

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

**Atezolizumab with chemotherapy for neoadjuvant treatment of resectable early or locally advanced invasive triple-negative breast cancer**

**Final scope**

**Remit/appraisal objective**

To appraise the clinical and cost effectiveness of atezolizumab within its marketing authorisation for neoadjuvant treatment of resectable early or locally advanced invasive triple-negative breast cancer.

**Background**

Breast cancer arises from the tissues of the ducts or lobules of the breast. It is described as invasive when the cancer cells have grown through the lining of the ducts into the surrounding tissue. 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 (clinical stages 1 and 2). It is described as 'locally advanced' if the cancer has spread from the breast to lymph nodes close to the breast, to the skin of the breast, or to the chest wall (clinical stage 3).<sup>1</sup>

Over 46,100 people were diagnosed with breast cancer in England in 2017<sup>2</sup> and there were approximately 9,600 deaths from breast cancer in England in 2018.<sup>3</sup> Around 15% of breast cancers are triple-negative breast cancers whereby the cancer cells test negative for oestrogen receptors and progesterone receptors (hormone-receptor-negative cancer) and human epidermal growth factor receptor 2 (HER2-negative cancer)<sup>4</sup>.

Triple-negative breast cancer is associated with poor prognosis with high risk of relapse and short progression-free survival and overall survival. As many as 50% of patients diagnosed with stage 1 to 3 triple-negative breast cancer experience disease recurrence, and 37% die in the first 5 years after surgery<sup>5</sup>. Depending on the stage of its diagnosis, triple-negative breast cancer can be particularly aggressive, is more likely to recur than other subtypes of breast cancer and is associated with poorer survival. It is diagnosed more frequently in younger women, and it is more frequent amongst women with BRCA1 mutations (a gene on chromosome 17 that normally helps to suppress cell growth, which is an inherited gene mutation that may increase the risk of breast cancer).<sup>6</sup>

NICE guideline 101 ([NG101](#)) recommends neoadjuvant chemotherapy for people with oestrogen receptor-negative invasive breast cancer as an option to reduce tumour size before surgery. It further recommends consideration of adding a platinum to an anthracycline-containing neoadjuvant chemotherapy regimen for triple-negative invasive breast cancer. Standard chemotherapy options used for neoadjuvant treatment of triple-negative breast cancer include doxorubicin, epirubicin, docetaxel and paclitaxel.

Final scope for the appraisal of atezolizumab with chemotherapy for neoadjuvant treatment of resectable early or locally advanced invasive triple-negative breast cancer

### The technology

Atezolizumab (Tecentriq, Roche) is a humanised, anti-programmed cell death ligand-1 (PD-L1) monoclonal antibody involved in the blockade of immune suppression and the subsequent reactivation of anergic T-cells. It is delivered by intravenous infusion.

Atezolizumab does not currently have a marketing authorisation in the UK for neoadjuvant treatment of resectable early or locally advanced invasive triple-negative breast cancer. It has been studied in a clinical trial as neoadjuvant treatment in combination with chemotherapy (nab-paclitaxel followed by doxorubicin and cyclophosphamide), compared with chemotherapy and placebo, in adults with previously untreated early or locally advanced triple-negative breast cancer.

<b>Intervention(s)</b>	Neoadjuvant atezolizumab in combination with chemotherapy
<b>Population(s)</b>	Adults with resectable early or locally advanced triple-negative invasive breast cancer
<b>Comparators</b>	Standard neoadjuvant chemotherapy without atezolizumab
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• overall survival</li> <li>• disease free survival</li> <li>• surgical outcomes</li> <li>• response rate</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>
<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will taken into account. The availability of any managed access arrangement for the intervention will be taken into account.</p>

Final scope for the appraisal of atezolizumab with chemotherapy for neoadjuvant treatment of resectable early or locally advanced invasive triple-negative breast cancer

<b>Other considerations</b>	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.
<b>Related NICE recommendations and NICE Pathways</b>	<p>Related Technology Appraisals:</p> <p>Atezolizumab with nab-paclitaxel for treating PD L1-positive, locally advanced or metastatic, triple-negative breast cancer (2020). NICE Technology Appraisal 639. Review date 2023.</p> <p>Appraisals in development (including suspended appraisals):</p> <p>Pembrolizumab in combination for untreated, locally advanced or metastatic, triple negative breast cancer. NICE technology appraisals guidance [ID1546]. Publication expected April 2021.</p> <p>Pembrolizumab in combination with chemotherapy for neoadjuvant treatment of triple negative breast cancer. NICE technology appraisals guidance [ID1500]. Publication date to be confirmed.</p> <p>Related Guidelines:</p> <p>Early and locally advanced breast cancer: diagnosis and management (2018). NICE guideline 101. Review date to be confirmed.</p> <p>Related Quality Standards:</p> <p>Breast cancer (2011). NICE quality standard 12.</p> <p>Related NICE Pathways:</p> <p><a href="#">Early and locally advanced breast cancer</a> (2019) NICE pathway</p>
<b>Related National Policy</b>	<p>The NHS Long Term Plan, 2019. <a href="#">NHS Long Term Plan</a></p> <p>NHS England (2018/2019) <a href="#">NHS manual for prescribed specialist services (2018/2019)</a></p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 3 to 5. <a href="https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017">https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</a></p>

## References

- 1 [Cancer Research UK \(2020\) Number stages of breast cancer](#). Accessed February 2021.
- 2 [Office for National Statistics \(2019\) Cancer registration statistics, England, 2017](#). Accessed February 2021.

Final scope for the appraisal of atezolizumab with chemotherapy for neoadjuvant treatment of resectable early or locally advanced invasive triple-negative breast cancer

- 3 [Cancer research UK \(2018\) Breast cancer mortality statistics](#). Accessed February 2021.
- 4 The Institute of Cancer Research (2016) [Promising drug target for aggressive 'triple negative' breast cancers identified](#). Accessed February 2021.
- 5 Costa RLB and Gradishar WJ. [Triple-negative breast cancer: current practice and future directions](#). Journal of Oncology Practice 13, no. 5 (May 1 2017) 301-303.
- 6 Couch FJ, Hart SN, Sharma P et al. [Inherited mutations in 17 breast cancer susceptibility genes among a large triple-negative breast cancer cohort unselected for family history of breast cancer](#). Journal of Clinical Oncology 2015;33(4):304-311