

A.15	Estradiol – induction of puberty – EML
<b>Draft recommendation</b>	<input checked="" type="checkbox"/> Recommended <input type="checkbox"/> Not recommended Justification: Although the conditions (ovarian failure) that need the proposed medications are rare, yet it is currently still the preferred treatment for the condition. Therefore, the availability of these medications is essential for treatment of the conditions.
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: The conditions that need the medication is quite rare, however the specific population that need the treatment would benefit the availability of the proposed medication in their country. Currently there is no medicine indicated for puberty induction in the EML.
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: Recommend as the preferred treatment approach for puberty induction or to sustain puberty in girls although the recommendation is based on low level of evidence. <sup>1</sup> Although the guideline stated a clear preference toward bioidentical human oestrogens (oestradiol/17 $\beta$ -oestradiol E2) compare to non-bioidentical, synthetic or derived from animal sources oestrogen, it doesn't any preference toward certain route of administration (oral vs patch).
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: Considered safer than other types of sex hormones <sup>2</sup>

<sup>1</sup> Nordenström A, Ahmed SF, van den Akker E, et al. Pubertal induction and transition to adult sex hormone replacement in patients with congenital pituitary or gonadal reproductive hormone deficiency: an Endo-ERN clinical practice guideline. Eur J Endocrinol. 2022;186(6):G9-G49. Published 2022 Apr 21. doi:10.1530/EJE-22-0073

<sup>2</sup> Dunkel L, Quinton R. Induction of puberty. European Journal of Endocrinology. 2014;170:R229–R239

24<sup>th</sup> WHO Expert Committee on Selection and Use of Essential Medicines  
Expert review

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: use of small-dose
Are there any special requirements for the safe, effective and appropriate use of the medicines?  (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable Comments: The conditions should be managed by endocrinologist
Are there any issues regarding cost, cost-effectiveness, affordability and/or access for the medicine in different settings?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not applicable Comments: The medicine is affordable
Are there any issues regarding the registration of the medicine by national regulatory authorities?  (e.g. accelerated approval, lack of regulatory approval, off-label indication)	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not applicable Comments: Has been approved by FDA, EMA, Australian Government, Health Canada, Japanese PMDA Available in the EML of 60+ countries, including the LMICs <sup>3</sup>
Is the proposed medicine recommended for use in a current WHO guideline?  (refer to: <a href="https://www.who.int/publications/who-guidelines">https://www.who.int/publications/who-guidelines</a> )	<input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Not applicable Comments: No WHO guideline existed for these conditions.

<sup>3</sup> <https://global.essentialmeds.org/dashboard/medicines/695>