

Appraisals

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Dear [REDACTED]

**Regarding: Breast cancer (metastatic hormone-receptor) - lapatinib and trastuzumab (with aromatase inhibitor)**

On behalf of the Commissioning Support, Appraisals Service (CSAS), I would like to submit our comments on the appraisal consultation document for Breast cancer (metastatic hormone-receptor) - lapatinib and trastuzumab (with aromatase inhibitor). CSAS is in agreement with the appraisal committee's decision that this technology does not represent a cost effective use of scarce NHS resources.

- **Adding lapatinib or trastuzumab to an aromatase inhibitor improves median progression free survival (PFS), but not overall survival.** Single RCTs found that adding lapatinib to letrozole improved median PFS from 3.0 months to 8.2 months, and that adding trastuzumab to anastrozole improved median PFS from 2.9 months to 5.8 months. Indirect comparisons from the manufacturers found no differences in PFS between these two combination regimens. The RCTs found that the combination regimens did not improve overall survival compared with aromatase inhibitors alone, and indirect comparisons found no difference in overall survival between the combination regimens.
- **Adding lapatinib or trastuzumab to an aromatase inhibitor increases adverse events.** Adding lapatinib to letrozole increased adverse events compared with letrozole alone, including diarrhoea (68% vs. 8%), rash (46% vs. 8%), and nausea (27% vs. 18%;  $p < 0.05$  for all three events). Adding trastuzumab to anastrozole increased adverse events compared with anastrozole alone (overall adverse events: 87% vs. 65%; serious adverse events: 23% vs. 6%). The most common adverse events with trastuzumab plus anastrozole included fatigue (21% vs. 10%), diarrhoea (20% vs. 8%), and vomiting (21% vs. 5%). Lapatinib and trastuzumab have been associated with cardiotoxicity therefore both drugs require cardiac monitoring (left ventricular function) before and during treatment. Liver function monitoring before and during treatment is also recommended with lapatinib.

