Title: **Trientine for Treatment of Wilson's Disease: Clinical and Cost-Effectiveness, and Safety**

DATE: 10 February 2014

RESEARCH QUESTIONS

1. What is the evidence for the clinical effectiveness and safety of trientine for patients with Wilson's disease?

2. What is the evidence for the cost-effectiveness of trientine for patients with Wilson's disease?

KEY MESSAGE

One relevant systematic review and three non-randomized studies were identified regarding the clinical effectiveness and safety of trientine for the treatment of Wilson's disease. No information on cost-effectiveness was identified.

METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 1), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2003 and February 4, 2014. Internet links were provided, where available.

RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, and economic evaluations.

One relevant systematic review and three retrospective non-randomized studies were identified regarding the clinical effectiveness and safety of trientine for the treatment of Wilson's disease. No health technology assessments, meta-analyses, randomized controlled trials, or economic evaluations were identified. Additional references of potential interest are provided in the appendix.

Health Technology Assessments
No literature identified.

Systematic Reviews and Meta-analyses

1. Wiggelinkhuizen M, Tilanus ME, Bollen CW, Houwen RH. Systematic review: clinical efficacy of chelator agents and zinc in the initial treatment of Wilson disease. Aliment Pharmacol Ther. 2009 May 1;29(9):947-58.
PubMed: PM19210288
Summary available from:
http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?AccessionNumber=12009104713#.UvO3zfldV8F

Randomized Controlled Trials
No literature identified.

Non-Randomized Studies

2. Weiss KH, Thurik F, Gotthardt DN, Schafer M, Teufel U, Wiegand F, et al. Efficacy and safety of oral chelators in treatment of patients with Wilson disease. Clin Gastroenterol Hepatol. 2013 Aug;11(8):1028-35.
PubMed: PM23542331

3. Walshe JM. The pattern of urinary copper excretion and its response to treatment in patients with Wilson's disease. QJM. 2011 Sep;104(9):775-8.
PubMed: PM21622540

4. Taylor RM, Chen Y, Dhawan A, EUROWILSON Consortium. Triethylene tetramine dihydrochloride (trientine) in children with Wilson disease: experience at King's College Hospital and review of the literature. Eur J Pediatr. 2009 Sep;168(9):1061-8.
PubMed: PM19066958

Economic Evaluations
No literature identified.

PREPARED BY:
Canadian Agency for Drugs and Technologies in Health
Tel: 1-866-898-8439
www.cadth.ca

APPENDIX – FURTHER INFORMATION:

Randomized Controlled Trial (Comparator other than penicillamine, zinc, or placebo)

5. Brewer GJ, Askari F, Lorincz MT, Carlson M, Schilsky M, Kluin KJ, et al. Treatment of Wilson disease with ammonium tetrathiomolybdate: IV. Comparison of tetrathiomolybdate and trientine in a double-blind study of treatment of the neurologic presentation of Wilson disease. Arch Neurol. 2006 Apr;63(4):521-7.
PubMed: PM16606763

Case Studies or Series on Trientine

6. Kim B, Chung SJ, Shin HW. Trientine-induced neurological deterioration in a patient with Wilson's disease. J Clin Neurosci. 2013 Apr;20(4):606-8.
PubMed: PM23274038

7. Kim YE, Yun JY, Yang HJ, Kim HJ, Jeon BS. Unusual epileptic deterioration and extensive white matter lesion during treatment in Wilson's disease. BMC Neurol [Internet]. 2013 [cited 2014 Feb 7];13:127. Available from:
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3851542
PubMed: PM24067156

8. Harada M, Miyagawa K, Honma Y, Hiura M, Shibata M, Matsuhashi T, et al. Excess copper chelating therapy for Wilson disease induces anemia and liver dysfunction. Intern Med. 2011;50(14):1461-4.
PubMed: PM21757830

9. Arnon R, Calderon JF, Schilsky M, Emre S, Shneider BL. Wilson disease in children: serum aminotransferases and urinary copper on triethylene tetramine dihydrochloride (trientine) treatment. J Pediatr Gastroenterol Nutr. 2007 May;44(5):596-602.
PubMed: PM17460493

10. Askari FK, Greenson J, Dick RD, Johnson VD, Brewer GJ. Treatment of Wilson's disease with zinc. XVIII. Initial treatment of the hepatic decompensation presentation with trientine and zinc. J Lab Clin Med. 2003 Dec;142(6):385-90.
PubMed: PM14713890

Case Studies or Series on Relevant Comparators

11. Kalita J, Kumar V, Chandra S, Kumar B, Misra UK. Worsening of Wilson disease following penicillamine therapy. Eur Neurol. 2013 Dec 17;71(3-4):126-31.
PubMed: PM24356057

12. Tan SS, Latif SA, Poh WY. Concurrent massive breast enlargement, myasthenia gravis and dermopathy as manifestations of penicillamine toxicity in a Wilson's disease patient. Med J Malaysia. 2012 Jun;67(3):323-5.
PubMed: PM23082426

13. Carlesimo M, Narcisi A, Cortesi G, Mari E, Fidanza L, De MG, et al. An 18-year follow-up of a case of D-penicillamine-induced Elastosis perforans serpiginosa. Int J Immunopathol

Pharmacol. 2011 Jan;24(1):257-9.
PubMed: PM21496412

14. Ping CC, Hassan Y, Aziz NA, Ghazali R, Awaisu A. Discontinuation of penicillamine in the absence of alternative orphan drugs (trientine-zinc): a case of decompensated liver cirrhosis in Wilson's disease. J Clin Pharm Ther. 2007 Feb;32(1):101-7.
PubMed: PM17286794

15. Chan KH, Cheung RT, Au-Yeung KM, Mak W, Cheng TS, Ho SL. Wilson's disease with depression and parkinsonism. J Clin Neurosci. 2005 Apr;12(3):303-5.
PubMed: PM15851088

Review Articles on Wilson's Disease

16. Purchase R. The treatment of Wilson's disease, a rare genetic disorder of copper metabolism. Sci Prog. 2013;96(Pt 1):19-32.
PubMed: PM23738435

17. Trocello JM, Broussolle E, Girardot-Tinant N, Pelosse M, Lachaux A, Lloyd C, et al. Wilson's disease, 100 years later... Rev Neurol (Paris). 2013 Dec;169(12):936-43.
PubMed: PM24119853

18. Lorincz MT. Recognition and treatment of neurologic Wilson's disease. Semin Neurol. 2012 Nov;32(5):538-43.
PubMed: PM23677665

19. Brewer GJ. Novel therapeutic approaches to the treatment of Wilson's disease. Expert Opin Pharmacother. 2006 Feb;7(3):317-24.
PubMed: PM16448326

20. Brewer GJ. Neurologically presenting Wilson's disease: epidemiology, pathophysiology and treatment. CNS Drugs. 2005;19(3):185-92.
PubMed: PM15740174

21. Ferenci P. Review article: diagnosis and current therapy of Wilson's disease. Aliment Pharmacol Ther. 2004 Jan 15;19(2):157-65.
PubMed: PM14723607

22. Ferenci P. Pathophysiology and clinical features of Wilson disease. Metab Brain Dis. 2004 Dec;19(3-4):229-39.
PubMed: PM15554419

Additional References

23. Schilsky ML. Wilson disease: treatment and prognosis. 2014 [cited Feb 7]. In: UpToDate [Internet]. Version 21.12. Waltham (MA): UpToDate; 1992- . Available from www.uptodate.com Subscription required.
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