Prescribing Information

(Please refer to the SmPC before prescribing Kisqali)

Kisqali® ▼ (ribociclib succinate)

Presentation: Film-coated tablet containing ribociclib succinate, equivalent to 200 mg ribociclib. **Indication:** Kisqali is indicated for the treatment of women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant as initial endocrine-based therapy, or in women who have received prior endocrine therapy. In pre- or perimenopausal women, the endocrine therapy should be combined with a luteinising hormone-releasing hormone (LHRH) agonist. **Dosage:** The recommended dose is 600 mg once daily; taken orally with or without food at the same time every day for 21 days, followed by 7 days off treatment, resulting in a complete cycle of 28 days. The treatment should be continued as long as the patient is deriving clinical benefit from therapy or until unacceptable toxicity occurs. Kisqali should be used together with 2.5 mg letrozole or another aromatase inhibitor (AI) or with 500 mg fulvestrant. The AI should be taken orally once daily continuously throughout the 28-day cycle. When Kisqali is used in combination with fulvestrant, fulvestrant is administered intramuscularly on days 1, 15 and 29, and once monthly thereafter.. If the patient vomits after taking the dose or misses a dose, an additional dose should not be taken. The next prescribing dose should be taken at the usual time. **Dose Modification:** Management of severe or intolerable adverse events (AEs) may require temporary dose interruption, reduction or discontinuation of Kisqali (See Special Warnings & Precautions). Dose reduction should be achieved by decrements of 200 mg daily. If further dose reduction below 200 mg/day is required, the treatment should be permanently discontinued. *Complete blood counts (CBC)* should be performed before and after initiating Kisqali treatment. CBC should be monitored every 2 weeks for the first 2 cycles, at the beginning of each of the subsequent 4 cycles, then as clinically indicated. For neutropenia, no dose modifications required for grade 1 or 2. For grade 3, interrupt the dose until recovery to grade ≤2, then resume at same dose level. If toxicity recurs at grade 3, interrupt the dose until recovery, then resume Kisqali and reduce by 1 dose level. For grade 3 febrile neutropenia interrupt the dose until recovery to grade ≤2, resume Kisqali and reduce by 1 dose level. For grade 4 interrupt the dose until recovery to grade ≤2, resume Kisqali and reduce by 1 dose level. *Liver function tests (LFTs)* should be performed before and after initiating Kisqali treatment. LFTs should be performed every 2 weeks for the first 2 cycles, at the beginning of each of the subsequent 4 cycles, then as clinically indicated. If grade ≥2 abnormalities are noted, more frequent monitoring is recommended. No dose adjustment is required for grade 1. For grade 2: if baseline at grade <2, interrupt until recovery to ≤ baseline grade, then resume Kisqali at same dose, and if grade 2 recurs, resume Kisqali at next lower dose level; if baseline = grade 2, no dose interruption. For grade 3: interrupt Kisqali until recovery to ≤ baseline grade then resume at next lower dose level. If grade 3 recurs, discontinue Kisqali. For grade 4: discontinue Kisqali. If patients develop ALT and/or AST >3xULN along with total bilirubin >2xULN irrespective of baseline grade, discontinue Kisqali. ECG should be assessed before and after initiating treatment with Kisqali. ECG should be repeated at approximately day 14 of the first cycle and at the beginning of the second cycle, then as clinically indicated. In case of QTcF prolongation during treatment, more frequent ECG monitoring is recommended. ECGs with QTcF >480 msec the dose should be interrupted. If the QTcF resolves to <481 msec, resume the treatment at next lower dose level and if QTcF >481 msec recurs, interrupt the dose until QTcF resolves to <481 and then resume Kisqali at the next lower dose level. If QTcF >500 msec, interrupt Kisqali until QTcF <481 msec then resume Kisqali at next lower dose level. If QTcF >500 msec or >60 msec change from baseline occurs in combination with torsade de pointes or polymorphic ventricular tachycardia or signs/symptoms of serious arrhythmia, permanently discontinue Kisqali. Interstitial lung disease(ILD)/pneumonitis, Grade 1: no dose adjustment is required. Grade 2: Dose interruption until recovery to grade ≤1, then resume Kisqali at the next lower dose level. Grade 3 or 4: discontinue Kisqali. For other toxicities no dose adjustment required for grade 1 or 2, initiate appropriate medical therapy and monitor as clinically indicated. For grade 3, interrupt until recovery to grade ≤1, then resume Kisqali at the same dose. If grade 3 recurs, resume Kisqali at the next lower dose level. For grade 4, discontinue Kisqali. Toxic epidermal necrolysis (TEN) has been reported with Kisqali treatment. If signs and symptoms suggestive of severe cutaneous reactions (e.g. progressive widespread skin rash often with blisters