Imatinib (for GIST)

Product:
IMATINIB (Gleevec®),
100mg and 400mg oral tablet

Class of drugs:
Protein kinase inhibitor/anti-cancer agent

Indication:
Treatment of gastrointestinal stromal tumours (GIST)

Manufacturer:
Novartis Pharmaceuticals Canada Inc.

CED Recommendation

The CED recommended that imatinib (Gleevec) be funded through Individual Clinical Review/Exceptional Access Program for the treatment of inoperable and/or metastatic gastrointestinal stromal tumours (GIST).

Executive Officer Decision

Based on the CED's recommendation, the Executive Officer has decided to provide public funding for imatinib (Gleevec) for the treatment of unresectable and/or metastatic gastrointestinal stromal tumours (GIST) through Individual Clinical Review/Exceptional Access Program according to specific criteria.

Status

Funding available through the Ontario Public Drug Programs under Individual Clinical Review/Exceptional Access Program, according to specific criteria.

Highlights of Recommendation:

- Imatinib (Gleevec) is used to treat gastrointestinal stromal tumours (GIST), a rare stomach and intestinal cancer.
- Imatinib (Gleevec) may benefit patients who cannot have their tumours surgically removed or who have metastatic (advanced) disease.
- Imatinib (Gleevec) therapy costs approximately $3,600 a month, at a dose of 400 mg daily.
- Imatinib (Gleevec) for GIST has been funded through the Individual Clinical Review (ICR) mechanism, where requests are reviewed on a case-by-case basis.
- The CED noted that there is no high-quality evidence to support whether imatinib (Gleevec) improves patients' survival and there is uncertainty about whether using imatinib (Gleevec) to treat GIST provides reasonable value-for-money.
- However, the CED also noted that there is currently no other treatment available for this rare cancer and imatinib (Gleevec) is being used as the standard treatment.
- **Overall, the CED felt that the current evidence is not strong enough to support formulary listing of imatinib (Gleevec) and consideration on a case-by-case basis is reasonable.**
- The Committee recommended that imatinib (Gleevec) continue to be considered through ICR/Exceptional Access Program for the treatment of unresectable and/or metastatic GIST according to specific clinical criteria. (Please refer to the "Detailed Discussion" section for details of the criteria.)

Background:

Gastrointestinal stromal tumours (GIST) are a type of rare stomach and intestinal cancer.

The term "metastatic" describes a cancer that has spread to organs distant from the original tumor site. Metastatic GIST is the most advanced stage of the disease.

Studies show that GIST that cannot be removed by surgery or that has spread is usually not responsive to chemotherapy.

Radiation therapy is also unsuitable for treating this type of disease.

Until recently, patients have usually been offered treatments that help with the symptoms GIST causes. Currently, imatinib (Gleevec) is the standard of treatment for this disease.

Detailed Discussion:

- The manufacturer, Novartis Pharmaceuticals Canada Inc., asked the Ministry of Health and Long-Term Care to consider listing imatinib (Gleevec) for GIST on the ODB Formulary as a Limited Use benefit, to allow more patients to access the medication.
- Imatinib (Gleevec) had been covered under the ICR mechanism for the treatment of inoperable and/or metastatic GIST.
- The Committee acknowledged that there are no randomized controlled trials comparing imatinib (Gleevec) either to placebo or to best supportive care. This makes quantifying the benefits attributed to imatinib (Gleevec) statistically difficult. The Committee also noted that treating such patients with imatinib (Gleevec) has already gained wide acceptance among oncologists around the world.

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- The published data available on imatinib (Gleevec) for the treatment of unresectable and/or metastatic GIST is Phase II data reporting improvements in response rates. As such, imatinib (Gleevec) has become a standard in the treatment of unresectable and/or metastatic GIST even though no Phase III randomized clinical trial data is available reporting overall survival benefits.
- The recommendation for an initial dose of 400mg per day is based on analyses of two clinical trials that compared two doses (400mg/day versus 800 mg/day) of imatinib (Gleevec). A higher dose has not been shown to increase overall survival in patients compared with the lower dose.
- One trial reported 23% of patients experienced serious adverse events. Another trial reported that 32.3% patients on imatinib (Gleevec) 400 mg/day and 50.2% patients on 800 mg/day had at least one serious adverse event. The most frequent adverse effects were anemia (93%) and granulocytopenia (42%), edema (80%), fatigue (74%), nausea (55%), and skin rash (37%), most of which were described as mild to moderate.
- A higher dose is generally tolerable, although there appears to be a significant increase in anemia and fatigue, according to one clinical trial.
- Overall, the Committee noted that although imatinib (Gleevec) has been adopted as the standard of care for the treatment of unresectable and/or metastatic GIST, the current evidence relies on response rates reported in Phase II data. However, it is unlikely that placebo controlled, randomized data will be forthcoming in this setting. With this gap in evidence, it is difficult to evaluate cost-effectiveness of this treatment regimen.
- Given that there is no alternative treatment for this rare cancer, the Committee felt that it was reasonable for requests to continue to be considered through ICR/Exceptional Access Program under the following criteria:
  - *For the treatment of patients with Gastrointestinal Stromal Tumours (GISTs), where:*
    - *Tumour is not surgically resectable (metastatic or recurrent)*
    - *Pathology has been confirmed with c-kit positivity*

Cancer Care Ontario (CCO) Information:

Information on CCO chemotherapy regimens for GIST is available at: http://www.cancercare.on.ca/index_chemoRegimensbyDisease.htm

The Sarcoma Disease Site Group (DSG) Program in Evidence Based Care guideline for imatinib (Gleevec) in GIST is available at: http://www.cancercare.on.ca/index_sarcomaGuidelines.htm

CEDAC Recommendation:

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

The Canadian Expert Drug Advisory Committee (CEDAC) did not review imatinib (Gleevec).

Ontario

Ministry of
Health and Long-Term Care
Ontario Public Drug Programs

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