Cost-effectiveness of Onco*type* DX® to target chemotherapy use in lymph-node-negative, oestrogen-receptor-positive, early-stage breast cancer in Ireland

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Summary

1. In May 2011, the NCPE received the revised submission from Genomic Health, Inc. on the cost-effectiveness of the gene-expression profiling assay, Onco*type* DX®, in lymph-node negative, oestrogen-receptor positive early stage breast cancer. Onco*type* DX® generates a Recurrence Score® (RS), ranging from 0 to 100, quantifying the likelihood of breast cancer distant recurrence: low-risk (RS < 18), intermediate-risk (RS 18-30), and high-risk (RS ≥ 31). Onco*type* DX® has been proposed to better estimate baseline risk and response to chemotherapy, to appropriately target chemotherapy to higher risk patients. In the cost-effectiveness model, decision making with Onco*type* DX in addition to standard decision-making tools is compared with standard decision making *without* Onco*type* DX®.

2. The economic benefits of Onco*type* DX® are modelled by an overall reduction in chemotherapy usage, thus avoiding associated costs and disutility, and an increase in chemotherapy usage in the high RS group, reducing the risk of recurrence and improving health outcomes. There is currently no direct evidence that the use of Onco*type* DX® leads to improvement in health outcomes. Indirect evidence for clinical utility comes from studies showing a correlation between RS and both risk of disease recurrence, and likelihood of chemotherapy benefit. The Onco*type* DX® NSABP B-20 validation study found that women with high RS showed significant benefit from chemotherapy (CMF) plus tamoxifen vs tamoxifen alone (RR=0.26; 95% CI: 0.13–0.53). Patients with tumours that had low RS derived minimal, if any, benefit from chemotherapy treatment (RR= 1.31; 95% CI: 0.46-3.78) while patients with tumours that had intermediate RS did not appear to receive a substantial benefit (RR 0.61; 95% CI, 0.24 to 1.59), but the uncertainty in this estimate cannot exclude a clinically important benefit. Relative risk reductions (RRR) in recurrence from this study are used in the cost-effectiveness model.

3. A number of studies have looked at the impact of Onco*type* DX® on clinical decision making. A meta-analysis of these studies (n=1154) showed a net reduction of 24% in chemotherapy recommendation following Onco*type* DX®. Methodological weaknesses inherent in some or all of the individual studies include: use of retrospective chart review to elicit treatment recommendations before and after Onco*type* DX® testing; lack of standardised decision-making

tools both within and between studies; non-standardised methods of patient selection for Onco*type* DX® testing; small sample sizes; minimal study details derived from conference abstracts and posters; *presumptive* estimates of treatment recommendations based on guidelines as opposed to *actual* treatment recommendations. Usage estimates based on studies which reported *actual* treatment recommendations are included in the results below.

4. A cost-utility analysis was performed over the lifetime of the patient using a state transition (Markov) model. The incremental cost-effectiveness ratio (ICER) under base case assumptions of the model was €25,615/QALY. In univariate sensitivity analysis, the parameters with greatest effect on the ICER are the RRR following chemotherapy, chemotherapy use before and after Onco*type* DX in high RS and frequency of high RS in the cohort. The ICER increased above €48,000/QALY within the uncertainty ranges of each of these parameters. The probability of Onco*type* DX® being cost-effective at a WTP threshold of €20,000 per QALY gained is 48 %.

5. The estimated gross budget impact of Onco*type* DX® ranged from €0.95 million in year 1 to €1.19 million by year 5, based on estimated uptake in one third of eligible patients. Genomic Health Inc. predicts cost-offsets due to a reduction in chemotherapy usage, resulting in a net budget impact of €0.38 million in year 1 increasing to € 0.48 million in year 5. Should Onco*type* DX® be used as part of the decision making process in all eligible patients the gross budget impact is estimated at € 3.43 million in year 5.

6. In this economic evaluation of Onco*type* DX® the base case ICER was estimated at € 25,615/QALY with a 48% probability of being cost-effective at the € 20,000/QALY threshold. The NCPE review group noted the considerable uncertainty associated with the estimates of cost-effectiveness. Therefore, we do not recommend the reimbursement of Onco*type* DX® at the submitted price.