A.25	Pertuzumab – HER2+ metastatic breast cancer
Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☐ No ☐ Not applicable Comments:
Briefly summarize the role of the proposed medicine(s) relative to other therapeutic agents currently included in the Model List, or available in the market.	It increases overall survival when added to trastuzumab and docetaxel in patients with HER 2 positive metastatic breast cancer who are treated in first line. This result is superior to what can be achieved with the current drugs on the EML. Another study. Ann Oncol. 2019;30(5):766-773. studied with inoperable HER2-positive advanced breast cancer (locally recurrent/metastatic) (LR/MBC) and no prior systemic therapy for LR/MBC (except endocrine therapy) received docetaxel, paclitaxel, or nab-paclitaxel with trastuzumab and pertuzumab until disease progression or unacceptable toxicity. The preliminary findings suggest that the safety and PFS effect of first-line pertuzumab, trastuzumab, and a taxane for HER2-positive LR/MBC are consistent with results from CLEOPATRA.
Have all important studies and all relevant evidence been included in the application?	☒ Yes ☐ No ☐ Not applicable If no, please provide brief comments on any relevant studies or evidence that have not been included:
Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed indication?	☒ Yes ☐ No ☐ Not applicable ESMO MCBS 4 The addition of pertuzumab increases overall survival from 40.8 months to 56.5 months when added to trastuzumab - docetaxel regimen in first line. The 8-year survival rates are 37% with pertuzumab versus 23%. Application is not requested for the curative setting where it obtains an ESMO-MCBS score A
Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☒ Yes ☐ No ☐ Not applicable Comments:

Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☒ No ☐ Not applicable Comments:
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	This medicine is clearly of benefit in first-line treatment of patients with HER2+ metastatic breast cancer
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	The quality of the evidence is good. A similar study done in China, with PFS results only
Are there any special requirements for the safe, effective and appropriate use of the medicine(s)**?** (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)	☐ Yes ☒ No ☐ Not applicable Comments:
Are you aware of any issues regarding the registration of the medicine by national regulatory authorities? (e.g. accelerated approval, lack of regulatory approval, off-label indication)	☐ Yes ☒ No ☐ Not applicable Comments: but I do not have sufficient know how
Is the proposed medicine recommended for use in a current WHO Guideline approved by the Guidelines Review Committee? (refer to: **https://www.who.int/publications/who-guidelines**)	☐ Yes ☐ No ☐ Not applicable Comments: ??
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	Relevant medicine, the major problem is the high price. The medicine has to be administered in first-line together with trastuzumab and docetaxel, which are on the EML list since 2015. For trastuzumab there are several biosimilars. Despite the availability of biosimilars the use of trastuzumab in the curative and non curative setting of trastuzumab in areas with resource constraints is suggested to be suboptimal. The addition of pertuzumab will enlarge this problem. Pertuzumab biosimilars are being developed. Paclitaxel and nab-paclitaxel might replace docetaxel. Paclitaxel and docetaxel are on the EML list.
Any additional comments	

Based on your assessment of the application, and any additional evidence / relevant information identified during the review process, briefly summarize your proposed recommendation to the Expert Committee, including the supporting rationale for your conclusions, and any doubts/concerns in relation to the listing proposal.	A relevant medicine as first line treatment in combination with trastuzumab and docetaxel for women with metastatic HER2 overexpressing breast cancer with long-term effect on OS. Current price of the medicine will preclude use in several countries. Additional information on relevant treatment duration might reduce costs as well.
References (if required)	