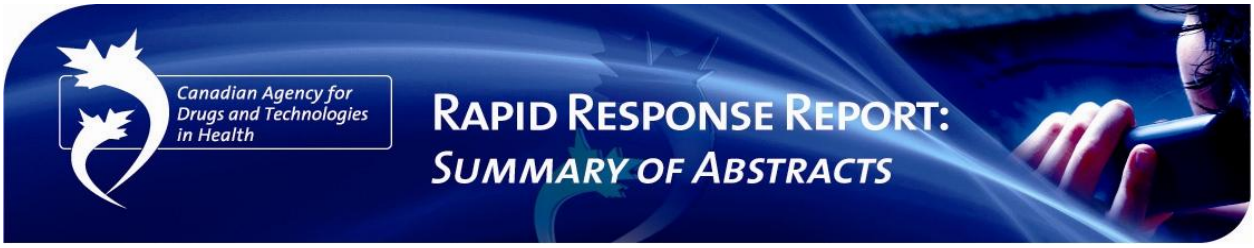

TITLE: Levetiracetam Treatment in Patients with Epilepsy: Clinical and Cost-Effectiveness and Safety

DATE: 06 April 2011

RESEARCH QUESTION

1) What is the comparative clinical effectiveness of levetiracetam versus standard drug therapies in patients with epilepsy?

2) What is the safety of levetiracetam versus standard drug therapies in patients with epilepsy?

3) What is the cost-effectiveness of levetiracetam versus standard drug therapies in patients with epilepsy?

KEY MESSAGE

There are a limited number of studies that directly compare levetiracetam to other antiepileptic agents, and the evidence available may be insufficient to inform a prescribing strategy. In adults, levetiratectam showed similar seizure rates compared to controlled release carbamazepine and lamotrigine in two randomized controlled trials (RCTs). Patients treated with levetiracetam may be more likely to continue epilepsy treatment compared to other agents. The cost-effectiveness of levetiracetam is not clear.

METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2011, Issue 3), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. To address research questions 1 and 3, methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, and economic studies. To address research question 2, a focused search (with main concepts appearing in title or major subject heading) was conducted and a methodological filter was applied to limit retrieval to non-randomized studies containing safety

data. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2006 and March 28, 2011.

The evidence selected to answer question 2 included HTAs, systematic reviews, meta-analyses, RCTs and non-randomized studies that compared levetiracetam to another antiepileptic drug. Uncontrolled cohort, case series or case reports were excluded.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

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.

The literature search identified one health technology assessment, four RCTs, seven non-randomized studies and one economic evaluation.

Two additional systematic reviews are listed in the appendix.

OVERALL SUMMARY OF FINDINGS

One health technology assessment evaluating the use of newer antiepileptic agents in children with epilepsy reported that the quality of RCTs available was generally poor and was insufficient to inform a prescribing strategy.[1] The newer agents showed similar efficacy to older antiepileptic drugs, and no clear conclusions on cost-effectiveness could be made.[1]

The four RCTs[2,3,4,5] varied in terms of patients studied, comparators used, study duration, and outcomes assessed. A summary of their characteristics and key findings with respect to both efficacy and safety is provided in Table 1.

Table 1. Safety and efficacy reported in RCTs

Study and Design Information	Population and Sample Size	Interventions	Results
Cho 2011[2]	Patients with epilepsy N=31	Levetiracetam vs. carbamazepine CR monotherapy duration: 4-6 weeks	Levetiracetam may increase sleep efficiency without major effects on sleep structure and with an overall effect on sleep parameters comparable to carbamazepine-CR
Labiner 2009[3] Double blind	Adults with partial seizures N=268	levetiracetam vs. lamotrigine adjunctive therapy	Adjunctive lamotrigine significantly improved Anger-Hostility and other mood symptom scale scores relative

Study and Design Information	Population and Sample Size	Interventions	Results
		duration: 20 weeks	to levetiracetam. Seizure frequency was similar.
Brodie 2007[4] Double blind, non-inferiority study	Adults with newly diagnosed epilepsy (partial or generalized tonic-clonic seizures) N=579	levetiracetam vs. carbamazepine CR monotherapy duration: 6 to 12 months	Seizure freedom rates were similar between groups. Withdrawals due to adverse events were 5% lower in levetiracetam group.
Coppola 2007[5] Open label	Children (aged 3.3 to 14 years) with newly diagnosed benign epilepsy with centrotemporal spikes N=39	levetiracetam vs. oxcarbazepine monotherapy duration: 12 to 24 months	No further seizures in 91% of levetiracetam and 72% of oxcarbazepine group. Similar rates of adverse events.

CR=controlled release

Three controlled, non-randomized studies[6,7,8] provided additional data on safety outcomes. One report stated that children exposed to levetiracetam in utero showed higher early cognitive development compared to those exposed to valproic acid.[6] One study used physician completed questionnaires to assess adverse events in patients with epilepsy and concluded that levetiracetam or lamotrigine use was associated with fewer adverse events than other antiepileptic drugs.[7] In another study, patients on levetiracetam monotherapy or combination therapy reported more behavioral changes than patients on other antiepileptic drugs.[8] The changes reported were both positive and negative, and aggression was a prominent feature.[8]

Four non-randomized studies[9,10,11,12] reported data regarding drug retention, a marker of drug tolerability and efficacy. Two studies showed higher retention rates with levetiracetam and lamotrigine than other antiepileptic agents.[9,10] Two reports, evaluating patients referred to the same tertiary epilepsy center, found that retention rates were higher and withdrawals due to adverse events were lower for those treated with levetiracetam than with topiramate.[11,12] Neurocognitive side effects from topiramate and mood disorders from levetiracetam led to drug discontinuation.[11,12]

A Korean economic study concluded that levetiracetam plus standard therapy in adults with refractory partial epilepsy has an incremental cost-effectiveness ratio of US$ 11,084 per quality adjusted life year gained (QALY) versus standard therapy alone.[13]

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Systematic reviews and meta-analyses

No literature identified

Randomized controlled trials

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Economic evaluations

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APPENDIX – FURTHER INFORMATION:

Systematic Review articles – study results not reported

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