# RECOMMENDATION on RECONSIDERATION and REASONS for RECOMMENDATION

## GEFITINIB 250 mg tablets (Iressa--AstraZeneca)

**Description:**
Gefitinib is an orally-active, selective epidermal growth factor receptor tyrosine kinase inhibitor, indicated as monotherapy for the third line treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of prior platinum-based and docetaxel chemotherapy. It has been granted conditional approval by the Therapeutics Products Directorate--conditional upon the completion of randomized controlled trials confirming clinical benefit.

**Recommendation on Reconsideration:**
CEDAC recommends that gefitinib not be listed.

**Reasons for the recommendation:**

1. There are no randomized controlled trials of gefitinib, either compared to placebo or to a non-gefitinib comparator in patients with locally advanced or metastatic non-small cell lung cancer who have failed prior platinum-based and docetaxel chemotherapy.

2. Only one of the two available randomized trials, comparing two different doses of gefitinib, (n=102 at the recommended dose of 250 mg) was performed exclusively in patients who had received two or more chemotherapy regimens – a study population that corresponds to the patients for which Health Canada conditionally approved gefitinib. For the 250 mg dose, the study found a tumor response rate of 11.8%, and symptomatic improvement in a disease-specific questionnaire in approximately 40% of patients which usually occurred relatively early after the onset of treatment (days-weeks).

3. The trials of gefitinib were performed in a relatively highly functional group of patients with locally advanced or metastatic non small cell lung cancer; thus, these patients would be expected to have a better outcome than most patients with advanced lung cancer.

4. Because there was no placebo group comparator in the randomized trial, it is impossible to determine how much of the tumor response rate and symptomatic improvement was due to gefitinib. Thus, effectiveness of the drug cannot be determined in patients for which gefitinib is indicated.

5. Gefitinib is associated with diarrhea, rash, vomiting and rarely, interstitial pneumonitis.

6. The U.S. FDA and Canadian Therapeutic Products Directorate approvals of gefitinib are conditional upon the manufacturer performing randomized controlled trials comparing gefitinib with best supportive care. These trials are underway.

7. Gefitinib costs approximately $2,000 per month. Because the effectiveness of gefitinib has not been established, it is not possible to demonstrate cost-effectiveness.

8. In summary, it was the Committee's opinion that although gefitinib holds promise, its degree of effectiveness is not known in patients with locally advanced or metastatic non-small cell lung cancer. Information from controlled trials is necessary to assess the effectiveness and cost-effectiveness of gefitinib.

**Of Note:**

1. Placebo-controlled trials in people with locally advanced or metastatic non small cell lung cancer are ethical and feasible. A randomized trial of a similar agent (erlotinib) compared to placebo has recently been completed in patients with advanced lung cancer.

2. Randomized trials of gefitinib in combination with two platinum-based chemotherapy regimens for patients who have advanced non small cell lung cancer and are chemotherapy-naïve have shown no early benefit from gefitinib.