# **U**NOVARTIS

## KISQALI - Mechanism of action - HCP

## Prescribing information

Image



Image



# KISQALI® (ribociclib) mechanism of action

## Indications:1

• 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

KISQALI is not recommended to be used in combination with tamoxifen.

To learn more about the safety profile of KISQALI, visit our portal page here.

For full safety profile information, please refer to the KISQALI <u>Summary of Product</u> <u>Characteristics</u>.



# KISQALI selectively inhibits cyclin-dependent kinases 4 and 6 (CDK4/6) in eligible patients with HR+/HER2aBC, thus potentially inhibiting tumour growth<sup>1</sup>

Information on this page is based on pre-clinical research. They should not be extrapolated to clinical response.

# The role of CDK4/6 in HR+/HER2- aBC

Image



#### Image

#### ER+ breast cancer cell dependency on CDK4/6

ER+ breast cancer cells are CDK4-dependent and show overexpression when compared to CDK6.4



#### Image

#### **References:**

- 1. KISQALI® (ribociclib) Summary of Product Characteristics.
- 2. Pavlovic D, et al. Ther Adv Med Oncol 2023;15:17588359231205848.
- 3. Peurala E, et al. Breast Cancer Res 2013;15:R5
- 4. Kim S, et al. Oncotarget 2018;9(81):35226-35240 and supplementary data.

#### Previous Next

#### CDK4 and CDK6 control of the cell division cycle

CDK4/6s are cell cycle checkpoint regulators that play a crucial role in the signalling pathways which lead to cellular proliferation.<sup>12</sup> Once bound to D-cyclins, CDK4/6s are activated. The cyclin D-CDK4/6 complex can then regulate cell cycle progression (from phase G1 to S) via phosphorylation of the retinoblastoma protein (pRb).<sup>2</sup>

#### Regulation of the G1/S phase transition by cyclin D1 and CDK4/6:<sup>3</sup>



Patients with HR+/HER2- aBC have dysregulated levels of CDK4/6, leading to increased ER pathway activation, promoting cancer cell growth.<sup>2,4</sup>

#### ER+ breast cancer cell dependency on CDK4/6

ER+ breast cancer cells are CDK4-dependent and show overexpression when compared to CDK6.<sup>4</sup>



#### **References:**

- 1. KISQALI® (ribociclib) Summary of Product Characteristics.
- 2. Pavlovic D, et al. Ther Adv Med Oncol 2023;15:17588359231205848.
- 3. Peurala E, et al. Breast Cancer Res 2013;15:R5
- 4. Kim S, et al. Oncotarget 2018;9(81):35226-35240 and supplementary data.

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# Mechanism of action of KISQALI

## KISQALI is a selective inhibitor of CDK4 and CDK6<sup>1,2</sup>

KISQALI works by binding to the cyclin-CDK4/6 complex to inhibit the function of CDK4 and arrest the cell cycle, reducing the proliferation of cancer cells.<sup>1,2</sup>

Image



Adapted from Sammons SL, et al. 2017.<sup>3</sup>

In biochemical assays, KISQALI results in 50% inhibition (IC<sub>50</sub>) values of 0.01 (4.3 ng/ml) and 0.039  $\mu$ M (16.9 ng/ml) for CDK4 and CDK6, respectively.<sup>1</sup>

aBC, advanced breast cancer; CDK4, cyclin-dependent kinase 4; CDK6, cyclin-dependent kinase 6; E2F, E2 transcription factor; ER, oestrogen receptor; HER2–, human epidermal growth factor receptor 2-negative; HR+, hormone receptor-positive;  $IC_{50}$ , half-maximal inhibitory concentration; pRb, retinoblastoma protein.

### References

- 1. KISQALI® (ribociclib) Summary of Product Characteristics.
- 2. Kim S, et al. Oncotarget 2018;9(81):35226-35240 and supplementary data.

3. Sammons SL, et al. *Curr Cancer Drug Targets* 2017;17(7):637-649.

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Adverse events should be reported. Reporting forms and information can be found at <u>www.mhra.gov.uk/yellowcard</u>. Adverse events should also be reported to Novartis online through the pharmacovigilance intake (PVI) tool at <u>www.novartis.com/report</u>, or alternatively email <u>medinfo.uk@novartis.com</u> or call 01276 698370.

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