Committee to Evaluate Drugs (CED)

Recommendations and Reasons

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Lurasidone for schizophrenia

Product: lurasidone hydrochloride (Latuda®)

Class of Drugs: second-generation antipsychotic (SGA)

Reason for Use: schizophrenia

Manufacturer: Sunovion Pharmaceuticals Canada Inc.

Date of Review: February 6, 2013 and January 15, 2014

CED Recommendation

The CED recommended that lurasidone (Latuda®) be funded for the management of schizophrenia according to specific criteria. The CED noted that although lurasidone has not been shown to provide clinical advantages over funded alternatives, the additional treatment choice provided by this drug could be valuable.

Executive Officer Decision*

Based on the CED's recommendation and an agreement with the manufacturer to help address concerns raised by the CED, the Executive Officer decided to fund lurasidone (Latuda®) on the Ontario Drug Benefit Formulary as a General Benefit.

Funding Status*

Funded on the Ontario Drug Benefit Formulary as a General Benefit.

* *This information is current as of the posting date of the document. For the most up-to-date information on Executive Officer decision and funding status, see: www.health.gov.on.ca/en/pro/programs/drugs/status_single_source_subm.aspx.*

Ontario

Highlights of Recommendation:

- Randomized controlled studies showed that lurasidone demonstrated benefit over placebo in mean change from baseline in the Positive and Negative Syndrome Scale (PANSS).
- Robust direct comparison studies are lacking to determine the effectiveness and safety of lurasidone relative to other antipsychotic drugs.
- The use of lurasidone is associated with extrapyramidal symptoms (movement disorders), specifically akathisia (restlessness) and Parkinsonism.
- At the list price, the cost of lurasidone falls in the middle of the price range for available alternatives.
- The CED noted that schizophrenia is an illness for which individualized treatment plans are necessary and a greater range of choice for patients is valuable.

Background:

Schizophrenia is a mental illness that interferes with the ability to perceive reality, manage emotions, organize thoughts and communicate with others. It is characterized by positive symptoms (e.g., delusions) and negative symptoms (e.g., lack of emotional expressiveness). Antipsychotic medications are the cornerstone of treatment for schizophrenia and are classified as either typical or atypical antipsychotics.

The typical antipsychotic drugs act at the dopamine D2 receptors in the brain and are associated with an increased incidence of extrapyramidal (EPS) side effects, such as rigidity or akathisia. The atypical, or second-generation, antipsychotic drugs (SGAs) act at both D2 receptors and serotonin (5-HT2a) receptors in the brain and are thought be be associated with lower risks of EPS.

Detailed Discussions:

- The CED reviewed lurasidone twice, initially in February 2013, and again in January 2014 following a resubmission from the manufacturer to Ontario and to the Common Drug Review.
- For these evaluations, the CED considered:
    - Findings of the Common Drug Review (CDR) and the recommendations of the Canadian Drug Expert Committee (CDEC);
    - Information in the manufacturer's submissions;
    - Submissions from two patient groups.
- The focus of the CED's initial review was nine double-blind, randomized controlled studies evaluating the efficacy and safety of lurasidone for the treatment of schizophrenia. The Positive and Negative Syndrome Scale (PANSS) was assessed as a primary or secondary endpoint in all nine studies. Several studied doses of lurasidone (i.e., 40mg, 80mg, 160mg) exceeded the minimal clinically important difference (MCID) of an absolute 15-point reduction in PANSS score from baseline.

- None of the nine studies were powered to determine the comparative efficacy of lurasidone versus other SGAs. The efficacy of lurasidone compared to other antipsychotics is uncertain.
- Notable side effects associated with lurasidone in the studies include extrapyramidal symptoms, specifically akathisia and Parkinsonism. These side effects were dose-related.
- At its January 2014 review, the CED evaluated additional data submitted by the manufacturer, including an indirect treatment comparison meta-analysis of lurasidone against other SGAs (aripiprazole and ziprasidone) and a second meta-analysis comparing safety and efficacy of 15 antipsychotic drugs and placebo for schizophrenia.
- The indirect meta-analysis failed to demonstrate a difference in the clinical benefit of lurasidone compared with aripiprazole and ziprasidone. The meta-analysis of 15 antipsychotics ranked lurasidone as one of the least efficacious drugs included in the analysis, although there may be a small advantage with respect to weight gain compared to older SGAs.
- The manufacturer submitted a confidential price for lurasidone. At the list price, the cost of lurasidone falls in the middle of the price range for available alternatives.
- At the CED's initial review in 2013, lurasidone was approved only for acute treatment of schizophrenia. Health Canada subsequently approved its use in the management of schizophrenia, removing previous CED concerns regarding off-label use in the chronic setting.
- The CED reviewed two patient group submissions. The submissions indicated that schizophrenia significantly impacts the lives of patients and families. Treatment wishes include access to drugs that are effective and have fewer side effects. The CED acknowledged that patients with schizophrenia respond differently to various antipsychotics and treatment is individualized.
- Overall, the CED noted that there is a lack of direct comparison data on the efficacy and safety of lurasidone relative to other SGAs. There is no evidence to indicate that lurasidone provides a clear therapeutic advantage over funded alternatives. The CED recognized that patients with schizophrenia could benefit from additional treatment choices.

Committee to Evaluate Drugs (CED)

The Committee to Evaluate Drugs (CED) is comprised of practicing physicians, pharmacists, health economists, and patient representatives. In conducting its review, the CED considers data contained in the drug manufacturer's submission, input provided by patient groups, findings from the national Common Drug Review and the pan-Canadian Oncology Drug Review, and other scientific information as necessary.

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