19th Expert Committee on the Selection and Use of Essential Medicines
April 8-12 2013

Expert peer review on application for adding Fomepizole

1. Assessment of efficacy
a. Have all relevant studies on efficacy been included
Yes
b. Summarize the data on efficacy, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)
Fomepizole blocks the metabolism of toxic alcohols (ethylene glycol, methanol etc.) so their toxic metabolites (plasma formic acid, plasma glycolate and urinary oxalates) do not accumulate.
It thus prevents or resolves metabolic acidosis induced by formic and glycolic acids.
Also it prevents or improves renal dysfunction induced by ethylene glycol poisoning and prevents or improves visual impairment due to methanol poisoning.
c. Please provide any additional relevant information with reference
No human randomized control studies exist.

2. Assessment of safety
a. Have all relevant studies on safety been included
Yes
b. Summarize the data on safety, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)
Fomepizole in therapeutic doses is quite a safe drug with very few and minor adverse effects that are usually not sufficient to discontinue treatment. These adverse effects occur in the CNS, GIT, and CVS systems with few skin, metabolic and blood events.
Also quite safe in children, though animal studies may indicate some teratogenicity to the foetus and thus is an FDA class “C” drug.
c. Please provide any additional relevant information with reference

3. Assessment of cost and availability
a. Have all relevant data on cost and availability been provided?
Yes
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)
Fomepizole has a very high acquisition cost but may be more cost effective in terms of outcome, ease of administering, simplicity of laboratory support and high dependency monitoring and the possibility of use without haemodialysis.
The use of the alternative ethanol which is not even listed on the WHO EML is more difficult to administer entailing frequent laboratory monitoring, use of haemodialysis. Toxicity and serious
adverse effects are frequent necessitating ICU use and more staff and personnel to monitor and manage them

c. Please provide any additional relevant information with reference

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

No

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

   Methanol, ethylene glycol and to a less extent other toxic alcohol poisoning is a worldwide phenomenon though the actual number of cases may not be that frequent. The occurrence is even more widespread in middle and low income countries for the very reason of their poverty and unscrupulousness, yet the medicine is not available in most developing countries.

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

   Yes, manufacturing pharmaceuticals approved by the FDA, the American Academy of Toxicology and the European Association of poison centres and Clinical Toxicology

5. **Are there special requirements for use or training needed for safe/effective use?**
   If yes, please provide details in 1-2 sentences

   No, for the drug per se, but for haemodialysis which is an adjunct?

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

7. **Any other comments**

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

   I recommend that it should be put on the WHO complimentary list. There is no doubt about its efficacy and safety and no gainsaying about its superiority to ethanol for the treatment of methanol and ethylene glycol poisoning. But its current cost, the relatively low actual case diagnoses and the spurious nature of epidemics make it a drug that cannot be termed core essential. Most pharmacies, even in the developed world, would not stock it; most developing countries will not buy it for their health services. Of what use will it be being on the WHO core EML?