Fomepizole

Essential medicine status

Section: 4. Antidotes and other substances used in poisonings > 4.2. Antidotes and other substances used in poisonings > Specific

EMLc | ATC codes: V03AB34

Indication	Harmful effects of or exposure to noxious substances, chiefly nonmedicinal as to source, not elsewhere classified ICD11 code: NE61
INN	Fomepizole
Medicine type	Chemical agent
List type	Complementary (EML) (EMLc)
Formulations	Parenteral > General injections > IV: 5 mg per mL in 20 mL ampoule (sulfate) ; 1 g per mL in 1.5 mL ampoule (base)
EML status history	First added in 2013 (TRS 985)
Sex	All
Age	Also recommended for children
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Fomepizole
DrugBank	Fomepizole

Summary of evidence and Expert Committee recommendations

An application to include fomepizole on both the EML and the EMLc was submitted by Guangduo Zhang, Kasumi Crews, Heather Wiseman and Nicola Bates of Medical Toxicology Information Services Ltd, London, United Kingdom; Dr Knut Erik Hovda of The National NBC Center, Department of Acute Medicine, Oslo University Hospital Ullevaal, Oslo, Norway; and Dr John Archer and Dr Paul Dargan of Clinical Toxicology, Guy's and St Thomas' NHS Foundation Trust and King's Health Partners, London, United Kingdom. Fomepizole is used for the treatment of toxic alcohol and glycol poisoning – principally methanol and ethylene glycol – in adults and children. Ethylene glycol poisoning occurs worldwide and in the majority of cases is due to the ingestion of substances such as antifreeze, vehicle screen wash and fuel additives. Methanol poisoning is usually associated with illicit alcohol. Epidemics of methanol poisoning (caused by ingestion of contaminated beverages) and of diethylene glycol poisoning (caused by adulterated medications) continue to occur worldwide, predominantly in developing countries and among economically disadvantaged communities. Poisoning with these agents is associated with severe morbidity and mortality. The toxicity associated with the toxic alcohols and glycols is due to their metabolism by the enzyme alcohol dehydrogenase to toxic intermediates. Fomepizole prevents formation of the toxic metabolites by competitively inhibiting alcohol dehydrogenase. Ethanol can also be used as an antidote and acts through the same mechanism. Experimental studies have demonstrated the ability of fomepizole to inhibit alcohol dehydrogenase, and animal studies have shown that fomepizole reverses the toxic effects of methanol and ethylene glycol poisoning. Prospective observational studies, clinical trials and retrospective case reviews have demonstrated that fomepizole improves outcomes by improving renal function, preventing visual impairment associated with methanol poisoning, and preventing metabolic acidosis (1, 2). In a retrospective case series, ethanol and fomepizole were equally effective but fomepizole provided practical advantages, such as ease of administration and monitoring, and a better adverse events profile (2-7). However, no high-quality studies have directly compared fomepizole with ethanol. Fomepizole is approved by the US FDA for these indications and is recommended by American and European associations of clinical toxicologists. Ethanol is not US FDA-approved for this indication.

The relative ease of use of fomepizole may confer some benefits through the potential avoidance of intensive therapy, although this would not apply to severely ill patients who would require intensive support. The limited data made it difficult to determine whether the greater cost of fomepizole was offset by any potential savings. The laboratory tests that are needed to initiate treatment and monitor therapy may not be available in all situations where poisonings occur. There are insufficient data from children and elderly people. However, most available information suggests that fomepizole is a safe medicine. It is classified as US FDA pregnancy category C. It was also noted that access to parenteral ethanol was problematic as this product was difficult to manufacture and pack in ampoule form. Though rare in some settings, toxic alcohol and glycol poisoning can lead to serious harm. Considering this need, the Expert Committee recommended the addition of fomepizole to the complementary list of the EML and EMLc. The need for specialist care was a consideration for inclusion on the complementary list rather than on the core list.

References: 1. Brent J, McMartin K, Phillips S, Burkhart KK, Donovan JW, Wells M, et al.; Methylpyrazole for Toxic Alcohols Study Group. Fomepizole for the treatment of ethylene glycol poisoning. N Engl J Med. 1999;340(11):832-8. http://dx.doi.org/10.1056/NEJM199903183401102 PMID:10080845 2. Brent J. Fomepizole for ethylene glycol and methanol poisoning. N Engl J Med. 2009;360(21):2216-23. http://dx.doi.org/10.1056/NEJMct0806112 PMID:19458366 3. Paasma R, Hovda KE, Hassanian-Moghaddam H, Brahmi N, Afshari R, Sandvik L, et al. Risk factors related to poor outcome after methanol poisoning and the relation between outcome and antidotes–a multicenter study. Clin Toxicol (Phila). 2012;50(9):823-31. http://dx.doi.org/10.3109/15563650.2012.728224 PMID:22992104 4. Miller H, Barceloux DG, Krenzelok EP, Olson K, Watson W; Ad Hoc Committee. American Academy of Clinical Toxicology practice guidelines on the treatment of ethylene glycol poisoning. J Toxicol Clin Toxicol. 1999;37(5):537-60. http://dx.doi.org/10.1081/CLT-100102445 PMID:10497633 5. Borron SW, Mégarbane B, Baud FJ. Fomepizole in treatment of uncomplicated ethylene glycol poisoning. Lancet. 1999;354(9181):831. http://dx.doi.org/10.1016/S0140-6736(99)80015-4 PMID:10485727 6. Cannarozzi AA, Mullins ME. A cost analysis of treating patients with ethylene glycol poisoning with fomepizole alone versus hemodialysis and fomepizole. Clin Toxicol. 2010;48(3):299-300. 7. Barceloux DG, Bond GR, Krenzelok EP, Cooper H, Vale JA; American Academy of Clinical Toxicology Ad Hoc Committee on the Treatment Guidelines for Methanol Poisoning. American Academy of Clinical Toxicology practice guidelines on the treatment of methanol poisoning. J Toxicol Clin Toxicol. 2002;40(4):415-46. http://dx.doi.org/10.1081/CLT-120006745 PMID:12216995