or mucosal lesions) appear, Kisqali should be discontinued immediately. Concomitant use of strong CYP3A4 inhibitors should be avoided and an alternative concomitant medicinal product with less potential to inhibit CYP3A4 inhibition should be considered. If patients must be given a strong CYP3A4 inhibitor concomitantly with ribociclib, the Kisqali dose should be reduced to 400 mg once daily. A starting dose of 400 mg is recommended in patients with severe renal impairment. **Contraindications:** Hypersensitivity to the active substance or to peanut, soya or any other listed excipients. **Special Warnings and Precautions:** Kisqali is not recommended to be used in combination with tamoxifen. *Critical Visceral Disease* The efficacy and safety of ribociclib have not been studied in patients with critical visceral disease. *Neutropenia* Based on the severity of the neutropenia, Kisqali treatment may have to be interrupted, reduced or discontinued.*QT Interval prolongation* Treatment with Kisqali should be initiated only in patients with QTcF values less than 450 msec. Appropriate monitoring of serum electrolytes (including potassium, calcium, phosphorus and magnesium) should be performed before initiating treatment, at the beginning of the first 6 cycles and then as clinically indicated. Any abnormality should be corrected before initiating treatment with Kisqali and during treatment with Kisqali. The use of Kisqali with medicinal products known to prolong QTc interval and/or strong CYP3A4 inhibitors should be avoided as this may lead to clinically meaningful prolongation of the QTcF interval. Kisqali should be avoided in patients with long QT syndrome, significant cardiac disease and electrolyte abnormalities, Hepatobiliary toxicity, CYP3A4 substrates, soya lecithin: see above. Women of childbearing potential should be advised to use an effective method of contraception while taking Kisqali and for at least 21 days after the last dose. *ILD/pneumonitis:* ILD/Pneumonitis has been reported with CDK4/6 inhibitors including Kisqali. Based on the severity of the ILD/Pneumonitis, which may be fatal, Kisqali may require dose interruption, reduction or discontinuation. Patients should be monitored for pulmonary symptoms indicative of ILD/Pneumonitis which may include hypoxia, cough and dyspnoea where dose modifications should be managed. Kisqali is not recommended during pregnancy and in women of childbearing potential not using contraception. Patients receiving Kisqali should not breast-feed for at least 21 days after the last dose. Kisqali may have a minor influence on the ability to drive and use machinery; patients should be cautious in case they experience fatigue, dizziness or vertigo. **Adverse Events:** *Very common*: Infections, abdominal pain, dyspepsia, abnormal liver function tests (ALT, AST & blood bilirubin increased), alopecia, anaemia, lymphopenia, asthenia, back pain, constipation, decreased appetite, diarrhoea, dyspnoea, cough, fatigue, headache, dizziness, leukopenia, nausea, neutropenia, peripheral oedema, pruritus, pyrexia, rash, stomatitis and vomiting. *Common*: Dry eye, dysgeusia, electrocardiogram QT prolonged, erythema, dry skin, vitiligo, dry mouth, oropharyngeal pain, febrile neutropenia, hepatotoxicity, hepatic failure, autoimmune hepatitis (single case), hypocalcaemia, hypokalaemia, hypophosphataemia, vertigo, lacrimation increased, blood increased creatinine, syncope and thrombocytopenia. *Not known*: Toxic epidermal necrolysis (TEN). **Interactions:** Ribociclib is primarily metabolised by CYP3A4. Medicinal products that can influence CYP3A4 enzyme activity may alter the pharmacokinetics of ribociclib. Ribociclib is a moderate to strong CYP3A4 inhibitor and may interact with medicinal substrates that are metabolised via CYP3A4, which can lead to increased serum concentrations of the concomitantly used medicinal product. Co-administration of Kisqali with medicinal products with a known potential to prolong the QT interval such as anti-arrhythmic medicinal products and other medicinal products that are known to prolong the QT interval should be avoided. Drug-drug interaction studies between ribociclib and oral contraceptives have not been conducted. Please refer to the SmPC for other possible interactions.**Basic NHS Cost:** 21 tablets = £983.33, 42 tablets = £1,966.67, 63 tablets = £2,950.00. **MA Number:** EU/1/17/1221/001-012 **Legal category:** POM. **Further information is available from** Novartis Pharmaceuticals UK Ltd,2nd Floor, The WestWorks Building, White City Place, 195 Wood Lane, London, W12 7FQ, UK. Tel: 01276 692255.

KIS20-C027 Date of preparation: July 2020

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.UK/yellowcard.

Adverse events should also be reported to Novartis via uk.patientsafety@novartis.com or online through the patient safety information (PSI) tool at https://psi.novartis.com.

If you have a question about the product, please contact Medical Information on 01276 698370 or by email at medinfo.uk@novartis.com.