

Formulary Drug Listing Decisions

PALIPERIDONE

Indication(s)

Treatment of schizophrenia.

DAC Recommendation

The Drug Advisory Committee (DAC) recommended that paliperidone 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 paliperidone on any of the formularies at this time.

Formulary Status

Paliperidone IS NOT listed on WSIB formularies at this time.

Recommendation Highlights

- Paliperidone is an antipsychotic medication marketed in Canada under the brand name Invega®. It is currently approved by Health Canada for the treatment of schizophrenia.
- No randomized-controlled (RCTs) studies of paliperidone 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 paliperidone appears to be more effective than placebo and *comparable* but *not superior* to olanzapine in improving psychotic symptoms.
- Most paliperidone trials have been of short duration and have not assessed clinically important outcomes like hospitalization, suicide or global severity and impression of illness.
- There is no evidence demonstrating any clear therapeutic or safety advantage for paliperidone over appropriate comparators in the treatment of psychotic symptoms.
- The average daily cost of paliperidone is significantly greater than most other medications proven effective and safe in treating psychotic symptoms. The cost-effectiveness of paliperidone 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 paliperidone did not indicate any therapeutic or non-therapeutic advantage over appropriate comparators in schizophrenia.** Consequently, the DAC recommended paliperidone NOT be listed on any WSIB formulary.

Drug Profile

Products available in Canada:

Invega®
(paliperidone)

Manufacturer:
Janssen-Ortho Inc

DETAILED DISCUSSION

Background

Paliperidone is a second-generation antipsychotic (SGA) marketed under the brand name Invega®. Paliperidone is the major active metabolite of risperidone; hence, both appear to exert their antipsychotic effects through the antagonism of dopamine-2 (D₂) and serotonin 5-HT_{2A} receptors in the brain.

Paliperidone is approved for the treatment of schizophrenia, an indication 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 paliperidone in the treatment of schizophrenia. Schizophrenia studies were considered in the review because no randomized-controlled trials (RCTs) investigating the efficacy of paliperidone in the treatment of illnesses common to the WSIB (e.g., psychotic depression, depression, PTSD, or sleep disturbance) were located.

One systematic review of five RCTs comparing paliperidone to placebo or olanzapine in the treatment of *schizophrenia* was located. Paliperidone appeared to be better than placebo and *similar, but not superior*, to olanzapine in terms of improving psychotic symptoms. 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).

Paliperidone was associated with a higher incidence of tachycardia, QT prolongation, weight gain, and movement disorders compared to placebo. Sustained increases in prolactin levels have also been observed

with paliperidone treatment. Compared to olanzapine, paliperidone is associated with less weight gain but a higher incidence of movement disorders. The long-term safety of paliperidone is difficult to determine given the short duration of the trials.

Two studies sponsored and co-authored by the manufacturer have assessed the cost-effectiveness of paliperidone compared to other SGAs in the treatment of schizophrenia. The conclusion of both studies, that paliperidone is more effective and less costly than other SGAs, is considered highly questionable (given that paliperidone has no evidence of benefit in effectiveness or overall safety and costs more than many other agents).

Key guidelines were consulted to establish standards of care. Olanzapine plus antidepressant therapy is recommended as second-line treatment for 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 over adverse effects.

The Canadian Expert Drug Advisory Committee (CEDAC) recommended that paliperidone not be listed. The Ontario Drug Benefit Program lists paliperidone as a general benefit based on a listing agreement with the manufacturers.

Based on the information considered, the DAC concluded that there was no compelling evidence demonstrating a therapeutic or non-therapeutic advantage for paliperidone 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 paliperidone not be listed on any WSIB formularies.

Revised: January 29, 2013

The WSIB will consider all relevant facts and circumstances, and shall make its decision based upon the merits and justice of a particular case.