

## CEDAC FINAL RECOMMENDATION and REASONS for RECOMMENDATION

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### ZIPRASIDONE HYDROCHLORIDE (Zeldox™ – Pfizer Canada Inc.)

**Description:**

Ziprasidone is an antipsychotic agent that is approved for the treatment of schizophrenia and related psychotic disorders.

**Dosage Forms:**

20 mg, 40 mg, 60 mg and 80 mg capsules. The recommended dose ranges from 20 mg to 80 mg given twice daily.

**Recommendation:**

The Canadian Expert Drug Advisory Committee (CEDAC) recommends that ziprasidone be listed for the treatment of schizophrenia and schizoaffective disorders in patients who have failed a trial of less expensive antipsychotic agents due to a contraindication, intolerance or lack of response.

**Reasons for the Recommendation:**

1. Randomized controlled trials (RCTs) have demonstrated that ziprasidone is generally as effective as comparative antipsychotic agents in patients with schizophrenia or schizoaffective disorders.
2. There is insufficient evidence from these trials that ziprasidone offers a therapeutic advantage over less expensive alternative antipsychotic agents.

**Summary of Committee Considerations:**

The Committee considered a systematic review of double-blind RCTs comparing ziprasidone with other antipsychotic agents in patients with schizophrenia and related psychotic disorders. Fifteen trials comparing ziprasidone with olanzapine (6 trials), haloperidol (4 trials), risperidone (2 trials), chlorpromazine (1 trial), clozapine (1 trial) and multiple comparators (1 trial), and ranging in duration from six weeks to 18 months met the inclusion criteria for the systematic review. Four of the trials also had extension phases with follow-up to a maximum of three years.

There is insufficient evidence from these trials that ziprasidone offers a therapeutic advantage or disadvantage compared to other antipsychotic agents with respect to clinically important

outcomes such as mortality, suicidal ideation, suicide attempts or quality of life. In general, ziprasidone produced improvements from baseline in the Positive and Negative Syndrome Scale (PANSS) that were similar to alternative antipsychotic agents.

Adverse events were reported in more ziprasidone than olanzapine subjects and in fewer ziprasidone than haloperidol subjects. Ziprasidone was associated with less weight gain versus olanzapine or clozapine, while nausea appeared to be more common with ziprasidone versus olanzapine and haloperidol. Ziprasidone also appeared to reduce total cholesterol and LDL cholesterol compared to olanzapine, and to a lesser extent, risperidone. Prolongation of the QT interval with potential for progression to torsades de pointes, is the most significant safety concern associated with ziprasidone.

Ziprasidone costs \$3.78 per day at doses of 40 mg to 80 mg twice daily. This is more costly compared to first generation antipsychotic agents such as haloperidol (\$0.21 to \$0.63 for 4 mg to 20 mg daily) and perphenazine (\$0.22 to \$0.50 for 12 mg to 64 mg daily) but similar in cost to generic risperidone (\$0.96 to \$4.79 for 2 mg to 10 mg daily) and less expensive compared to the daily cost of olanzapine (\$2.53 to \$10.13 for 5 mg to 20 mg daily) and quetiapine (\$3.86 to \$7.73 for 300 mg to 600 mg daily).

**Of Note:**

1. Both published and unpublished data were reviewed and taken into consideration in making this recommendation.
2. The Committee was aware that antipsychotic agents are widely used to treat agitation and behavioural problems in elderly patients with dementia, but concerns have been raised regarding the safety of treating these patients with antipsychotics.

**Background:**

CEDAC provides formulary listing recommendations to publicly funded drug plans. Recommendations are based on an evidence-based review of the medication's effectiveness and safety and an assessment of its cost-effectiveness in comparison to other available treatment options. For example, if a new medication is more expensive than other treatments, the Committee considers whether any advantages of the new medication justify the higher price. If the recommendation is not to list a drug, the Committee has concerns regarding the balance between benefit and harm for the medication, and/or concerns about whether the medication provides good value for public drug plans.

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**Common Drug Review**