

A.12	Cyclin-dependent kinase 4/6 inhibitors – HR-positive/ HER2-negative advanced breast cancer – EML
Draft recommendation	<input type="checkbox"/> Recommended <input checked="" type="checkbox"/> Not recommended Justification: <ul style="list-style-type: none"> Not cost effective
Does the proposed medicine address a relevant public health need?	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable Comments: <ul style="list-style-type: none"> Breast cancer is the leading cause of morbidity, disability, and mortality in women, worldwide. In 2018, 60% of the breast cancer incident cases and two-third of the related mortality occurred in low- and middle-income countries.
Does adequate evidence exist for the efficacy/effectiveness of the medicine for the proposed indication? (this may be evidence included in the application, and/or additional evidence identified during the review process)	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable Comments: <ul style="list-style-type: none"> CDK4/6 inhibitors showed a significant improvement of the survival outcome and for some of them, of the quality of life Adding a CDK4/6 inhibitor to endocrine therapy appeared to be provide relative benefits in terms of PFS and OS The selection of patients eligible for treatment with CDK4/6 inhibitors (CDK4/6i) is not based on a predictive biomarker or specific molecular profile.
Does adequate evidence exist for the safety/harms associated with the proposed medicine? (this may be evidence included in the application, and/or additional evidence identified during the review process)	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable Comments: <ul style="list-style-type: none"> The use of CDK4/6i, in fact, is associated with a predictable, reversible, and generally not infection- prone neutropenia – related to the cell cycle effects on the hematopoiesis of the cell cycle blockade the occurrence of febrile neutropenia has been registered in <1% of the trial population, with all these compounds

24th WHO Expert Committee on Selection and Use of Essential Medicines
Expert review

<p>Are there any adverse effects of concern, or that may require special monitoring?</p>	<p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input type="checkbox"/> Not applicable</p> <p>Comments: neutropenia</p>
<p>Are there any special requirements for the safe, effective and appropriate use of the medicines?</p> <p>(e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)</p>	<p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input type="checkbox"/> Not applicable</p> <p>Comments:</p> <ul style="list-style-type: none"> • CBC control at the begin of each cycle and, precautionarily after 2 weeks for the first 2 cycles • EMA and FDA recommend an initial ECG monitoring for patients receiving ribociclib
<p>Are there any issues regarding cost, cost-effectiveness, affordability and/or access for the medicine in different settings?</p>	<p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input type="checkbox"/> Not applicable</p> <p>Comments:</p> <ul style="list-style-type: none"> • Most of the studies were based on high-income countries • Cost- effectiveness was commonly not met with CDK4/6 inhibitors, related to their high cost
<p>Are there any issues regarding the registration of the medicine by national regulatory authorities?</p> <p>(e.g. accelerated approval, lack of regulatory approval, off-label indication)</p>	<p><input type="checkbox"/> Yes</p> <p><input checked="" type="checkbox"/> No</p> <p><input type="checkbox"/> Not applicable</p> <p>Comments:</p>
<p>Is the proposed medicine recommended for use in a current WHO guideline?</p> <p>(refer to: https://www.who.int/publications/who-guidelines)</p>	<p><input type="checkbox"/> Yes</p> <p><input checked="" type="checkbox"/> No</p> <p><input type="checkbox"/> Not applicable</p> <p>Comments:</p>