19th Expert Committee on The Selection and Use of Essential Medicines

April 8-12 2013

Expert peer review on application to add azithromycin under ophthalmological preparations

1. Assessment of efficacy
   a. Have all relevant studies on efficacy been included

   No  (if no, please provide reference and information)

   Single dose of oral azithromycin is effective in trachoma and reduces its prevalence. Most of the trials compare oral azithromycin with topical tetracycline. There is only one study in which azithromycin eye drops (twice daily for three days) has been compared with single dose oral azithromycin. This is a study in children conducted in Pakistan (ref. no.2 in the review) which proved that azithromycin topical eye drops are as efficacious as oral azithromycin. The quality of evidence is low.

   b. Summarize the data on efficacy, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

   Topical azithromycin is effective in the treatment of trachoma and can be used for mass treatments. However there is very little data on comparison of oral and topical azithromycin. Whatever data has been found is of low quality. Topical azithromycin (drops) has not been compared with tetracycline ointment. However, tetracycline ointment is not as patient friendly as azithromycin drops. WHO guidelines have been modified and now recommend single dose oral azithromycin in trachoma. Previous versions recommended tetracycline ointment.

   c. Please provide any additional relevant information with reference

2. Assessment of safety
   a. Have all relevant studies on safety been included

   No  (if no, please provide reference and information)


   There are no significant differences in safety between topical azithromycin and oral single dose azithromycin. However this information is from a limited number of children.

   b. Summarize the data on safety, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

   Topical azithromycin is better tolerated than tetracycline ointment. There are no significant differences in safety between single dose oral azithromycin and topical azithromycin. On local application to the eye stinging and burning sensation and ocular discomfort is common. Hypersensitivity reactions are rare.

   c. Please provide any additional relevant information with reference
3. Assessment of cost and availability

a. Have all relevant data on cost been provided
   No. There is no information on cost or comparative cost effectiveness provided in the review.

b. Summarize the data on cost and cost effectiveness, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

   Azithromycin drops are more expensive than tetracycline ointment. However, considering that it is used only twice a day for three days, the quantity (total dose) needed for each person is very little, which is why the review suggests the packaging of six single dose vials into a box. However, the cost of this is not known.

c. Please provide any additional relevant information with reference.
   Topical azithromycin is not expensive and is available in many countries. Generic forms of this medicine are available. The provided review states that six single dose vials each containing 25mg of azithromycin will be put into a box (presumably for each patient). This probably will be costlier than a single dose of oral azithromycin. However since the costs are not known a definitive statement cannot be made. One 10ml vial of azithromycin (1.5%) costs approximately one dollar in India.

d. Is the product available in several low and middle income countries?
   Yes. Azithromycin 1.5% is available in many countries. 1% solution is available in USA. Six single dose vials packed in a box are not available in India. The cost of this packaging is not known.

4. Assessment of public health need

a. Please provide the public health need for this product (1-2 sentences)

   Trachoma is a large problem in many countries in Africa, Asia, middle-east, Latin America etc. Topical azithromycin would be a good alternative to tetracycline if clinical trials are done to provide the necessary evidence on efficacy and safety.

b. Do guidelines (especially WHO guidelines) recommend this product? If yes, which ones? List 1 or 2 international preferable

   No. None of the guidelines state the use of azithromycin drops for the management of trachoma. WHO guidelines now state single oral dose of azithromycin as the antibiotic for trachoma.

5. Are there special requirements for use or training needed for safe/effective use?

   If yes, please provide details in 1-2 sentences

   No.

6. Is the proposed product registered by a stringent regulatory authority?

   Yes

7. Any other comments

   There is only one clinical trial in which oral and topical azithromycin have been compared (reference 2 in the review). The quality of evidence in that trial is low. The trials in which mass administration of azithromycin drops were given in Cameroon was an uncontrolled open study (references 3 & 4 in the review).
Azithromycin eye drops (1.5%) are commonly sold in a 10 ml vial. The packing of azithromycin into a box with six single dose vials to be given to a patient with trachoma is not commonly found. This kind of packaging may be costlier than a single dose of oral azithromycin (1 gm) which costs around 2 US dollars in India. On the other hand the convenience of use and safety (especially of contamination) of many people sharing a 10ml vial of azithromycin has not been tested in the field.

Under section 15 of the review (proposed text for the WHO formulary) – it is stated that the name of the medicinal product is Azyter. Brand names should be avoided and only generic names should be proposed as is the norm in all WHO documents. The review on azithromycin which has been provided is a very superficial one and there has been no attempt to evaluate the quality of evidence or provide information on cost.

8. What is your recommendation to the committee (please provide the rationale)

Topical azithromycin drops should not be included in the EML at the moment as there is very little evidence of the superiority of this to oral azithromycin which is the present treatment recommended by WHO. The packing of azithromycin drops into a box containing six single dose vials is not common and the cost for this type of packing is not known.