NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Talazoparib for treating BRCA 1 or 2 mutated advanced breast cancer after prior chemotherapy

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of talazoparib within its marketing authorisation for treating BRCA 1 or 2 mutated advanced breast cancer.

Background

Breast cancer arises from the tissues of the ducts or lobules of the breast. The cancer is said to be 'advanced' if it has spread to other parts of the body such as the bones, liver, and lungs (metastatic cancer), or if it has grown directly into nearby tissues and cannot be completely removed by surgery. Some people have gene mutations that may increase the risk of breast cancer. Mutated inherited genes that increase the risk of breast cancer include BRCA 1 and 2.

Over 45,960 people were diagnosed with breast cancer in England in 2016, and there were approximately 9,685 deaths from breast cancer in 2016[1,2]. The 5-year survival rate for people with metastatic breast cancer in England is 15%[3]. Approximately 6-7% of people with invasive breast cancers have metastatic disease when they are diagnosed[4], and around 30% of people who present with localised disease will later develop metastases. A person's lifetime risk of developing breast and/or ovarian cancer is greatly increased if they inherit the BRCA 1 or BRCA 2 mutation[5]. About 12% of women in the general population will develop breast cancer at some point during their lives. In contrast, 72% of women who inherit the BRCA 1 mutation and around 69% of women who inherit the BRCA 2 mutation will develop breast cancer by the age of 80 years[5]. Current treatments for metastatic breast cancer aim to relieve symptoms, prolong survival and maintain a good quality of life with minimal adverse events. Treatment may depend on whether the cancer cells have particular receptors (oestrogen receptor or HER2), the extent of the disease and previous treatments; options include endocrine therapies, biological therapies and chemotherapy.

For people having chemotherapy for advanced breast cancer, NICE clinical guideline 81 (CG81) recommends anthracycline-based regimens as the initial treatment, followed by sequential lines of treatment with docetaxel first line followed by capecitabine and vinorelbine as second or third line. Gemcitabine monotherapy is also used in clinical practice in the UK. Patients for whom anthracyclines are not suitable (because of contraindication or progression on

prior anthracycline treatment) are offered sequential treatment with systemic chemotherapy. NICE Technology Appraisal guidance 423 recommends eribulin for treating locally advanced or metastatic breast cancer that has progressed after at least 2 chemotherapy regimens (which may include an anthracycline or a taxane, and capecitabine).

The technology

Talazoparib (brand name unknown, Pfizer) is a poly-ADP-ribose polymerase (PARP) inhibitor. PARP proteins are involved in the detection and initiation of DNA repair. In cells deficient in other DNA repair pathways, such as those seen with BRCA gene mutations, inhibition of PARP can lead to cancer cell death. It is administered orally.

Talazoparib does not currently have a marketing authorisation in the UK for treating breast cancer. It has been studied in a clinical trial in adults with germline BRCA 1 or 2 mutated, HER2 negative advanced or metastatic breast cancer who have had prior therapy with a taxane and/or anthracycline, but no more than 3 prior chemotherapy-inclusive regimens. Talazoparib was compared with 'physician's-choice' (that is capecitabine, eribulin, gemcitabine or vinorelbine).

Intervention	Talazoparib
Population	Adults with BRCA 1 or 2 mutated, HER2-negative advanced breast cancer that has previously been treated with a taxane and/or an anthracycline
Comparators	• Vinorelbine • Capecitabine • Gemcitabine • Eribulin (after at least 2 chemotherapy regimens)
Outcomes	The outcome measures to be considered include: • overall survival • progression free survival • response rate • 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 patient access schemes for the intervention or comparator technologies will be taken into account. The economic modelling should include the cost associated with diagnostic testing in people with BRCA 1 or 2 mutated metastatic 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	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: Eribulin for treating locally advanced or metastatic breast cancer after one prior chemotherapy regimen (2018) NICE technology appraisal guidance 515. Fulvestrant for untreated locally advanced or metastatic oestrogen-receptor positive breast cancer (2018) NICE technology appraisal guidance 503. Ribociclib with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer (2017) NICE technology appraisal guidance 496. Palbociclib with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer (2017) NICE technology appraisal guidance 495.

	Eribulin for treating locally advanced or metastatic breast cancer after 2 or more chemotherapy regimens (2016) NICE technology appraisal guidance 423. Everolimus with exemestane for treating advanced breast cancer after endocrine therapy (2016) NICE technology appraisal guidance 421 Fulvestrant for the treatment of locally advanced or metastatic breast cancer (2011) NICE technology appraisal guidance 239. Placed on the static list (2014). Gemcitabine for the treatment of metastatic breast cancer (2007) NICE technology appraisal guidance 116 Placed on the static list (2010). Appraisal in development (including suspended appraisals) 'Taselisib for previously treated ER-positive, HER2-negative, PIK3CA-positive breast cancer in postmenopausal women' Proposed NICE technology appraisal [ID1401] Publication date to be confirmed. 'Olaparib for treating BRCA 1 or 2 mutated metastatic breast cancer after prior chemotherapy' Proposed NICE technology appraisal [ID1382] Publication date to be confirmed 'Neratinib for treating HER2-positive breast cancer after 2 therapies' Proposed technology appraisal [ID981] Publication date to be confirmed 'Ribociclib in combination with fulvestrant for treating advanced hormone-receptor positive, HER2-negative breast cancer' Proposed technology appraisal [ID1318] Publication date to be confirmed 'Veliparib for treating HER2-negative, BRCA-positive breast cancer' Proposed technology appraisal [ID1404] Publication date to be confirmed Related Guideline: Advanced breast cancer: diagnosis and treatment (2009 updated 2017) NICE guideline CG81 Related Quality Standards:

	http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp 'Breast cancer' (2016) NICE quality standard 12 Related NICE Pathways: Advanced breast cancer (2017) NICE pathway http://pathways.nice.org.uk/
Related National Policy	NHS England (2017) Manual for Prescribed Specialised Services 2017/18. https://www.england.nhs.uk/wp-content/uploads/2017/10/prescribed-specialised-services-manual-2.pdf Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 2, 4, 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Is talazoparib likely to be used in HER2 negative advanced breast cancer only, in line with the clinical evidence?
Have all relevant comparators for talazoparib been included in the scope?
Which treatments are considered to be established clinical practice in the NHS for BRCA 1 or 2 mutated, HER2-negative advanced breast cancer that has previously been treated with a taxane and/or an anthracycline?
Where do you think at which line of therapy do you anticipate talazoparib will be used?
Are the outcomes listed appropriate?

Are there any subgroups of people in whom talazoparib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider talazoparib will fit into the existing NICE pathway, 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 telazoparib 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 telazoparib 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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Office for National Statistics (2018) Cancer registration statistics, England, 2016. Accessed June 2018.

2. Cancer Research UK (2016) Breast cancer mortality statistics. Accessed June 2018.

3. Cancer Research UK (2016) Breast cancer survival statistics. Accessed June 2018.

4. Cancer Research UK (2017) Breast cancer incidence statistics. Accessed June 2018.

5. National Cancer Institute (2018). BRCA1 and BRCA2: Cancer risk and genetic testing. Accessed June 2018.