



Canadian Agency for  
Drugs and Technologies  
in Health

# COMMON DRUG REVIEW

## CEDAC FINAL RECOMMENDATION

### **ARIPIPRAZOLE – REQUEST FOR ADVICE**

**(Abilify – Bristol-Myers Squibb Canada)**

**Indication: Schizophrenia and Related Psychotic Disorders**

This recommendation supersedes the CEDAC recommendation for this drug and indication dated April 27, 2010.

#### **Recommendation:**

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

#### **Reason for the Recommendation:**

At the new submitted price, the average daily cost of treatment with aripiprazole is within the range of most of the costs of atypical agents currently reimbursed by participating drug plans.

#### **Background:**

Aripiprazole has a Health Canada indication for the treatment of schizophrenia and related psychotic disorders, which is the focus of this recommendation. Aripiprazole also has a Health Canada indication for the acute treatment of manic or mixed episodes in bipolar I disorder. It has partial agonist activity at the dopamine D2 and serotonin 5-HT1A receptors and antagonist activity at the serotonin 5-HT2A receptors.

The Health Canada-recommended starting dose for aripiprazole is 10 mg to 15 mg once a day, with a maximum daily dose of 30 mg. It is available as 2 mg, 5 mg, 10 mg, 15 mg, 20 mg, and 30 mg tablets.

#### **Submission History:**

Aripiprazole was previously reviewed by CEDAC for the same indication (schizophrenia and related psychotic disorders) and received a recommendation of “do not list” (see Notice of CEDAC Final Recommendation, April 27, 2010), with an “of note” that indicated that a reduced price would increase the likelihood of a recommendation to “list” or “list with criteria.” This updated aripiprazole recommendation is being made subsequent to a Request for Advice from

## Common Drug Review

CEDAC Meeting – June 15, 2011

Notice of CEDAC Final Recommendation – July 18, 2011

© 2011 CADTH

Page 1 of 3

the Common Drug Review (CDR) participating drug plans, based on a reduced price that the manufacturer is offering to individual drug plans.

## Summary of CEDAC Considerations:

### ***Clinical Evidence***

In addition to the information prepared by the CDR for the original consideration of aripiprazole, the Committee considered a clinical brief indicating that no new studies met the inclusion criteria of the original systematic review.

The original systematic review included 12 randomized controlled trials (RCTs) comparing aripiprazole with other antipsychotic agents. Two RCTs reported no statistically significant differences in total Positive and Negative Syndrome Scale (PANSS) scores between aripiprazole and haloperidol or perphenazine. In two RCTs evaluating olanzapine, statistically significantly greater improvements in the total PANSS score were observed for olanzapine compared with aripiprazole; however, the improvement was less than 15 points in both trials and the clinical significance of these results is uncertain. Brief Psychiatric Rating Scale (BPRS) results generally correlated with PANSS results. In one trial, ziprasidone was non-inferior to aripiprazole based on changes in clinical global impression of severity, but not based on changes in the BPRS. The only study reporting quality of life found no statistically significant difference between aripiprazole and perphenazine. In all studies, serious adverse events, adverse events, and withdrawals due to adverse events were similar between treatment groups.

As there was no additional clinical information to supplement the 2010 CDR review of aripiprazole, the Committee maintained that the efficacy of aripiprazole is similar to other atypical antipsychotic agents. As in the discussion at the 2010 CEDAC meeting, the Committee noted that antipsychotic agents are often used off-label to treat agitation and behavioural problems in elderly patients with dementia, and concerns have been raised regarding the safety and efficacy of treating these patients with antipsychotic agents.

### ***Cost and Cost-Effectiveness***

The Committee considered new pricing information available since the original review of aripiprazole. At the time of the original review, the average daily cost of aripiprazole was \$4.50 (15 mg).

Since the original review of aripiprazole, the price of aripiprazole has been reduced to \$3.78 for strengths of 10 mg and higher. The prices for the 2 mg and 5 mg tablets remain the same as in the original submission (\$2.91 and \$3.28, respectively). In addition, the costs of some comparator atypical agents have also changed.

There is significant variation in drug prices for atypical agents across the participating drug plans; as a result, there were no consistent findings. For example, in Ontario, at recommended daily doses, aripiprazole (\$3.78; 10 mg to 30 mg) is similar in cost to ziprasidone (\$3.30 to \$3.78; 40 mg to 160 mg), lower than paliperidone (\$3.52 to \$10.41; 3 mg to 12 mg), but higher than generic olanzapine (\$0.90 to \$3.59; 5 mg to 20 mg), risperidone (\$1.21 to \$2.42; 4 mg to 8 mg), and quetiapine (\$0.97 to \$1.93; 400 mg to 800 mg). For other drug plans (such as British Columbia, Alberta, Manitoba, New Brunswick, Nova Scotia, and Newfoundland), the range in daily costs of olanzapine (\$1.62 to \$11.24), quetiapine (\$1.75 to \$5.90), and risperidone

---

## Common Drug Review

## Common Drug Review

(\$2.07 to \$5.26) is wider, resulting in less pronounced differences compared with aripiprazole. At current prices, the daily cost of aripiprazole is within the range of most of the costs of atypical agents currently reimbursed by participating drug plans.

The Committee noted that prices and the listing status of the above agents differ across the jurisdictions, and that any potential listing recommendation of aripiprazole should allow for such differences.

### **CEDAC Members:**

Dr. Robert Peterson (Chair), Dr. Anne Holbrook (Vice-Chair), Dr. Michael Allan, Dr. Ken Bassett, Dr. Bruce Carleton, Dr. Doug Coyle, Mr. John Deven, Dr. Alan Forster, Dr. Laurie Mallery, Mr. Brad Neubauer, Dr. Lindsay Nicolle, Dr. Yvonne Shevchuk, and Dr. James Silvius.

### **June 15, 2011 Meeting**

#### **Regrets:**

One CEDAC member did not attend

#### **Conflicts of Interest:**

None

### **About this Document:**

CEDAC provides formulary listing recommendations to publicly funded drug plans. Both a technical recommendation and plain language version of the recommendation are posted on the CADTH website when available.

CDR clinical and pharmacoeconomic reviews are based on published and unpublished information available up to the time that CEDAC made its recommendation.

The manufacturer has reviewed this document and has not requested the removal of confidential information in conformity with the *CDR Confidentiality Guidelines*.

The Final CEDAC Recommendation neither takes the place of a medical professional providing care to a particular patient nor is it intended to replace professional advice.

CADTH is not legally responsible for any damages arising from the use or misuse of any information contained in or implied by the contents of this document.

The statements, conclusions, and views expressed herein do not necessarily represent the view of Health Canada or any provincial, territorial, or federal government or the manufacturer.

---

## Common Drug Review