NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Olaparib for adjuvant treatment of high-risk HER2-negative, BRCA-positive early breast cancer after chemotherapy

Final scope

Final remit/appraisal objective

To appraise the clinical and cost effectiveness of olaparib within its marketing authorisation for adjuvant treatment of high-risk HER2-negative, BRCA-positive early or locally advanced breast cancer after chemotherapy and surgery.

Background

Breast cancer arises from the tissues of the ducts or lobules of the breast. Breast cancer is described as 'early' if it is restricted to the breast, or the breast and nearby lymph nodes, and has not spread to other parts of the body. Locally advanced cancer means that the cancer has spread into nearby tissue and lymph nodes around the breast, including lymph nodes around the collar bone and breastbone, but hasn't spread to other organs. Some people have mutations in the BRCA1 and BRCA2 genes that may increase the risk of breast cancer. Cancers are described as HER2-negative when the cancer cells test negative for human epidermal growth factor receptor 2. Additionally, when cancer cells also test negative for oestrogen and progesterone receptors (hormone receptor-negative cancer) cancers are described as triple negative breast cancer.

In 2017, there were about 45,908 new diagnoses of breast cancer in England.[1] Of these, 36,601 (80%) were diagnoses of early breast cancer.[1] It is estimated that approximately 80-85% of women with breast cancer have HER2-negative tumours.[2] Around 15% of breast cancers (approximately 7,500 cases a year in England and Wales) are triple negative breast cancers.[3]

Treatment may depend on whether the cancer cells have particular receptors (hormone receptor status or HER2 status), the extent of the disease, and previous treatments.

Adjuvant therapy is used to reduce the risk of the cancer coming back after surgery. The decision about whether to have adjuvant therapy is based on the assessment of the risk of the cancer coming back and the potential benefits and side effects of the treatment. If the risk of the cancer recurring is sufficiently high, NICE guideline 101 recommends adjuvant chemotherapy with a regimen containing both an anthracycline and a taxane such as docetaxel or paclitaxel for invasive, HER2-negative disease. For people with hormone receptor-positive early breast cancer, NICE guideline 101 recommends adjuvant endocrine therapy (tamoxifen or aromatase inhibitors such as anastrozole and letrozole). It also recommends considering ovarian function suppression for premenopausal women and extended endocrine therapy (total duration of endocrine therapy of more than 5 years). Adjuvant radiotherapy and adjuvant bisphosphonate therapy (for post-menopausal women) are also recommended for HER2-negative early breast cancer.

The technology

Olaparib (Lynparza, AstraZeneca) is a poly-ADP-ribose polymerase (PARP) inhibitor which inhibits PARP proteins involved in DNA repair. It is administered orally.

Olaparib does not currently have a marketing authorisation in the UK for the adjuvant treatment of high risk HER2-negative, BRCA1- or BRCA2-positive early breast cancer after chemotherapy. It has been studied in a clinical trial as monotherapy compared to placebo, in adults with high risk HER2-negative, BRCA1 or BRCA2-positive early breast cancer that has been treated with neoadjuvant or adjuvant chemotherapy.

Intervention(s)	Olaparib
Population(s)	Adults with BRCA1- or BRCA2-positive, HER2-negative, high risk early breast cancer that has been treated with surgery and neoadjuvant or adjuvant chemotherapy.
Comparators	Established clinical management without olaparib
Outcomes	The outcome measures to be considered include: • distant disease-free survival • invasive disease-free survival • overall survival • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account. The use of olaparib is conditional on the presence of mutations in the BRCA1 or BRCA2 genes. The economic modelling should include the costs associated with diagnostic testing for BRCA1 or BRCA2 mutations in people with high-risk early breast cancer who would not otherwise have been tested. A sensitivity analysis should be provided without the

	cost of the diagnostic test. See section 5.9 of the Guide to the Methods of Technology Appraisals.
Other considerations	If the evidence allows, subgroups based on hormone receptor status will be considered. The availability and cost of biosimilar and generic products should be taken into account. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals** None **Appraisals in development** 'Abemaciclib for adjuvant treatment of hormone receptor-positive, HER2-negative, node-positive early breast cancer' [ID3857]. Publication date to be confirmed. 'Pembrolizumab with neoadjuvant chemotherapy and adjuvant endocrine therapy for treating ER-positive, HER2-negative early breast cancer' Proposed NICE technology appraisal [ID3993]. Publication date to be confirmed. 'Palbociclib for treating high-risk early breast cancer after neoadjuvant chemotherapy' Proposed NICE technology appraisal [ID3846]. Publication date to be confirmed. **Related Guidelines** Early and locally advanced breast cancer: diagnosis and management (2018) NICE guideline 101 Suspected cancer: recognition and referral (2015, updated 2020) NICE guideline 12 Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer (2013, updated 2019) NICE guideline CG164 **Related Interventional Procedures** Endoscopic mastectomy and endoscopic wide local excision for breast cancer (2009) NICE interventional procedures guidance 296 Image-guided radiofrequency excision biopsy of breast lesions (2009) NICE interventional procedures guidance 308 Endoscopic axillary lymph node retrieval for breast cancer (2005) NICE interventional procedures guidance 147 Interstitial laser therapy for breast cancer (2004) NICE

	interventional procedures guidance 89 **Related Quality Standards** Suspected cancer (2016) NICE quality standard 124 Breast cancer (2011) NICE quality standard 12
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018) NHS England Funding and Resource 2018/19: Supporting 'Next Steps for the NHS Five Year Forward View' NHS England (2016) Radiotherapy after primary cancer for breast cancer. Clinical Commissioning Policy. Reference: 16038/P NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 31: Breast radiotherapy injury rehabilitation service (a discrete cohort of adult females), pp103-4 Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 1. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

1 National Cancer Registration and Analysis Service (2019). Stage breakdown by CCG 2017. Accessed October 2021.

2 Macmillan Cancer Support (2021). Receptors for breast cancer. Accessed October 2021.

3 Cancer Research UK (2020). Triple negative breast cancer. Accessed October 2021.