19th Expert Committee on the Selection and Use of Essential Medicines
April 8-12; 2013
Expert peer review on application for “Ophthalmological preparation: Addition of Ketotifen”

1. Assessment of efficacy
a. Have all relevant studies on efficacy been included
   No

b. Summarize the data on efficacy, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)
   N/A. No ophthalmological preparation of Antihistamines is currently on the List.

c. Please provide any additional relevant information with reference

2. Assessment of safety
a. Have all relevant studies on safety been included
   No

b. Summarize the data on safety, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)
   N/A. No ophthalmological preparation of Antihistamines is currently on the List.

c. Please provide any additional relevant information with reference

3. Assessment of cost and availability
a. Have all relevant data on cost and availability provided
   No

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)
   N/A. No ophthalmological preparation of Antihistamines is currently on the List.

c. Please provide any additional relevant information with reference

d. Is the product available in several low and middle income countries?
   Yes, in middle income countries.

4. Assessment of public health need
b. Do guidelines (especially WHO guidelines) recommend this product?
   WHO has not included ophthalmological preparation of Antihistamines in its guidelines.
5. Are there special requirements for use or training needed for safe/effective use?
   No.

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

7. Any other comments
   This application is part of six applications submitted by the International Council of Ophthalmology for updating the Ophthalmological Preparations section of the EML. The applications are as following:
   1. Addition of Bevacizumab
   2. Addition of Ketorolac
   3. Addition of Latanoprost
   4. Addition of Ofloxacin
   5. Addition of Azithromycin
   6. Addition of Ketotifen

   1. Ophthalmic antihistamine preparations provide symptomatic relief of seasonal allergic conjunctivitis (SAC). Ophthalmic formulations of alcaftadine, azelastine, bepotastine, epinastine, ketotifen, and olopatadine have both H1-antihistamine and mast-cell stabilizing properties.
   2. Compared to oral antihistamines and ophthalmic mast cell stabilizers, the topical antihistamines have been shown to have a faster onset of action.
   3. While a few studies have reported some differences between agents, the overall clinical significance of these differences is not known.
   4. Current therapies for the relief of the signs and symptoms associated with SAC include nonpharmacological management and pharmacological therapies. When adequate relief of SAC signs and symptoms is not achieved by nonpharmacological therapies, topical or systemic pharmacological therapies are initiated.
   5. The initial treatment options for SAC are saline solution or artificial tears to physically irrigate, dilute and remove the allergens from the ocular surface. If these fail to provide adequate relief, pharmacological treatment options include topical decongestants, antihistamines, mast cell stabilizers, nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids could be used.
   6. Topical application of antihistamines can be irritating to the eye and can potentially lead to sensitivity reactions and aggravation of allergic responses.

7. What is your recommendation to the committee (please provide the rationale)
   1. SAC is not generally a sight-threatening disease. However it may cause patients’ discomfort and have a impact on morbidity and quality of life of the patients.
   2. Systemic antihistamines may be used to control the symptoms of rhinoconjunctivitis, but these agents may have partial efficacy for ocular symptoms.
3. Chlorphenamine (chlorpheniramine) as a systemic antihistamine is already listed under section 3 of the EML. These medicines are already reviewed by other reviewers. Therefore, recommendations from reviewer of the antihistamine section should also be considered.

4. Final recommendation “**Listing of ophthalmic Ketotifen is not recommended**”.