100 to < 1/10):* Herpes zoster, Herpes simplex, Gastroenteritis, Urinary tract infections, Pneumonia, Thrombocytosis > 600 x 10^9 cells/L, Nausea, ALT increased ≥ 3 x ULN *Uncommon (≥ 1/1,000 to < 1/100):* Neutropaenia < 1 x 10^9 cells/L, Hypertriglyceridaemia, AST increased ≥ 3 x ULN, Creatine phosphokinase increased > 5 x ULN. *For full details of these and other side-effects, please see the Summary of Product Characteristics, which is available at* ***United Kingdom****: http://www.medicines.org.uk/emc/, or* ***Ireland****: http://www.medicines.ie/.* **Legal Category** POM **Marketing Authorisation Numbers and Holder** EU/1/16/1170/002, EU/1/16/1170/010, EU/1/16/1170/014, Eli Lilly Nederland B.V., Papendorpseweg 83, 3528 BJ Utrecht, The Netherlands. **Cost (UK only)** £805.56 per pack of 28 x 2 mg film-coated tablets, £805.56 per pack of 28 x 4 mg film-coated tablets, £2,416.68 per pack of 84 x 4 mg film-coated tablets. *An Irish price is available on request; please see section below for contact information.* **Date of Preparation or Last Review:** September 2018 **Further information is available from** Eli Lilly and Company Limited, Lilly House, Priestley Road, Basingstoke, Hampshire, RG24 9NL. Telephone: **UK:** + 44-(0) 1256 315000, **Ireland:** + 353-(0) 1 661 4377, E-mail: ukmedinfo@lilly.com, Website: www.lilly.co.uk; www.lilly.ie.

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Adverse events and product complaints should also be reported to Lilly: please call **Lilly UK** on **01256 315 000**, or **Lilly Ireland** on **01 664 0446**.