NOVARTIS

Kisqali - ebc safety - HCP

Prescribing information

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KISQALI® (ribociclib) safety profile in early breast cancer (eBC)

Indications:[1]

- KISQALI in combination with an aromatase inhibitor (AI), is indicated for the adjuvant treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence (see section 5.1 of the SmPC for eligibility criteria)

- In pre- or perimenopausal women, or in men, the AI should be combined with a luteinising hormone-releasing hormone (LHRH) agonist

Please refer to the Summary of Product Characteristics (SmPC) for the full safety profile and guidance regarding managing adverse events (AEs).

For information on dosing and dose modifications, please click here.

KISQALI 400 mg has a generally manageable and well characterised safety profile[1-4]

NATALEE study design: (N=5101) international, randomised, open-label, Phase III trial in patients with HR+/HER2– eBC. Premenopausal and postmenopausal women, and men, were randomised to receive either KISQALI 400 mg/day plus NSAI or NSAI alone. The primary endpoint was invasive disease-free survival as per Standardised Definitions for Efficacy Endpoints (STEEP) criteria version 1.0, assessed by the investigator.[3]

- NATALEE safety analysis

- Adverse reactions in the SmPC

- Contraindications/Precautions

In an exploratory analysis at 4 years, KISQALI 400 mg had a generally manageable and well characterised safety profile with no new safety signals identified after extended follow-up[1,2]

NATALEE AEs at 4 years (exploratory analysis)[2]

	KISQALI + NSAI (n=2526)		NSAI (n=2441)	
AEIS, %	**Any grade**	**Grade ≥3**	**Any grade**	**Grade ≥3**
Neutropenia*	62.8	44.4	4.5	0.9
Febrile neutropenia	0.3	0.3	0.0	0.0

Liver-related AEs[†]	26.7	8.6	11.4	1.7
QT interval prolongation[‡]	5.4	1.0	1.6	0.7
ECG QT prolonged	4.4	0.2	0.8	<0.1
Interstitial lung disease (ILD)/pneumonitis[§]	1.6	0.0	0.9	0.1
Other clinically relevant AEs, %				
Arthralgia	38.8	1.0	44.4	1.3
Nausea	23.5	0.2	7.9	<0.1
Headache	22.9	0.4	17.2	0.2
Fatigue	22.8	0.8	13.5	0.2
Diarrhoea	14.6	0.6	5.5	0.1
Venous thromboembolism[¶]	1.1	0.6	0.5	0.3

Adapted from Fasching PA, et al. 2024.[2]

Dose adjustments and discontinuations at 3 years[3]

	KISQALI + NSAI (n=2525)	NSAI (n=2442)
KISQALI discontinuation due to AEs	**19.5%**	**N/A**
NSAI discontinuation due to AEs	**5.1%**	**4.4%**
Dose reduction of KISQALI due to AEs	**22.8%**	**N/A**
Most frequent any-grade AE leading to discontinuation	**9.9% Liver-related**[‖] **1.5% Arthralgia**	**0.1% Liver-related 2.0% Arthralgia**

Adapted from Hortobagyi GN, et al. 2025.[3]

In the KISQALI + NSAI arm, rates of discontinuation due to AEs were consistent and remained stable at 4 years (20.0%), with a <1.0% increase from the 3-year final analysis[2]

AEs generally occurred early in treatment, allowing for prompt dose adjustments[4]

For KISQALI, median time to discontinuation due to AEs was 4.17 months (range: 0.10–35.75 months)[4]

The majority of ≥grade 3 AEs were laboratory findings that were generally

identifiable and manageable[4]

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The most common AEs (reported at a frequency ≥20%) in the dataset for which the frequency for KISQALI + AI exceeds the frequency for AI alone were neutropenia, infections, nausea, headache, fatigue, leukopenia and abnormal liver function tests. The most common grade 3/4 ADRs (reported at a frequency of ≥2%) in the dataset for which the frequency for KISQALI + AI exceeds the frequency for AI alone were neutropenia, abnormal

liver function tests and leukopenia.[1]

Corresponding frequency category for each AE based on the CIOMS III: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1000 to <1/100); rare (≥1/10,000 to <1/1000); very rare (<1/10,000) and not known (cannot be estimated from the available data).[1]

Adverse events in patients with eBC with starting dose of 400mg KISQALI

AEs	FREQUENCY
Infections and infestations	
Infections**	Very common
Blood and lymphatic system disorders	
Neutropenia, leukopenia	Very common
Anaemia, thrombocytopenia, lymphopenia	Common
Febrile neutropenia	Uncommon
Metabolism and nutrition disorders	
Hypocalcaemia, hypokalaemia, appetite decreased	Common
Nervous system disorders	
Headache	Very common
Dizziness	Common
Respiratory, thoracic and mediastinal disorders	
Cough	Very common
Dyspnoea, ILD/pneumonitis	Common
AEs	**FREQUENCY**
Gastrointestinal disorders	
Nausea, diarrhoea, constipation, abdominal pain††	Very common
Vomiting, stomatitis‡‡	Common
Hepatobiliary disorders	
Hepatotoxicity§§	Common
Skin and subcutaneous tissue disorders	

Alopecia	Very common
Rash,[¶¶] pruritus	Common
General disorders and administration site conditions	
Fatigue, asthenia, pyrexia	Very common
Peripheral oedema, oropharyngeal pain	Common
Investigations	
Abnormal liver function tests[‖‖]	Very common
Blood creatinine increased, ECG QT prolonged	Common

Adapted from KISQALI Summary of Product Characteristics.[1]

For further safety profile information, please refer to the SmPC.[1]

- NATALEE safety analysis

- Adverse reactions in the SmPC

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Contraindications[1]

Image

Hypersensitivity to the active substance or to peanut, soya or any of the excipients listed in

the SmPC.

