F.2	Doxorubicin, pegylated liposomal – injection 2 mg/mL – EML and EMLc
Draft recommendation	☒ Recommended ☐ Not recommended **Justification:** WHO EML currently lists doxorubicin (and other treatments) for Kaposi's sarcoma. The addition of pegylated liposomal doxorubicin (PLD) would be a new formulation that is included. In PLD, doxorubicin is encapsulated within pegylated liposomes, which preferentially distribute into tumours due to the greater permeability of the vasculature in KS tumours compared to that in healthy tissue. This allows the concentration of doxorubicin to be higher within tumours, while keeping concentrations in the systemic circulation the same. The ability to use PLD as single-agent chemotherapy also means the toxicities that are more specific to bleomycin (e.g. pulmonary fibrosis) and vincristine (e.g. neuropathy) can be decreased or avoided.
Does the proposed medicine address a relevant public health need?	☒ Yes ☐ No ☐ Not applicable **Comments:** Doxorubicin is already listed in the EML and EMLc for this condition. This is a request for an additional formulation to be included.
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)	☒ Yes ☐ No ☐ Not applicable **Comments:** Doxorubicin is already listed in the EML and EMLc for this condition. This is a request for an additional formulation to be included.
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)	☒ Yes ☐ No ☐ Not applicable **Comments:** Doxorubicin is already listed in the EML and EMLc for this condition. This is a request for an additional formulation to be included. Reduced side effects are noted with this formulation.
Are there any adverse effects of concern, or that may require special monitoring?	☒ Yes ☐ No ☐ Not applicable **Comments**: As per SOC with administration of cytotoxic agents.

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)	☒ Yes ☐ No ☐ Not applicable **Comments:** Provision of chemotherapy drugs requires adequate infrastructure (e.g. pharmacy, laminar flow) for preparation of the drugs, as well as a level of expertise with trained staff to ensure that the drugs are administered correctly and monitored appropriately to minimize potential side effects and ensure that serious toxicities are identified and managed. Since the drugs are largely available as liquid vials, they need to be reconstituted with calculation for a specific dose for each patient, which requires access to a laminar flow hood and appropriate training
Are there any issues regarding cost, cost-effectiveness, affordability and/or access for the medicine in different settings?	☒ Yes ☐ No ☐ Not applicable **Comments:** The doxorubicin-bleomycin-vincristine regimen, which is no longer considered the first choice in high income countries and some international guidelines, was the most rational treatment option in a resource-limited country like Brazil. Indeed the incremental cost per additional responder of using PEG liposomal doxorubicin instead of ABV was as high as US$20,990. [1] Thus having a number of formulation options for treatment are important for countries.
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)	☐ Yes ☒ No ☐ Not applicable **Comments**: The formulation is available on the global market.
Is the proposed medicine recommended for use in a current WHO guideline? (refer to: https://www.who.int/publications/who-guidelines)	☒ Yes ☐ No ☐ Not applicable **Comments:** Another formulations of the medicine is already listed on the EML/EMLc for the same indication.

[1] Vanni T, Lopes Fonseca BA, Polanczyk CA. Cost-effectiveness analysis comparing chemotherapy regimens in the treatment of AIDS-related Kaposi's sarcoma in Brazil. HIV Clin Trials. 2006;7(4):194–202