RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Iressa (gefitinib) is a tyrosine kinase inhibitor indicated for metastatic non-small cell lung cancer (NSCLC) that has certain epidermal growth factor receptor (EGFR) mutations. EGFR is expressed on the cell surface of both normal and cancer cells and plays a role in the processes of cell growth and proliferation. Some EGFR activating mutations (exon 19 deletion or exon 21 point mutation L858R) within NSCLC cells have been identified as contributing to the promotion of tumor cell growth, blocking of apoptosis, increasing the production of angiogenic factors and facilitating the processes of metastasis. Iressa as a higher binding affinity for EGFR exon 19 deletion and exon 21 (L858R) substitution mutation than for wild-type EGFR (1).

Regulatory Status

FDA-approved indication: Iressa is a tyrosine kinase inhibitor indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21(L858R) substitution mutations as detected by an FDA-approved test (1).

<u>Limitations of Use:</u>

Safety and efficacy of Iressa have not been established in patients whose tumors have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution mutations (1).

Iressa label contains warnings for interstitial lung disease (ILD), hepatotoxicity, gastrointestinal perforation, diarrhea, ocular disorders including keratitis, bullous and exfoliative skin disorders, and embryo-fetal toxicity (1).

Withhold Iressa during evaluation of patients with suspected ILD and patients who present with worsening of respiratory symptoms. Discontinue Iressa in patients with confirmed ILD. Obtain periodic liver function testing. Withhold Iressa for Grade 2 or higher for ALT and/or AST elevations. Discontinue for severe hepatic impairment. Permanently discontinue Iressa in patients who develop gastrointestinal perforation. Withhold Iressa for higher than Grade 3 or severe/persistent (up to 14 days) diarrhea. Discontinue Iressa in patients who develop life-threatening bullous, blistering, or exfoliating lesions. Withhold Iressa for signs and symptoms of severe or worsening ocular disorders including keratitis, characterized as acute or worsening eye inflammation,

lacrimation, light sensitivity, blurred vision, eye pain, and/or red eye. Discontinue if patient develops persistent ulcerative keratitis. Iressa can cause harm to fetus. Advise of potential risk to a fetus and use of effective contraception (1).

Safety and effectiveness of Iressa in pediatric patients have not been established (1).

Summary

Iressa (gefitinib) is a tyrosine kinase inhibitor indicated for metastatic non-small cell lung cancer (NSCLC) that has certain epidermal growth factor receptor (EGFR) mutations. Iressa label contains warnings for interstitial lung disease (ILD), hepatotoxicity, gastrointestinal perforation, diarrhea, ocular disorders including keratitis, bullous and exfoliative skin disorders, and embryo-fetal toxicity. Safety and effectiveness of Iressa in pediatric patients have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Iressa while maintaining optimal therapeutic outcomes.

References

1. Iressa [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; February 2023.
2. NCCN Drugs & Biologics Compendium® Gefitinib 2025. National Comprehensive Cancer Network, Inc. Accessed on January 14, 2025.