20th Expert Committee on Selection and Use of Essential Medicines

Peer Review Report #2

[Cisplatin for EARLY STAGE CERVICAL CANCER, Union for International Cancer Control 2014 Review of Cancer Medicines on the WHO List of Essential Medicines]

(1) Does the application adequately address the issue of the public health need for the medicine?

Yes [ ] No [x]

Please provide brief details:
GLOBOCAN indicates that global cervical cancer prevalence in 2012 was 1,547,000 and labels it as the fourth most common cancer in women. There were an estimated 528,000 new incidences in 2012. About 85% (444,300) of all new cases in 2012 occurred in less developed regions, and the remaining 15% (83,000) occurred in more developed regions. Highest-risk regions include Eastern and Middle Africa. Cervical cancer is highly preventable and treatable, if detected in early states. GLOBOCAN estimated that in 2012 there were 266,000 deaths from cervical cancer. 87% of deaths (8.3 with an ASR per 100,000) occurred in less developed regions.

While GLOBOCAN does not provide specifics about early stage cervical cancer, the data do suggest that overall cervical cancer disproportionately impacts less developed regions.

(2) Have all important studies that you are aware of been included in the application?

Yes [ ] No [x]

Please provide brief comments on any relevant studies that have not been included:

The application did not specify the magnitude of the problem (early stage cervical cancer) globally and in less developed countries in particular.

(3) Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed use?

Yes [ ] No [x]

Briefly summarise the reported outcomes (e.g. clinical, surrogate, other) and comment, where possible, on the magnitude of clinical benefit associated with use of the medicine:

The evidence reported came from two systematic reviews, the first on Radiotherapy with concurrent cisplatin-based doublet or weekly cisplatin for cervical cancer: A systematic review and meta-analysis. It included all stages and not only early stages. It concluded that platinum-based combination therapy plus RT should be the preferred treatment over weekly CDDP plus RT for stage IB-IVA CC.
The other systematic review on Chemotherapy for metastatic and recurrent cervical cancer and not early stage cervical cancer.

(4) Is there evidence of efficacy in diverse settings and/or populations?

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Please provide brief details:
The application did not clarify these points.

(5) Has the application adequately considered the safety and adverse effects of the medicine? Are there any adverse effects of concern, or that may require special monitoring?

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Please provide brief details: Cisplatin is highly emetogenic, Mild peripheral neuropathy is common with cisplatin. Ototoxicity is observed with cisplatin and is more common with increasing dose and number of cycles. Renal toxicity caused by cisplatin can be significant and may result in electrolyte abnormalities. The application stressed the importance of monitoring these adverse effects.

ADDITIONAL CONSIDERATIONS:

(6) Are there special requirements or training needed for the safe, effective and/or appropriate use of the medicine?

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Please provide brief details: The administration of chemotherapy with platinum base requires that the patient to have regular access to clinical care and adequate venous access. This entails laboratory investigations, audiometry, neurological assessment, parenteral fluids, and medications for vomiting.

(7) Are there any issues regarding the registration of the medicine by regulatory authorities? (e.g., recent registration, new indications, off-label use)

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Please provide brief details:
Carboplatin is currently in the WHO Essential Medicines List for Adults (2013, 18th Edition). Cisplatin belongs to same group.

(8) Is the medicine recommended for use in a current WHO GRC-approved Guideline (i.e., post 2008)?

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Please provide brief details:
Not mentioned in the application.

(9) Please comment briefly on issues regarding cost and affordability of this medicine.
Not mentioned in the application

(10) Any additional comments?

(11) Please summarise the action you propose the Expert Committee takes. The present proposal calls for the explicit addition of Cisplatin to the EML given its distinct use in the treatment of a number of cancers. However the application does not cover all aspects needed (efficacy and safety in early stage cervical cancer, cost, and comparability to carboplatin). At this stage, the reviewer does not endorse this application.