RATIONAL FOR INCLUSION IN PA PROGRAM

Background
Tykerb (lapatinib) is approved for the treatment of Human Epidermal Growth Factor Receptor – 2 (HER2) - overexpressing (positive) cancers to be used in combination with capecitabine (Xeloda) and in patients who have received prior therapy including an anthracycline, a taxane and trastuzumab. Tykerb is also indicated for use with letrozole (Femara) in the treatment of postmenopausal women with HER-2 overexpressing (positive) cancer for whom hormonal therapy is indicated (1).

Regulatory Status
FDA-approved indication: Tykerb (lapatinib) is a kinase inhibitor indicated in combination with: (1)
1. Capecitabine, for the treatment of patients with advanced or metastatic breast cancer whose tumors overexpress HER2 and who have received prior therapy including an anthracycline, a taxane, and trastuzumab.
2. Letrozole (Femara) for the treatment of postmenopausal women with hormone receptor positive metastatic breast cancer that overexpresses the HER2 receptor and for whom hormonal therapy is indicated.

Limitation of Use:
Patients should have disease progression on trastuzumab prior to initiation of treatment with Tykerb in combination with capecitabine.

Off-Label Use:
Tykerb has also been shown to be effective for HER2+ gastric cancer when used together with, or following, Herceptin (trastuzumab). The combination of Tykerb and Herceptin has been shown to be superior to lapatinib alone in the second-line treatment of HER2+ breast cancer. The use of Tykerb in combination with Herceptin has been shown to be safe and effective in metastatic HER2+ breast cancer. The treatment is recommended in the NCCN guidelines and is an accepted standard of care (2-4).

Tykerb carries a boxed warning for hepatotoxicity in clinical trials and post-marketing experience. The hepatotoxicity may be severe. Tykerb has been associated with interstitial lung disease and pneumonitis. Tykerb should be discontinued if patients experience severe pulmonary symptoms.
Tykerb carries a pregnancy category D warning based on treatment studies in pregnant rats and rabbits. It is important to verify pregnancy status prior to the initiation of Tykerb and to advise patients not to become pregnant due to the risks of embryo-fetal death and birth defects (1).

The safety and effectiveness of Tykerb have not been established in pediatric patients (1).

Summary
Tykerb (lapatinib) is approved for the treatment of Human Epidermal Growth Factor Receptor – 2 (HER2) - overexpressing (positive) cancers. Tykerb is indicated to be used in combination with capecitabine in patients who have received prior therapy with an anthracycline, a taxane and trastuzumab. Tykerb is approved in combination with letrozole for the treatment of HER-2 overexpressing (positive) cancers in postmenopausal women for whom hormonal therapy is indicated. The use of lapatinib (Tykerb) in combination with trastuzumab has been shown to be safe and effective in metastatic HER2+ breast cancer. Tykerb may also be used in HER2+ gastric cancer when used in conjunction with or after trastuzumab (Herceptin) therapy (1-4).

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

References