

Paliperidone

Product:

PALIPERIDONE (Invega®) 3mg, 6mg, 9mg extended-release tablets

Class of drugs:

Antipsychotic

Indication:

Treatment of schizophrenia

Manufacturer:

Janssen-Ortho Inc.

CED Recommendation

The CED recommended that paliperidone (Invega) not be funded on the basis that this drug has not been shown to provide important clinical benefits. Moreover, there is no evidence that paliperidone (Invega) offers any therapeutic or economic advantages over currently available treatments.

Executive Officer Decision

Taking the CED's recommendation into consideration, the Executive Officer decided list paliperidone (Invega) on the Ontario Drug Benefit Formulary based on a listing agreement with the manufacturer that addresses price and utilization.

Status

Listed on the Ontario Drug Benefit Formulary.

Highlights of Recommendation:

- ◆ Paliperidone (Invega) is an antipsychotic drug used to treat schizophrenia.
- ◆ The Committee considered six clinical studies, all of which were of short duration. When compared against placebo, paliperidone (Invega) was shown to provide small improvements in symptoms of schizophrenia, social functioning, and quality of life. However, long-term data are not available. Therefore, it is not known whether paliperidone (Invega) improves important clinical outcomes, such as rates of hospitalization and suicide.
- ◆ Few clinical studies compared paliperidone (Invega) directly with other antipsychotic drugs; therefore, it is difficult to draw conclusions about its efficacy relative to other treatments. There is no convincing evidence that paliperidone is clinically better than alternative therapies.
- ◆ The Committee noted that the parent drug of paliperidone (Invega) is risperidone. Risperidone is an antipsychotic drug that is listed on the Formulary. In the body, risperidone gets converted into paliperidone by the liver. The Committee questioned whether paliperidone (Invega) offers any meaningful benefits over risperidone. Although there are no direct comparison studies between the two drugs, their clinical effects are likely to be similar given that paliperidone is the active end-product of risperidone.
- ◆ Currently available clinical studies were too short to adequately assess this drug's harm, including the risk of hyperprolactinemia (abnormally high levels of the prolactin hormone in the blood), heart disorders, and weight gain. Because these are adverse effects seen with risperidone, it is likely that these are safety concerns with paliperidone (Invega) as well.
- ◆ Paliperidone (Invega) costs \$3.38 to \$10.12 per day, depending on the dose. This is significantly more expensive than risperidone at \$0.96 to \$4.79 per day. Without evidence that paliperidone (Invega) provides any efficacy or safety advantages over risperidone, the higher price could not be justified.
- ◆ The Committee expressed concerns regarding the risk of off-label use. Paliperidone belongs to a class of drugs called atypical antipsychotics. This class of drugs is often prescribed for the management of agitation in elderly patients with dementia, even though this indication is not approved and these drugs can cause significant harm, including death.
- ◆ **Overall, the Committee noted that paliperidone (Invega) has not been demonstrated to provide clinically important benefits, and its relative efficacy compared to other schizophrenia treatments has not been established. Paliperidone (Invega) is also more costly than risperidone. For these reasons, the Committee recommended that paliperidone (Invega) not be funded through the Ontario Public Drug Programs.**

Background:

Schizophrenia is a complex mental illness. Researchers believe that a biochemical imbalance in the brain causes the symptoms of schizophrenia, which may include hallucinations, delusions, disorganized thinking, impaired judgment, impulsiveness, social withdrawal, and difficulties with perception, memory, or abstract thinking.

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Although there is no cure for schizophrenia, antipsychotic medications can help control the symptoms of the illness by changing the balance of chemicals in the brain. Antipsychotic medications are only a part of a comprehensive treatment plan that includes education, counseling and social support programs.

Antipsychotic medications are grouped into classes according to their side effect profiles. Older, first-generation medications are known as conventional antipsychotics or neuroleptics; newer, second-generation agents are known as atypical antipsychotics. There are currently four oral atypical antipsychotics and 12 oral conventional agents listed on the Ontario Drug Benefit Formulary.

Paliperidone (Invega) is an atypical antipsychotic. Its parent drug is risperidone. In the body, risperidone is converted into paliperidone (Invega), which is the main active end-product responsible for the therapeutic effects of risperidone.

Detailed Discussion:

- ◆ The Committee considered six double-blind, randomized controlled studies in the review of paliperidone (Invega). Limitations of the studies included their short duration (6-10 weeks) and the high rates of patient withdrawal (upwards of 40-50% in some studies). All six were trials compared paliperidone (Invega) to placebo; only one study included a comparison to quetiapine (another atypical antipsychotic).
- ◆ When compared against placebo, paliperidone (Invega) was shown to provide improvements in symptoms of schizophrenia, social functioning and quality of life. When compared against quetiapine, paliperidone (Invega) was shown to provide small improvements in symptoms of schizophrenia. The Committee questioned whether the magnitudes of the reported improvements constitute meaningful benefits in clinical practice, when patients are not as closely monitored and the drug is used in a broad range of patients compared to those studied in the trial.
- ◆ Direct comparison studies are lacking to establish the relative efficacy and safety of paliperidone (Invega) compared with other schizophrenia treatments, most notably with risperidone.
- ◆ There are currently no long-term studies to assess whether paliperidone (Invega) impacts relevant clinical outcomes, such as rates of hospitalization and suicide.

- ◆ Furthermore, the clinical studies were too short to adequately evaluate the adverse effects of this drug. Side effects reported with paliperidone (Invega) are similar to those observed with risperidone and may include stomach upset, sleepiness, weight gain, extrapyramidal symptoms (e.g. slow or stiff movement), hyperprolactinemia, and cardiac disorders (e.g. fast, irregular heartbeat).
- ◆ Paliperidone (Invega) costs \$3.38 to \$10.12 per day, when taken in doses ranging from 3mg to 12mg. This is significantly more expensive than risperidone at \$0.96 to \$4.79 per day.
- ◆ Current evidence does not suggest that atypical antipsychotics have major advantages over the conventional antipsychotics when overall benefit, harm and withdrawals are considered. The Committee indicated that atypical antipsychotics are much more expensive than conventional antipsychotics, therefore must be closely evaluated for value for money.
- ◆ The Committee noted the risk for off-label use of this drug in patients with dementia. Atypical antipsychotic drugs are frequently used in the management of dementia, even though studies have found that their use in elderly patients has no important benefit and can cause significant harm, including death.
- ◆ Overall, the Committee noted that paliperidone (Invega) has not been demonstrated to provide clinically important benefits, and its relative efficacy compared to other schizophrenia treatments has not been established. Paliperidone (Invega) is also more costly than risperidone. For these reasons, the Committee recommended that paliperidone (Invega) not be funded through the Ontario Public Drug Programs.

CEDAC Recommendation:

(<http://www.cadth.ca/index.php/en/cdr/recommendations>)

The Canadian Expert Drug Advisory Committee (CEDAC) recommended that paliperidone (Invega) not be listed.



Ministry of
Health and Long-Term Care
Ontario Public Drug Programs

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