Lopinavir/Ritonavir

Product:
LOPINAVIR/RITONAVIR (Kaletra®) 200/50mg tablet

Class of drugs:
Antiretroviral agent; protease inhibitor

Indication:
Treatment of HIV infection

Manufacturer:
Abbott Laboratories Ltd.

CED Recommendation

The CED recommended that lopinavir/ritonavir (Kaletra) 200mg/50mg tablet be listed on the Ontario Drug Benefit (ODB) Formulary as a General Benefit via the Facilitated Access Mechanism. The CED's recommendation was made on the basis that this new formulation of lopinavir/ritonavir (Kaletra) appears to be comparable in efficacy, safety and cost to the currently funded 133/33mg soft gel capsule.

Executive Officer Decision

Based on the CED's recommendation and a negotiated pricing agreement with the manufacturer, the Executive Officer decided to list lopinavir/ritonavir (Kaletra) 200/50mg tablet on the ODB Formulary as a General Benefit via the Facilitated Access Mechanism.

Status

Funding available through the Ontario Public Drug Programs.

Highlights of Recommendation:

- Lopinavir/ritonavir (Kaletra) is a combination product that contains two drugs used to treat Human Immunodeficiency Virus (HIV), the virus that causes Acquired Immune Deficiency Syndrome (AIDS). Kaletra 133mg/33mg soft gel capsule is already listed on the Formulary. Lopinavir/ritonavir (Kaletra) 200mg/50mg tablet is a new formulation that does not require refrigeration and can be taken with or without food. The manufacturer intends to phase out the 133mg/33mg soft gel capsule.
- Available evidence appears to support that lopinavir/ritonavir (Kaletra) 200mg/50mg tablet is similar to the 133mg/33mg soft gel capsule in terms of efficacy and safety.
- There is no evidence to support that lopinavir/ritonavir (Kaletra) 200mg/50 mg tablet offers any therapeutic advantages (e.g. improved tolerability, improved adherence) over the soft gel capsule.
- The Ministry negotiated a pricing agreement with the manufacturer.
- **Overall, the Committee noted that lopinavir/ritonavir (Kaletra) 200mg/50mg tablet is comparable to the currently listed 133mg/33mg soft gel capsule with respect to efficacy, safety and cost.**

Background:

Human Immunodeficiency Virus (HIV) is the virus that causes Acquired Immune Deficiency Syndrome (AIDS). Although there is no cure for HIV, antiretroviral drugs can help patients avert the clinical consequences of HIV infection by restoring immune function, improving quality of life and reducing HIV-related complications and death. Antiretroviral drugs work by lowering the amount of virus in the patient's blood (called the viral load).

Lopinavir/ritonavir (Kaletra) contains two drugs that belong to a class called protease inhibitors. Protease inhibitors work by blocking an enzyme that is required for the reproduction of the HIV. Ritonavir increases the blood levels of lopinavir by interfering with its metabolism, resulting in higher and more sustained levels of lopinavir in the blood.

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Detailed Discussion:

- The Committee reviewed this drug on two occasions, initially in February 2007 and again in July 2007. Both published and unpublished data were considered as a part of this review.
- Evidence supporting lopinavir/ritonavir (Kaletra) 200mg/50mg tablet comes from clinical trial data as well as bioequivalence data.
- Results from the submitted bioequivalence study comparing lopinavir/ritonavir (Kaletra) 200mg/50mg tablet to the 133mg/33mg soft gel capsule demonstrated that the two formulations are not bioequivalent. In particular, the peak concentration (Cmax) of ritonavir was higher in the tablet formulation.
- Evidence from clinical trials indicated that the difference in bioavailability between the 200mg/50mg tablet and the 133mg/33mg soft gel capsule did not result in any clinically important differences in safety or tolerability.
- There is no evidence that lopinavir/ritonavir (Kaletra) 200mg/50mg tablet offers any therapeutic advantages (e.g. improved tolerability, improved adherence) over the soft gel capsule.
- The most common adverse events reported with lopinavir/ritonavir were gastrointestinal symptoms, fatigue, and headache.
- The Ministry negotiated a pricing agreement with the manufacturer.
- Overall, the Committee noted that lopinavir/ritonavir (Kaletra) 200mg/50mg tablet is comparable to the currently listed Kaletra 133mg/33mg soft gel capsule with respect to efficacy, safety, tolerability, and cost.

CEDAC Recommendation:

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

The Canadian Expert Drug Advisory Committee (CEDAC) did not review lopinavir/ritonavir (Kaletra) 200mg/50mg tablet.

Ontario

Ministry of
Health and Long-Term Care
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