Formulary Drug Listing Decisions

ZIPRASIDONE

Indication(s)

Treatment of schizophrenia and related psychotic disorders, the treatment of acute manic or mixed episodes associated with bipolar disorder.

DAC Recommendation

The Drug Advisory Committee (DAC) recommended that ziprasidone not be listed on any WSIB formularies as there are no trials providing evidence that it demonstrates an advantage to comparators currently listed on the WSIB formularies.

The WSIB Decision

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

Formulary Status

*Ziprasidone is **NOT LISTED** on WSIB formularies at this time.*

Recommendation Highlights

- Ziprasidone is an antipsychotic medication marketed under the brand name Zeldox®. It is currently approved for the treatment of schizophrenia and acute manic or mixed episodes in bipolar affective disorder.
- No randomized-controlled (RCTs) studies of ziprasidone in the treatment of illnesses common to the WSIB (e.g., psychotic depression, depression, post-traumatic stress disorder [PTSD], or sleep disturbances) were located.
- A systematic review of RCTs in schizophrenia concluded that ziprasidone is *less effective* than olanzapine and risperidone, and as *effective (but not superior) to* quetiapine in improving core schizophrenia symptoms.
- Most ziprasidone trials have been of short duration and have not assessed clinically important outcomes like hospitalization, suicide and global severity and impression of illness.
- There is no evidence demonstrating any clear therapeutic or safety advantage for ziprasidone compared to other comparable agents in the treatment of psychotic symptoms.
- The average daily cost of ziprasidone is significantly greater than most other medications proven effective and safe in treating psychotic symptoms. The cost-effectiveness of ziprasidone in an environment similar to the WSIB has not been established.
- **The DAC concluded that an independent review of the clinical efficacy, safety, and cost-effectiveness of ziprasidone did not indicate any therapeutic or non-therapeutic advantage over appropriate comparators in schizophrenia.** Consequently, the DAC recommended ziprasidone NOT be listed on any WSIB formulary.

Drug Profile

Products available in Canada:

Zeldox® (ziprasidone)

Manufacturer:
Pfizer Canada Inc

wsib ONTARIO

DETAILED DISCUSSION

Background

Ziprasidone is a second-generation antipsychotic (SGA) marketed under the brand name Zeldox®. It is believed to exert its therapeutic effects through the antagonism of dopamine-2 (D_2) and serotonin 5-HT_{2A} receptors in the brain.

Ziprasidone is approved for the treatment of schizophrenia and acute manic or mixed episode of bipolar affective disorder, indications not common to work-related injuries/illnesses.

Summary of Committee Considerations

The DAC considered an external, independent review of the clinical efficacy, safety, and cost-effectiveness of ziprasidone in the treatment schizophrenia. Schizophrenia studies were considered in the review because no randomized-controlled trials (RCTs) investigating the efficacy of ziprasidone in the treatment of illnesses common to the WSIB (e.g., psychotic depression, depression, PTSD, or sleep disturbance) were located.

One systematic review and meta-analysis of RCTs with head-to-head comparisons of SGAs in the treatment of *schizophrenia* was identified, (the review included 9 ziprasidone trials). Ziprasidone was found to be *less effective* than olanzapine and risperidone. Ziprasidone was also found to be as effective as, *but not superior* to, quetiapine. Changes in the Positive and Negative Symptoms Scale (PANSS), a research tool measuring the severity of psychotic symptoms, were used to assess antipsychotic effect in all trials. Hospitalization rates, suicide, and global severity and impression of illness were not assessed (outcomes that are considered to be of greater clinical relevance). All trials were of short duration (up to six weeks).
The most commonly reported adverse events with ziprasidone included extrapyramidal symptoms, somnolence, nausea, and respiratory tract infection. Furthermore, ziprasidone was associated with an increased risk of QT prolongation, rash (in some cases utricaria), and weight gain. The long-term safety of ziprasidone is difficult to determine given the short duration of the trials.

Multiple studies, most of which were sponsored or co-authored by the manufacturer, have assessed the cost-effectiveness ziprasidone in the treatment of schizophrenia. A review of these studies concluded that their methodologies were generally weak. The cost or ziprasidone is higher than most comparators, yet there is insufficient evidence of clinical or quality of life benefits to justify its use over less costly alternatives.

Key guidelines were consulted to establish standards of care. Olanzapine plus antidepressant therapy is recommended as second-line in the treatment of psychotic depression. Adjunctive SGAs are considered second- or third-line in the treatment of PTSD. SGAs are not recommended in the treatment of sleep disorders in most individuals due to concerns regarding adverse effects.

The Canadian Expert Drug Advisory Committee (CEDAC) recommended that ziprasidone ONLY be listed for schizophrenia and schizoaffective disorder in patients who have failed a less expensive antipsychotic. The Ontario Drug Benefit Program lists ziprasidone due to a listing agreement with the manufacturer.

Based on the information considered, the DAC concluded that there was no compelling evidence demonstrating a therapeutic or non-therapeutic advantage for ziprasidone over comparators in the treatment of schizophrenia. Furthermore, several alternative medications are available on the WSIB formularies that can meet the treatment needs of the majority of workers. Hence, the DAC recommended ziprasidone not be listed on any WSIB formularies.

Revised: January 29, 2013