

**Important Information on  
IRESSA® (gefitinib) 250 mg Tablets**

December 20, 2004

**Subject: UPDATED EFFICACY INFORMATION: IRESSA® FAILS TO SHOW STATISTICALLY SIGNIFICANT SURVIVAL ADVANTAGE IN TRIAL 1839IL/0709:**

*A double blind, placebo controlled, parallel group, multicentre, randomized, Phase III survival study comparing IRESSA® (gefitinib) (250 mg tablet) plus best supportive care versus placebo plus best supportive care in patients with advanced NSCLC who have received one or two prior chemotherapy regimens and are refractory or intolerant to their most recent regimen.*

Dear Health Professional:

AstraZeneca would like to inform you of important new efficacy data related to the use of IRESSA® (gefitinib). The top-line data from the ISEL trial, a trial that compared IRESSA to placebo in advanced non-small cell lung cancer patients (NSCLC) who had progressed or could no longer tolerate chemotherapy, have now been analyzed.

The trial was closed to randomization on August 2, 2004 with 1692 enrolled patients. The analysis of the primary endpoint of the study shows that IRESSA did not significantly prolong survival in the overall population (HR 0.89, p=0.11, Median 5.6 vs 5.1 months for IRESSA and placebo respectively), or in patients with adenocarcinoma (HR 0.83, p=0.07, Median 6.3 vs 5.4 months for IRESSA and placebo respectively).

There was a statistically significant improvement in tumor shrinkage (objective response rate), which did not translate into an overall statistically significant survival benefit. Prospective subgroup analyses may suggest survival benefits in some patient groups but more analysis is needed.

These data are especially surprising in light of the consistent survival data that we have seen in the large number of patients from our Expanded Access (compassionate use) program. There is no methodological explanation for these findings and analysis of EGFR and other biomarkers is still underway. We firmly believe that IRESSA

provides significant benefit for some patients and more work is needed to isolate and study these populations.

AstraZeneca is providing the ISEL data to you in a rapid fashion to enable you to best treat your current and future patients. In light of these data, AstraZeneca urges you to discuss suitable treatment options for patients with recurrent non-small cell lung cancer. Individual patients currently on IRESSA and doing well may be part of a sub-population that is particularly sensitive to the drug. For those individual patients whom you deem appropriate, AstraZeneca intends to continue to make the drug available.

These top-line results are currently being reviewed and discussed with Health Canada. Full results of the data will be available in the first half of 2005 and publicly presented as soon as possible. At this time, AstraZeneca is suspending promotion of IRESSA while these trial data are further analyzed.

Should you have any questions or require additional information regarding the use of IRESSA® please contact AstraZeneca Canada Inc., Medical Information at 1-800-668-6000.

***Original signed by:***

ASTRAZENECA CANADA Inc.

Karen Feltmate

Vice President, Operations and Regulatory Affairs

IRESSA® is a trademark of the AstraZeneca group of companies.

**Any suspected adverse drug reactions can also be reported to:**

Canadian Adverse Drug Reaction Monitoring Program (CADRMP)  
Health Product Safety Information Division  
Marketed Health Products Directorate  
HEALTH CANADA  
Address Locator: 0201C2  
OTTAWA, Ontario, K1A 1B9  
Tel: (613) 957-0337 or Fax: (613) 957-0335  
Toll free for consumers and health professionals:  
Tel: 866 234-2345, Fax: 866 678-6789  
cadrmp@hc-sc.gc.ca

**The ADR Reporting Form can be found in *The Canadian Compendium of Pharmaceuticals and Specialties*, or on the TPD web site, along with the ADR Guidelines at:**

[http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adverse\\_e.html](http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adverse_e.html)  
[http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adr\\_guideline\\_e.html](http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adr_guideline_e.html)