Special warnings and precautions for use[1]

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Critical visceral disease

The efficacy and safety of KISQALI have not been studied in patients with critical visceral disease.

Image

Neutropenia

Based on the severity of the neutropenia, treatment with KISQALI may have to be interrupted, reduced or discontinued.

Image

Hepatobiliary toxicity

Liver function tests should be performed before initiating treatment with KISQALI. After initiating treatment, liver function should be monitored.

Based on the severity of the transaminase elevations, treatment with KISQALI may have to be interrupted, reduced or discontinued as described in the SmPC. Recommendations for patients who have elevated AST/ALT grade ≥3 at baseline have not been established.

Image

QT interval prolongation

ECG should be assessed before initiating treatment with KISQALI in all patients. Treatment with KISQALI should be initiated only in patients with QTcF values less than 450 msec. ECG should be repeated at approximately Day 14 of the first cycle, then as clinically indicated.

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 should be avoided in patients who already have or who are at significant risk of developing QTc prolongation. This includes patients with:

- Long QT syndrome
- Uncontrolled or significant cardiac disease, including recent myocardial infarction, congestive heart failure, unstable angina and bradyarrhythmias
- Electrolyte abnormalities

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. If co-administration of KISQALI with a strong CYP3A4 inhibitor cannot be avoided, the KISQALI dose should be changed as described in the SmPC.

Based on the observed QT prolongation during treatment, treatment with KISQALI may have to be interrupted, reduced or discontinued.

Image

Severe cutaneous reactions

Toxic epidermal necrolysis 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.

Image

Interstitial lung disease (ILD)/pneumonitis

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 in accordance with the SmPC. Based on the severity of the ILD/pneumonitis, which may be fatal, KISQALI may require dose interruption, reduction or discontinuation as described in the SmPC.

Image

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.

Image

CYP3A4 substrates

KISQALI is a moderate CYP3A4 inhibitor at the 400 mg dose. Thus, KISQALI may interact with medicinal products that are metabolised via CYP3A4, which may lead to increased serum concentrations of 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.

Image

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 of 600 mg in advanced or metastatic breast cancer 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.

Image

Women of childbearing potential

Pregnancy status should be verified prior to starting treatment with KISQALI. Women of childbearing potential should be advised to use an effective method of contraception while taking KISQALI and for at least 21 days after stopping treatment with KISQALI.

Pregnancy: KISQALI is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breastfeeding: Patients receiving KISQALI should not breastfeed for at least 21 days after the last dose.

Fertility: There are no clinical data available regarding the effects of KISQALI on fertility. Based on animal studies, KISQALI may impair fertility in males of reproductive potential.

Image

Soya lecithin

KISQALI contains soya lecithin. Patients who are hypersensitive to peanut or soya should not take KISQALI.

Find out more about the safety profile of KISQALI in aBC

Discover more

Click here to learn more about dosing and monitoring with KISQALI

Discover more

*Grouped term that combines neutropenia and neutrophil count decreased.[2]
†Grouped term that includes all preferred terms identified by standardised MedDRA queries for drug-related hepatic disorders.[2]
‡Grouped term.[2]
§Grouped term that includes all preferred terms identified by standardised MedDRA queries for ILD.[2]
¶Grouped term that includes all preferred terms identified by standardised MedDRA queries for venous thromboembolism.[2]
‖Liver-related: ALT increase 7.1%, AST increase 2.8%.[3]
**Infections: urinary tract infections, respiratory tract infections, gastroenteritis (only in patients with advanced or metastatic breast cancer), sepsis (<1% only in patients with advanced or metastatic breast cancer).[1]
††Abdominal pain: abdominal pain, abdominal pain upper.[1]
‡‡Stomatitis for eBC includes: stomatitis, mucositis.[1]
§§Hepatotoxicity: hepatic cytolysis, hepatocellular injury (only in patients with advanced or metastatic breast cancer), drug-induced liver injury (<1% in patients with eBC and in patients with advanced or metastatic breast cancer), hepatotoxicity, hepatic failure (only in patients with advanced or metastatic breast cancer), autoimmune hepatitis (single case in patients with eBC and single case in patients with advanced or metastatic breast cancer).[1]
¶¶Rash: rash, rash maculopapular, rash pruritic.[1]
‖‖Abnormal liver function tests: ALT increased, AST increased, blood bilirubin increased.[1]

AE, adverse event; AEIS, adverse event of special interest; AI, aromatase inhibitor; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CIOMS, Council for International Organizations of Medical Sciences; eBC, early breast cancer; ECG, electrocardiogram; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; ILD, interstitial lung disease; LHRH, luteinising hormone-releasing hormone; MATE1, multidrug and toxin extrusion protein 1; MeDRA, Medical Dictionary for Regulatory Activities; NSAI, non-steroidal aromatase inhibitor; OCT2, organic cation transporter 2; QTcF, corrected QT interval by Fridericia’s formula; SmPC, summary of product characteristics.

References

1. KISQALI (ribociclib) Summary of Product Characteristics.

2. Fasching PA, et al. Oral LBA13. European Society for Medical Oncology Congress, 13–17 September 2024, Barcelona, Spain.

3. Hortobagyi GN, et al. *Ann Oncol* 2025;36(2):149–157.

4. Barrios C, et al. Oral presentation 113MO. European Society for Medical Oncology Breast Cancer Congress, 15–17 May 2024, Berlin, Germany.

5. Slamon DJ, et al. *N Engl J Med* 2024;390:1080–1091; protocol.

UK | July 2025 | FA-11344823

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.

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