Canadian Expert Drug Advisory Committee
Final Recommendation – Plain Language Version

ARIPIPRAZOLE – REQUEST FOR ADVICE
(Abilify – Bristol-Myers Squibb Canada)
Indication: Schizophrenia and Related Psychotic Disorders

This recommendation takes the place of the CEDAC recommendation for this drug and indication dated April 27, 2010.

Recommendation:

The Canadian Expert Drug Advisory Committee (CEDAC) recommends that Abilify, which is also called aripiprazole, be listed by Canada's publicly funded drug plans for the treatment of schizophrenia and schizoaffective disorders in patients who have a contraindication (unable to take a drug for medical reasons) to less expensive antipsychotic agents, or who tried and failed treatment with less expensive antipsychotic agents due to side effects or a lack of response.

Reason for the Recommendation:

At the new submitted price, the average daily cost of treatment with Abilify is within the range of most of the costs of other newer antipsychotic medications currently reimbursed by participating drug plans.

Background:

Abilify belongs to a class of drugs called antipsychotics. Antipsychotic medications affect the chemicals that allow communication between nerve cells (neurotransmitters). Illnesses that affect the brain, such as schizophrenia, may be due to certain chemicals in the brain being out of balance. These imbalances may cause some of the symptoms that the patient may be experiencing. Exactly how Abilify works is unknown. However, it seems to adjust the balance of chemicals called dopamine and serotonin.

Abilify has a Health Canada indication for the treatment of schizophrenia and related psychotic disorders, which is the focus of this recommendation. Abilify also has a Health Canada indication for the treatment of manic or mixed episodes in bipolar I disorder.

The Health Canada-recommended starting dose for Abilify 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:

Abilify 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" stating that a reduced price would increase the likelihood of a recommendation to "list" or "list with criteria". This updated Abilify recommendation is being made after a Request for Advice was received from 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 that the CDR prepared for the original consideration of Abilify, the Committee considered a clinical brief indicating there were no new studies that met the inclusion criteria of the original CDR review.

The original CDR review included 12 studies comparing Abilify with other antipsychotic medications. Two studies found that Abilify compared with haloperidol (also called Haldol) or perphenazine (also called Trilafon) had about the same total Positive and Negative Syndrome Scale (PANSS) scores. In two studies that looked at olanzapine (also called Zyprexa), greater improvements in the total PANSS score were seen for olanzapine compared with Abilify; however, the improvement was less than 15 points in both studies, and the importance of these results is not certain. Brief Psychiatric Rating Scale (BPRS) results generally were linked with PANSS results. In one study, ziprasidone (also called Zeldox) was not worse than Abilify 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 real difference between Abilify and perphenazine. In all studies, serious side effects, side effects, and stopping participation in the study because of side effects were similar, regardless of the treatment that the patient received.

As there was no additional clinical information to add to the 2010 CDR review of Abilify, the Committee kept its previous conclusion that the effectiveness of Abilify is similar to other, newer antipsychotic medications. As in the discussion at the 2010 CEDAC meeting, the Committee noted that antipsychotic medications are often used off label (without Health Canada indication) to treat agitation and behaviour problems in elderly patients with dementia, and concerns have been raised regarding the safety and effectiveness of treating these patients with antipsychotic medications.

Cost and Cost-Effectiveness

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

Since the original review of Abilify, the price of Abilify has been reduced to $3.78 for strengths of 10 mg and higher. The prices of 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 of the other, newer antipsychotic medications have also changed.

There is a wide range in drug prices for newer antipsychotic medications across the participating drug plans; as a result, there were no constant findings. For example, in Ontario, at

recommended daily doses, Abilify ($3.78; 10 mg to 30 mg) is similar in cost to ziprasidone ($3.30 to $3.78; 40 mg to 160 mg), costs less than paliperidone (also called Invega, $3.52 to $10.41; 3 mg to 12 mg), but costs more than the following generic medications: 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; 300 mg to 600 mg). For other drug plans (such as British Columbia, Alberta, Manitoba, New Brunswick, Nova Scotia, and Newfoundland), the ranges in daily costs of olanzapine ($1.62 to $11.24), quetiapine ($1.75 to $5.90), and risperidone ($2.07 to $5.26) are wider, and therefore closer to the costs of Abilify. At current prices, the daily cost of Abilify is within the range of most of the costs of newer antipsychotic medications currently reimbursed by participating drug plans.

The Committee noted that prices and the listing status of the above medications vary across the jurisdictions, and that any potential listing recommendation of Abilify 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
The information contained within this plain language version of the Canadian Expert Drug Advisory Committee (CEDAC) Recommendation about this drug is based on the information found within the corresponding technical version of the CEDAC Recommendation.

In making its recommendation, CEDAC considered the best clinical and pharmacoeconomic evidence available, up to that time. Health care professionals and those requiring more detailed information are advised to refer to the technical version available in the CDR Drug Database on the CADTH website (www.cadth.ca).

Background on CEDAC

CEDAC is a committee of the Canadian Agency for Drugs and Technologies in Health (CADTH). The committee is made up of drug evaluation experts and public members. CEDAC provides recommendations about whether or not drugs should be listed for coverage through the participating publicly funded drug plans; however, the individual drug plans make their own decision about whether or not to cover a drug.

In making its recommendations, CEDAC decides if the drug under review ought to be covered by the participating public drug plans based on an evidence-informed review of the medication's effectiveness and safety, and based on an assessment of its cost-effectiveness in comparison with other available treatments. Patient information submitted by Canadian patient groups is included in the CDR reviews and used in the CEDAC deliberations.

The 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.

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The manufacturer has reviewed this document and has not requested the deletion of any confidential information.