Great Britain Prescribing Information

KISQALI® (ribociclib succinate)

Important note: Before prescribing, consult Summary of Product Characteristics (SmPC).

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 and administration:** 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. The tablets should be swallowed whole and should not be chewed, crushed or split prior to swallowing. **Dose Modification:** Management of severe or intolerable adverse reactions (ARs) may require temporary dose interruption, reduction or discontinuation of Kisqali (See 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 to grade ≤2, 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 >3x upper limit of normal (ULN) 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 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 msec 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, initiate appropriate medical therapy and monitor as clinically indicated. 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. 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. In patients who have had their dose reduced to 200 mg ribociclib daily and in whom initiation of co-administration of a strong CYP3A4 inhibitor cannot be avoided, Kisqali treatment should be interrupted. These recommended dose adjustments for Kisqali use with strong CYP3A4 inhibitors may not be optimal in all patients, for further information please refer to the SmPC. A starting dose of 200 mg is recommended in patients with severe renal impairment. Patients with moderate (Child Pugh class B) and severe hepatic impairment (Child Pugh class C) can have increased (less than 2 fold) exposure to ribociclib and the starting dose of 400 mg Kisqali once daily is recommended. **Contraindications:** Hypersensitivity to the active substance or to peanut, soya or any other listed excipients. **Warnings/ 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. *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. 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, uncontrolled or significant cardiac disease and electrolyte abnormalities. *Blood creatinine increase*: Kisqali may cause blood creatinine increase as an inhibitor of the renal transporters organic cation transporter 2 (OCT2) and multidrug and toxin extrusion protein 1 (MATE1), which are involved in the active secretion of creatinine from the proximal tubules. In case of blood creatinine increase while on treatment, it is recommended that further assessment of the renal function be performed to exclude renal impairment. *Renal impairment:* The recommended starting dose of 200 mg for patients with severe renal impairment is estimated to result in approximately 45% lower exposure compared with the standard starting dose in patients with normal renal function. The efficacy at this starting dose has not been studied. Caution should be used in patients with severe renal impairment with close monitoring for signs of toxicity. *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:* Interstitial lung disease (ILD)/Pneumonitis has been reported with Kisqali. Patients should be monitored for pulmonary symptoms indicative of ILD/pneumonitis which may include hypoxia, cough and dyspnoea and dose modifications should be managed. Based on the severity of the ILD/Pneumonitis, which may be fatal, Kisqali may require dose interruption, reduction or discontinuation. *Hepatobiliary toxicity*: Liver function tests should be performed before initiating treatment with Kisqali. After initiating treatment, liver function should be monitored as advised in the SmPC. Based on the severity of the transaminase elevations, treatment with Kisqali may have to be interrupted, reduced or discontinued as advised in the SmPC. Recommendations for patients who have elevated AST/ALT grade ≥ 3 at baseline have not been established. CYP3A4 substrates: Caution is recommended in case of concomitant use with sensitive CYP3A4 substrates with a narrow therapeutic index and the SmPC of the other product should be consulted for the recommendations regarding co-administration with CYP3A4 inhibitors. *CYP3A4 substrates*: see Interactions. *Soya lecithin*: see Contraindications. **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. **Fertility, pregnancy and lactation**: 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. There are no clinical data available regarding effects of ribociclib on fertility. Based on animal studies, ribociclib may impair fertility in males of reproductive potential. **Other:** 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. **Undesirable effects:** *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, interstitial lung disease (ILD)/pneumonitis. *Rare:* Erythema multiforme. *Not known*: Toxic epidermal necrolysis (TEN). **Basic NHS Cost:** 21 tablets = £983.33, 42 tablets = £1,966.67, 63 tablets = £2,950.00. **MA Number:** PLGB 00101/1100 **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.

Date of preparation: October 2024
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Adverse Event reporting:

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 online through the pharmacovigilance intake (PVI) tool at www.novartis.com/report or alternatively email medinfo.uk@novartis.com or call 01276 698370

Northern Ireland Prescribing Information

KISQALI® (ribociclib succinate)

Important note: Before prescribing, consult Summary of Product Characteristics (SmPC).

