Formulary Drug Listing Decisions

DESVENLAFAXINE

Indication(s)

Symptomatic relief of major depressive disorder (MDD).

DAC Recommendation

The Drug Advisory Committee (DAC) has recommended that desvenlafaxine not be listed on any WSIB formularies, as there is no evidence that it provides an advantage to comparators in the treatment of MDD.

The WSIB Decision

Based on the DAC's recommendation, the WSIB has decided **NOT** to list desvenlafaxine on any of the formularies at this time.

Formulary Status

Desvenlafaxine is NOT LISTED on WSIB formularies at this time.

Recommendation Highlights

- Desvenlafaxine is a selective serotonin and norepinephrine reuptake inhibitor (SNRI) and is marketed as Pristiq® in Canada. It is currently approved for the treatment of MDD.
- Desvenlafaxine is the active metabolite of venlafaxine (Effexor XR®, generics).
- Placebo-controlled trials have demonstrated modest efficacy for desvenlafaxine in the treatment of MDD. However, there are no randomized, controlled trials comparing desvenlafaxine to venlafaxine (its parent drug) which has a similar pharmacology and safety profile. There are also no head-to-head trials comparing desvenlafaxine with other antidepressants (e.g. selective serotonin reuptake inhibitors [SSRIs]).
- An independent review did not locate any trials assessing the efficacy of desvenlafaxine in the treatment of chronic non-cancer pain or anxiety disorders (e.g., post-traumatic stress disorder, generalized anxiety disorder, etc.).
- There is no evidence demonstrating any clear therapeutic or safety advantage for desvenlafaxine compared to venlafaxine or other comparators in the treatment of MDD.
- Desvenlafaxine is more costly than most relevant comparators proven efficacious and safe (e.g., venlafaxine, SSRIs). However, it has not demonstrated superior efficacy. Only one pharmacoeconomic study has been conducted. This cost-minimization study conducted by the manufacturer was considered flawed and its conclusions unsupported by the literature.
- **The DAC concluded that an independent review of the clinical efficacy, safety, and cost-effectiveness of desvenalfaxine in the treatment of MDD did not demonstrate any significant therapeutic or non-therapeutic advantage over appropriate comparators available in Canada.** Consequently, the DAC recommended that desvenlafaxine **NOT** be listed on any WSIB formulary.

Drug Profile

Products available in Canada:

Pristiq® (desvenlafaxine succinate)

Manufacturer: Wyeth Canada

wsib ONTARIO

DETAILED DISCUSSION

Background

Desvenlafaxine is a new antidepressant marketed as Pristiq® in Canada. The drug exerts its antidepressant effects through the inhibition of serotonin and norepinephrine reuptake in the central nervous system. Desvenlafaxine is an active metabolite of venlafaxine (Effexor XR®, generics). It has similar pharmacology and a nearly identical safety profile as venlafaxine.

Summary of Committee Considerations

The DAC considered an external, independent review of the clinical efficacy, safety, and cost-effectiveness of desvenlafaxine in the treatment of MDD and chronic non-cancer pain (CNCP). The review included published and unpublished randomized controlled trials (RCTs) that were at least single-blind.

No RCTs of desvenlafaxine in the treatment of CNCP were located. Accordingly, the review focused on the evidence of desvenlafaxine in the treatment of MDD. Desvenlafaxine has been compared to placebo in the treatment of MDD in eight published short-term (8-week) placebo-controlled trials (one placebo-controlled trial remains unpublished). Results from these trials were not consistent; some trials found no significant difference in changes from baseline in the Hamilton Rating Scale for Depression (HAM-D17) total score between desvenlafaxine and placebo, while others did. Doses studied ranged from 50mg to 400mg daily. A meta-analysis demonstrated there was no increased efficacy for doses over 50 mg daily. There are no published head-to-head trials comparing desvenlafaxine to other antidepressants in MDD.

One cost-minimization study conducted by the manufacturer was considered. This study compared the price of desvenlafaxine to venlafaxine and SSRIs. The results of this study showed that at standard doses, relevant comparators would be less costly than desvenlafaxine (except duloxetine and Paxil CR®). A major drawback of this study was that it assumed equal efficacy between drugs. This assumption is not supported by any randomized controlled trials, as there are no comparative studies available.

Pooled data from placebo-controlled trials indicate that desvenlafaxine has an adverse effect profile similar to other SRNIs. Some of the most commonly reported side effects including nausea, headache, and dry mouth appear to be dose-dependent. Desvenalfaxine appears to cause more nausea than venlafaxine while venlafaxine appears to be associated with greater loss of appetite.

Key guidelines were reviewed to establish standards of care. Current guidelines suggest the use of SSRIs, SNRIs, or other second-generation antidepressants as first-line treatment for MDD. There is currently no data to justify the choice of any second-generation antidepressant over another on the basis of efficacy, effectiveness, or quality of life.

The Ontario Drug Benefit Program does not list desvenlafaxine. The independent body that makes recommendations regarding drug listings to provincial plans has recommended that desvenlafaxine ***NOT*** be listed.

Based on the available evidence, the DAC concluded that there was no compelling evidence demonstrating a therapeutic or non-therapeutic advantage for desvenlafaxine over comparators in the treatment of depression. Furthermore, several alternative drug classes are available on the WSIB formularies that can meet the treatment needs of the majority of injured/ill workers. Hence, the DAC recommended that desvenlafaxine products not be listed on any WSIB formularies.

Revised: January 29, 2013