



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.

Disclaimer: The Rapid Response Service is an information service for those involved in planning and providing health care in Canada. Rapid responses are based on a limited literature search and are not comprehensive, systematic reviews. The intent is to provide a list of sources of the best evidence on the topic that CADTH could identify using all reasonable efforts within the time allowed. Rapid responses should be considered along with other types of information and health care considerations. The information included in this response is not intended to replace professional medical advice, nor should it be construed as a recommendation for or against the use of a particular health technology. Readers are also cautioned that a lack of good quality evidence does not necessarily mean a lack of effectiveness particularly in the case of new and emerging health technologies, for which little information can be found, but which may in future prove to be effective. While CADTH has taken care in the preparation of the report to ensure that its contents are accurate, complete and up to date, CADTH does not make any guarantee to that effect. CADTH is not liable for any loss or damages resulting from use of the information in the report.

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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.

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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. *Trientine, Page 5. (Subscription required)*