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 and administration:** 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. The tablets should be swallowed whole and should not be chewed, crushed or split prior to swallowing. **Dose Modification:** Management of severe or intolerable adverse reactions (ARs) may require temporary dose interruption, reduction or discontinuation of Kisqali (See 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 to grade ≤2, 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. For hepatobiliary toxicity, 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 >3x upper limit of normal (ULN) 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 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 msec 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, initiate appropriate medical therapy and monitor as clinically indicated. 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. 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. In patients who have had their dose reduced to 200 mg ribociclib daily and in whom initiation of co- administration of a strong CYP3A4 inhibitor cannot be avoided, Kisqali treatment should be interrupted. These recommended dose adjustments for Kisqali use with strong CYP3A4 inhibitors may not be optimal in all patients, for further information please refer to the SmPC.A starting dose of 200 mg is recommended in patients with severe renal impairment. Patients with moderate (Child Pugh class B) and severe hepatic impairment (Child Pugh class C) can have increased (less than 2 fold) exposure to ribociclib and the starting dose of 400 mg Kisqali once daily is recommended. **Contraindications:** Hypersensitivity to the active substance or to peanut, soya or any other listed excipients.

Warnings/ 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. *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. *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, uncontrolled or significant cardiac disease and electrolyte abnormalities. *Blood creatinine increase*: Kisqali may cause blood creatinine increase as an inhibitor of the renal transporters organic cation transporter 2 (OCT2) and multidrug and toxin extrusion protein 1 (MATE1), which are involved in the active secretion of creatinine from the proximal tubules. In case of blood creatinine increase while on treatment, it is recommended that further assessment of the renal function be performed to exclude renal impairment. *Renal impairment:* The recommended starting dose of 200 mg for patients with severe renal impairment is estimated to result in approximately 45% lower exposure compared with the standard starting dose in patients with normal renal function. The efficacy at this starting dose has not been studied. Caution should be used in patients with severe renal impairment with close monitoring for signs of toxicity. *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:* Interstitial lung disease (ILD)/Pneumonitis has been reported with Kisqali. Patients should be monitored for pulmonary symptoms indicative of ILD/ pneumonitis which may include hypoxia, cough and dyspnoea and dose modifications should be managed. Based on the severity of the ILD/Pneumonitis, which may be fatal, Kisqali may require dose interruption, reduction or discontinuation. *Hepatobiliary toxicity*: Liver function tests should be performed before initiating treatment with Kisqali. After initiating treatment, liver function should be monitored as advised in the SmPC. Based on the severity of the transaminase elevations, treatment with Kisqali may have to be interrupted, reduced or discontinued as advised in the SmPC. Recommendations for patients who have elevated AST/ALT grade ≤ 3 at baseline have not been established.*CYP3A4 substrates*: Caution is recommended in case of concomitant use with sensitive CYP3A4 substrates with a narrow therapeutic index and the SmPC of the other product should be consulted for the recommendations regarding co-administration with CYP3A4 inhibitors. See Interactions. *Soya lecithin*: see Contraindications. **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 which can lead to increased serum concentrations of the concomitantly used medicinal product. Caution is recommended in case of concomitant use with sensitive CYP3A4 substrates with a narrow therapeutic index and the SmPC of the other product should be consulted for the recommendations regarding co-administration with CYP3A4 inhibitors. 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. **Fertility, pregnancy and lactation:** 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. There are no clinical data available regarding effects of ribociclib on fertility. Based on animal studies, ribociclib may impair fertility in males of reproductive potential.

Other: 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. **Undesirable effects:** *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, Interstitial lung disease (ILD)/ pneumonitis. *Rare*: Erythema multiforme. *Not known*: Toxic epidermal necrolysis (TEN). **Basic NHS Cost**: 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.
Date of preparation: September 2024 **MLR ID**: FA-11268668

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