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Healthcare Improvement Scotland | SMC Advice on new medicines

Advice document
SMC2737

olaparib film-coated tablets (Lynparza®)

AstraZeneca UK Limited

10 January 2025

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutics Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following an abbreviated submission

olaparib (Lynparza®) is accepted for use within NHSScotland.

Indication under review: monotherapy for the treatment of adult patients with germline *BRCA1/2*-mutations, who have HER2 negative locally advanced or metastatic breast cancer. Patients should have previously been treated with an anthracycline and a taxane in the (neo)adjuvant or metastatic setting unless patients were not suitable for these treatments. Patients with hormone receptor (HR)-positive breast cancer should also have progressed on or after prior endocrine therapy, or be considered unsuitable for endocrine therapy.

Olaparib offers an additional treatment choice in the therapeutic class of poly (ADP-ribose) polymerase (PARP) inhibitors.

Another medicine within this therapeutic class has been accepted for use via the end of life medicine process.

This advice applies only in the context of approved NHSScotland Patient Access Scheme (PAS) arrangements delivering the cost-effectiveness results upon which the decision was based, or PAS/ list prices that are equivalent or lower.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Olaparib selectively inhibits poly (ADP-ribose) polymerase (PARP) enzymes (PARP-1, PARP-2 and PARP-3), thereby blocking PARP-mediated DNA repair. [1, 2]

Patients must have confirmation of a deleterious or suspected deleterious germline *BRCA1/2*-mutation before commencing olaparib treatment, determined by an experienced laboratory using a validated test method. Genetic counselling for patients tested for mutations in *BRCA1/2* genes should be performed according to local regulations. [1, 2]

The recommended dose of olaparib is 300 mg (2 x 150 mg tablets) orally twice daily. The dose may be reduced or interrupted to manage adverse reactions. It is recommended that treatment be continued until progression of the underlying disease or unacceptable toxicity. See Summary of Product Characteristics for further information. [1, 2]

1.2. Relevant comparator(s)

The submitting company compared olaparib to talazoparib (Talzenna®), which is an inhibitor of PARP-1 and PARP-2. Talazoparib is accepted for use within NHSScotland as monotherapy for the treatment of adult patients with germline *BRCA1/2*-mutations, who have HER2 -negative locally advanced or metastatic breast cancer (SMC2607). Patients should have been previously treated with an anthracycline and/or a taxane in the (neo)adjuvant, locally advanced or metastatic setting unless patients were not suitable for these treatments. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine-based therapy, or be considered unsuitable for endocrine-based therapy. [3]

2. Summary of Clinical Evidence

2.1. Evidence to support comparable efficacy with relevant comparators

Evidence to support the efficacy and safety of olaparib for the indication under review is available from a phase III, multicentre, open-label, randomised study, OlympiAD, that compared olaparib monotherapy with the physician's choice (TPC) of chemotherapy (capecitabine, eribulin, or vinorelbine) in patients with a confirmed deleterious or suspected deleterious germline *BRCA1/2*-mutation and HER2-negative metastatic breast cancer who had received no more than two previous chemotherapy regimens for metastatic disease. The primary endpoint was progression free survival (PFS), assessed by blinded independent central review (BICR) using Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1. At data cut-off (9 December 2016), median PFS was significantly longer in the olaparib group than the TPC group (7 months versus 4 months, respectively; Hazard Ratio (HR) 0.58, 95% CI 0.43 to 0.80, p = <0.001). [4]

In the absence of direct evidence comparing olaparib with talazoparib, the submitting company provided evidence from two published indirect treatment comparisons (ITCs), which each included two studies, OlympiAD and EMBRACA. EMBRACA was a multicentre, phase III, multi-centre, open-label, randomised study that compared talazoparib with TPC (capecitabine, eribulin, gemcitabine or vinorelbine) in the indication under review. [5, 6]

In the ITC conducted by McCrea et al, a Bayesian fixed-effect analysis found no evidence of a difference between olaparib and talazoparib for PFS, any serious adverse event (SAE) and any treatment-related SAE. The authors reported that patients receiving olaparib had a higher rate of nausea and vomiting, while those receiving talazoparib had a higher rate of alopecia and anaemia. [5]

These findings were supported by a second ITC, conducted by Wang et al, which used a random effect model within a Bayesian framework. The ITC demonstrated no evidence of a difference between olaparib and talazoparib for PFS, overall survival and objective response rate. [6]

The submitting company concluded that although there is no direct evidence to compare olaparib versus talazoparib, the results from the two ITCs suggest olaparib is likely to provide similar health benefits to talazoparib.

3. Company Estimate of Eligible Population, Uptake and Budget Impact

3.1. Company's number of patients assumed to be eligible for treatment

SMC is unable to publish the estimated patient numbers as the company considered that these were commercial in confidence.

3.2. Budget Impact assumption

Medicines reviewed under the abbreviated submissions process are estimated to have a limited net budget impact and resource allocation across NHS Scotland.

Other data were also assessed but remain confidential*

References

1. AstraZeneca. Olaparib tablets (Lynparza®) Summary of product characteristics. Electronic Medicines Compendium www.medicines.org.uk/emc/ Last updated [2 February 2024]
2. The European Medicines Agency (EMA) European Public Assessment Report. Olaparib (Lynparza®) 28/02/2019, EMEA H-C-003726-II-0020. www.ema.europa.eu
3. Pfizer Limited. Talazoparib tablets (Talzenna®) Summary of product characteristics. Electronic Medicines Compendium www.medicines.org.uk/emc/ Last updated [17 April 2024]
4. Robson M, Im SA, Senkus E, Xu B, Domchek SM, Masuda N, et al. Olaparib for Metastatic Breast Cancer in Patients with a Germline BRCA Mutation. N Engl J Med. 2017;377(6):523-33. Epub 20170604. 10.1056/NEJMoa1706450
5. McCrea C, Hettle R, Gulati P, Taneja A, Rajora P. Indirect treatment comparison of olaparib and talazoparib in germline BRCA-mutated HER2-negative metastatic breast cancer. J Comp Eff Res. 2021;10(13):1021-30. Epub 20210707. 10.2217/cer-2021-0097
6. Wang J, Zhang Y, Yuan L, Ren L, Zhang Y, Qi X. Comparative efficacy, safety, and acceptability of single-agent poly (ADP-ribose) polymerase (PARP) inhibitors in BRCA-mutated HER2-negative metastatic or advanced breast cancer: a network meta-analysis. Aging (Albany NY). 2020;13(1):450-9. Epub 20201130. 10.18632/aging.202152

This assessment is based on data submitted by the applicant company up to and including **26 November 2024.**

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:https://www.scottishmedicines.org.uk/about-us/policies-publications/*

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice is based on the estimation of at least similar comparative efficacy and limited net budget impact compared with other medicinal products, within the same therapeutic class, that are in routine use within NHSScotland.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after evaluation of the evidence submitted by the company. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.