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

Draft scope

Draft remit

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] Around 35% of people with early or locally advanced disease will progress to metastatic breast cancer.[4]

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. NICE guideline 101 recommends adjuvant chemotherapy (a regimen containing both an anthracycline and a taxane such as docetaxel or paclitaxel) for treating invasive, HER2-negative early breast cancer. For people with hormone receptor-positive and HER2-negative 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.

Olaparib is indicated for treating BRCA1 or BRCA2-positive, HER2 negative locally advanced or metastatic breast cancer, after treatment with an anthracycline and a taxane in the neoadjuvant, adjuvant or metastatic setting.

Intervention(s)	Olaparib
Population(s)	Adults with germline BRCA1 or BRCA2 mutations, and high risk HER2-negative breast cancer which has been treated with surgery and neoadjuvant or adjuvant chemotherapy.
Comparators	Standard adjuvant therapy 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.

Other considerations	If the evidence allows the following subgroups will be considered. These include: • people with hormone receptor-positive breast cancer • people with triple-negative breast cancer 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 NICE Pathways** Early and locally advanced breast cancer (2020) NICE pathway
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

Questions for consultation

How is high-risk, early or locally advanced breast cancer defined in clinical practice?

Have all relevant comparators for olaparib been included in the scope? Which treatments are considered to be established clinical practice in the NHS for high-risk HER2-negative, BRCA-positive early breast cancer after chemotherapy?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom olaparib is expected to be more clinically effective and cost effective or other groups that should be examined separately? OR Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom olaparib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider olaparib will fit into the existing NICE pathway, early and locally advanced breast cancer?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which olaparib will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider olaparib to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of olaparib can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

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.

4 Dewis R and Gribbin J (2009). Breast cancer: diagnosis and treatment, an assessment of need. Accessed October 2021.