I.11	Doxorubicin - rhabdomyosarcoma
Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: Rhabdomysarcoma is the most common soft tissue sarcoma in children and adolescents. The incidence is 4.4 million cases under the age of 20 years.
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.	The current standard of care includes combination chemotherapy regimens 1) IVA: Ifosamide, vincristine, Dactinomycin 2) VAC: vincristine, Dactinomycin, cyclophosphamide Single agent doxorubicin is currently not standard of care as first line therapy for advanced/metastatic rhabdomyosarcoma.
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 Briefly summarize the reported benefits (e.g. hard clinical versus surrogate outcomes) and comment, where possible on the actual magnitude and clinical relevance of benefit associated with use of the medicine(s). Only 1 randomized trial compared addition of doxorubicin to IVA. versus IVA alone. The suggested results increase in progression free survival (HR 0.87, 95% CI 0.65 – 1.16). Overall survival was however not increased HR 1.17, 95% CI0.82 – 1.67). There are no recent trials available. Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)? NA
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: Monitoring of short- and long-term cardiac function.
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	The current standard of care for rhabdomyosarcoma is VAC or IVA. Doxorubicin is an effective therapeutic option for patients in low resource settings where it is difficult to administrator combination chemotherapy either due to lack of availability of drugs, financial constraints or lack of trained personnel to manage side effects of the combination therapy.
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	NA
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: Routine laboratory tests including CBC, Liver function test. Echocardiogram.
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:
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: Doxorubicin can be used as single agent as palliative therapy. 1) Locally advanced/metastatic rhabdomyosarcoma 2) Most important it is of benefit for the treatment of non-metastatic rhabdomyosarcoma in settings where combination chemotherapy regimens are not available/affordable and cannot be given.

Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	Doxorubicin is cost effective, accessible and easily available all over the world where cancer treatment is provided.
Any additional comments	NO
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.	The addition of doxorubicin to standard chemotherapy for non-metastatic rhabdomyosarcoma is not associated with increased survival benefit and is associated with increased toxicity. For this reason, it was not proposed for inclusion in EML by applicants. However, single agent doxorubicin is nevertheless considered to be an effective treatment option for non-metastatic/metastatic rhabdomyosarcoma and has a place in cases where standard chemotherapy regimens are not available. As such it is a valuable treatment option. It is currently of use and is used in low resource settings and where cost constraints and toxicities prevent use of combination chemotherapy. Therefore, doxorubicin should NOT BE EXCUDED from the EMLc for use as a single agent in the treatment of rhabdomyosarcoma when standard triplet therapies (IVA, VAC) are not available/affordable.
On the MOReferences (if required)	