TITLE:  Pregabalin Treatment for Patients with Fibromyalgia: Clinical Effectiveness

DATE:  30 July 2010

RESEARCH QUESTIONS:

1. What is the clinical effectiveness of pregabalin treatment for the management of symptoms of fibromyalgia?

2. What is the evidence regarding the use of pregabalin as a second-line therapy option for patients with fibromyalgia?

3. What are the adverse events and safety associated with pregabalin treatment for patients with fibromyalgia?

METHODS:

A limited literature search was conducted on key health technology assessment resources, including PubMed, Ovid: EMBASE, the Cochrane Library (Issue 7, 2010) University of York Centre for Reviews and Dissemination (CRD) databases, ECRI (Health Devices Gold), EuroScan, international health technology agencies, and a focused Internet search. The search was limited to English language articles published between January 1, 2005 and July 21, 2010. No filters were applied to limit the retrieval by study type. Internet links were provided, where available.

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:

HTIS 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 and non-randomized studies.

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One systematic review, three meta-analyses, and five randomized controlled trials were identified pertaining to the clinical effectiveness of and safety associated with pregabalin treatment for patients with fibromyalgia. No relevant health technology assessment reports or non-randomized trials were identified, and no information regarding the use of pregabalin as a second-line therapy option for patients with fibromyalgia was found. Additional information that may be of interest has been included in the appendix.

OVERALL SUMMARY OF FINDINGS:

Overall, evidence from meta-analyses and randomized controlled trials (RCTs) indicates that treatment with pregabalin at doses of 300 milligrams per day (mg/d) or more is effective in reducing pain\textsuperscript{1-5,7-9} and sleep disturbances\textsuperscript{1,2,5,7,8} and improving health-related quality of life\textsuperscript{3,9}, Patient Global Impression of Change scores\textsuperscript{5,7} and Fibromyalgia Impact Questionnaire scores\textsuperscript{5,7}. With respect to anxiety and depressed mood, two meta-analyses found no evidence for the effectiveness of pregabalin in treating depressed mood\textsuperscript{1,3}, one meta-analysis found pregabalin to be effective in decreasing anxiety\textsuperscript{3}, and one RCT found that pregabalin treatment effect on pain scores is not dependant on baseline depression or anxiety\textsuperscript{8}. Although most of the included studies concluded that pregabalin is a safe treatment option for patients with fibromyalgia\textsuperscript{2,5-7,9}, adverse events (e.g., somnolence\textsuperscript{2,4,7}, dizziness\textsuperscript{2,4,7}) were generally more common in patients taking pregabalin compared to placebo, and one trial reported a higher rate of discontinuation due to adverse events in the pregabalin group than in the placebo group.\textsuperscript{6} No relevant information regarding pregabalin as a second-line therapy was identified. Additional details regarding the included studies can be found in Table 1.

<table>
<thead>
<tr>
<th>Study Type, year</th>
<th>Interventions compared</th>
<th>Results</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meta-analysis, 2010\textsuperscript{1}</td>
<td>Duloxetine* (DLX)</td>
<td>PGB was superior to placebo for all outcomes except for depressed mood.</td>
<td>The drugs have different effects on the key symptoms of fibromyalgia.</td>
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<td></td>
<td>Milnacipran* (MLN)</td>
<td>PGB was superior to MLN for reduction in pain and sleep disturbance; superior to DLX for reducing fatigue.</td>
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<tr>
<td></td>
<td>Pregabalin* (PGB)</td>
<td>Risk of headache and nausea was lower for patients taking PGB than MLN and DLX; risk of diarrhea was lower for PGB than DLX.</td>
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<td></td>
<td>Placebo</td>
<td>There is evidence for short term (six month) efficacy of PGB.</td>
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<tr>
<td>Meta-analysis, 2010\textsuperscript{2}</td>
<td>Pregabalin*</td>
<td>Pain and sleep scores were better in patients receiving PGB.</td>
<td>All trial information was provided by Pfizer.</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>Proportion of patients achieving at least 50% pain relief was higher in the PGB group.</td>
<td></td>
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<tr>
<td>Study Type</td>
<td>Intervention</td>
<td>Key Findings</td>
<td>Limitations/Conclusion</td>
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<td>Meta-analysis, 2009³</td>
<td>Gabapentin* (GPT) Pregabalin*</td>
<td>No difference between placebo and PGB for serious adverse events, but more patients taking PGB had adverse effects (e.g., somnolence and dizziness).</td>
<td>External validity considered to be limited due to the exclusion of patients with severe somatic and mental disorders.</td>
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<tr>
<td>Systematic review and meta-analysis, 2009⁴</td>
<td>Pregabalin Placebo</td>
<td>Strong evidence for reduction of pain, improved health-related quality of life, and non-substantial reductions in fatigue and of anxiety, but no evidence for a reduction in depressed mood. Abstract does not specify which drug was superior.</td>
<td>Authors concluded that most patients who benefit from PGB will have moderate benefits and a minority will have substantial benefits.</td>
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<tr>
<td>RCT, 2008⁵</td>
<td>Pregabalin 300 mg/d, 450 mg/d, or 600 mg/d Placebo</td>
<td>PGB doses of 300 mg, 450 mg, and 600 mg are effective for pain reduction in patients with fibromyalgia. 600 mg PGB resulted in somnolence in 15% to 25% and dizziness in 27% to 46% of patients. Treatment discontinuation due to adverse events occurred in 19% to 28% of patients. Proportion of patients reporting an adverse event or a serious adverse event was not affected by dose. Serious adverse events were not more common in patients taking PGB.</td>
<td>Authors concluded that PGB is an important treatment option for patients with fibromyalgia.</td>
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<tr>
<td>RCT, 2008⁶</td>
<td>Pregabalin</td>
<td>Loss of response was longer in PGB-</td>
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<tr>
<td>Study</td>
<td>Treatment</td>
<td>Comparator</td>
<td>Results</td>
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<tr>
<td>RCT, 2008&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Pregabalin 300 mg/d, 450 mg/d, or 600 mg/d</td>
<td>Placebo</td>
<td>All three doses of PGB were associated with significant improvement in PGIC scores, pain scores, and sleep assessments.</td>
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<td>RCT, 2007&lt;sup&gt;8&lt;/sup&gt;</td>
<td>Pregabalin*</td>
<td>Placebo</td>
<td>PGB treatment effect on pain scores is not dependent on baseline depression or anxiety.</td>
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<tr>
<td>RCT, 2005&lt;sup&gt;9&lt;/sup&gt;</td>
<td>Pregabalin 150 mg/d, 300 mg/d, 450 mg/day</td>
<td>Placebo</td>
<td>450 mg/d PGB was associated with reduced average severity of pain, greater number of patients with improved pain scores, and improvement in several domains of health-related quality of life.</td>
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450 mg/d and 300 mg/d PGB were associated with significant improvements in sleep quality, fatigue, and global measures of change.

Discontinuation rates due to adverse events were similar in all medication and placebo groups.

*Authors concluded that PGB 450 mg/d was efficacious.

**Study abbreviations:**
- RCT = randomized controlled trial

**Dosages not provided in the abstract.**
REFERENCES SUMMARIZED:

Health technology assessments
No literature identified.

Systematic reviews and meta-analyses


Randomized controlled trials


Non-randomized studies
No literature identified.

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APPENDIX – FURTHER INFORMATION:

Systematic reviews and meta-analyses


Secondary analyses


Review articles


20. Yousefi P, Coffey J. For fibromyalgia, which treatments are the most effective? J Fam Pract. 2005;54(12):1094-5.

Additional references