

A.12	Cyclin-dependent kinase 4/6 inhibitors – HR-positive/ HER2-negative advanced breast cancer – EML
Draft recommendation	<input checked="" type="checkbox"/> Recommended <input type="checkbox"/> Not recommended Justification: <ul style="list-style-type: none"> • Many patients that can benefit • + endocrine therapy provide meaningful overall survival benefits vs. placebo/ aromatase inhibitors or placebo/fulvestrant. • Oral medication
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: high patient volume, the disease is main cause of death in 110 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: Uncertainties exist related to dose and treatment duration, and whether relevant clinical differences exist between agents within the pharmacological class.
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:
Are there any adverse effects of concern, or that may require special monitoring?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not applicable Comments:

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

<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 type="checkbox"/> Yes</p> <p><input checked="" type="checkbox"/> No</p> <p><input type="checkbox"/> Not applicable</p> <p>Comments:</p>
<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: Average monthly in Europe examples</p> <p>Palbociclib US\$ 2000—7000 (Netherlands €2000)</p> <p>Ribociclib US\$ 8900 (Netherlands €5540)</p> <p>Abemaciclib US\$ 3500 -12000</p> <ul style="list-style-type: none"> At the current high price, cdk 4/6 inhibitors have not been found to be cost-effective in most settings and would pose serious affordability challenges, especially in low-resource settings. Ideal candidates for voluntary license mechanisms through the Medicines Patent Pool.
<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: Not available in SSA LMICs</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> <p>But given the high costs of the treatment, this may influence the final decision.</p> <p>There is uncertainty whether all cdk4-6 inhibitors are equally effective</p>