

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Trastuzumab deruxtecan for treating HER2-positive unresectable or metastatic breast cancer after 1 or more anti-HER2 therapies (MA review TA704 and TA862)**Final Scope****Remit/appraisal objective**

To appraise the clinical and cost effectiveness of trastuzumab deruxtecan within its marketing authorisation for treating HER2-positive unresectable or metastatic breast cancer after 1 or more anti-HER2 therapies.

Background

Breast cancer arises from the tissues of the ducts or lobules of the breast. Metastatic breast cancer is when the cancer has spread beyond the breast and nearby lymph nodes to other organs in the body. Unresectable means that the cancer cannot be treated by surgery. Human epidermal growth factor receptor 2 (HER2) is a receptor for a growth factor which occurs naturally in the body. When human epidermal growth factor attaches itself to HER2 receptors on breast cancer cells, it can stimulate the cells to divide and grow. Some breast cancer cells have more HER2 receptors than others. In this case, the tumour is described as being HER2-positive.

In 2017, there were 46,109 new diagnoses of breast cancer in England.¹ There were approximately 2,300 cases of breast cancer in stage 4 in the UK in 2016 according to the National Cancer Registration and Analysis Service.² In 2017 in England, there were 10,219 deaths from breast cancer.³ It is estimated that approximately 15-20% of people with breast cancer will have HER2-positive tumours.⁴

Current treatments for advanced breast cancer aim to relieve symptoms, prolong survival and maintain a good quality of life with few adverse events. Treatment depends on whether the cancer cells have particular receptors (hormone receptor status or HER2 status), the extent of the disease and previous treatments.

For people with HER2-positive unresectable or metastatic breast cancer who have not had previous anti-HER2 treatment or chemotherapy for their metastatic disease, NICE technology appraisal guidance [509](#) recommends pertuzumab with trastuzumab and docetaxel as first line treatment. In addition, NICE technology appraisal guidance [34](#) recommends trastuzumab with paclitaxel as an option for people with tumours expressing HER2 who have not received chemotherapy for metastatic breast cancer and in whom anthracycline is not appropriate. For disease that has progressed, NICE technology appraisal guidance [458](#) recommends trastuzumab emtansine as an option for treating HER2-positive unresectable, locally advanced or metastatic breast cancer after trastuzumab and a taxane. There is currently no standard of care for HER2-targeted therapy in people with metastatic HER2-positive breast cancer whose disease has progressed on or after trastuzumab emtansine. NICE clinical guideline (CG81) recommends that patients may receive treatment with non-targeted chemotherapies such as capecitabine or vinorelbine. NICE technology appraisal guidance [423](#) recommends eribulin for locally advanced or metastatic breast cancer after 2 or more chemotherapy regimens. NICE technology appraisal guidance 786

Scope for the appraisal of trastuzumab deruxtecan for treating HER2-positive unresectable or metastatic breast cancer after 1 or more anti-HER2 therapies

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recommends tucatinib with trastuzumab and capecitabine for HER2- positive locally advanced or metastatic breast cancer after 2 or more anti HER2 treatment therapies.

This evaluation is a review of [NICE technology appraisal guidance 704](#), which recommends trastuzumab deruxtecan within the Cancer Drugs Fund for HER2- positive unresectable or metastatic breast cancer after 2 or more anti-HER2 treatments and [NICE technology appraisal guidance 862](#) which recommends trastuzumab deruxtecan for use within managed access for treating HER2-positive unresectable or metastatic breast cancer after 1 or more anti-HER2 treatments.

The technology

Trastuzumab deruxtecan (Enhertu, Daiichi-Sankyo) has a marketing authorisation in the UK as a monotherapy for the treatment of adults with unresectable or metastatic HER2-positive breast cancer who have had 1 or more prior anti-HER2-based regimens.

Intervention(s)	Trastuzumab deruxtecan
Population(s)	People with HER2-positive, unresectable or metastatic breast cancer who have received 1 or more prior anti-HER2 therapies
Comparators	<p>For people who have had 1 prior therapy with trastuzumab and a taxane:</p> <ul style="list-style-type: none"> • trastuzumab emtansine <p>For people who have had 2 or more prior anti-HER2 therapies:</p> <ul style="list-style-type: none"> • capecitabine • vinorelbine • eribulin (for people who have had 2 or more chemotherapy regimens) • tucatinib with trastuzumab and capecitabine
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • progression free survival • overall survival • response rate • duration of response • adverse effects of treatment • health-related quality of life.

Economic analysis	<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 be taken into account.</p>
Other considerations	<p>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.</p> <p>The availability and cost of biosimilar and generic products should be taken into account.</p>
Related NICE recommendations and NICE Pathways	<p>Related Technology Appraisals:</p> <p>Trastuzumab deruxtecan for treating HER2-positive unresectable or metastatic breast cancer after 1 or more anti-HER2 treatments (2023) NICE technology appraisal guidance 862.</p> <p>Tucatinib with trastuzumab and capecitabine for treating HER2-positive advanced breast cancer after 2 or more anti-HER2 therapies (2022) NICE technology appraisal guidance 786.</p> <p>Trastuzumab deruxtecan for treating HER2-positive unresectable or metastatic breast cancer after 2 or more anti-HER2 therapies (2021) NICE technology appraisal guidance 704.</p> <p>Trastuzumab emtansine for treating HER2-positive advanced breast cancer after trastuzumab and a taxane (2017) NICE technology appraisal guidance 458.</p> <p>Eribulin for treating locally advanced or metastatic breast cancer after 2 or more chemotherapy regimens (2016) NICE technology appraisal guidance TA423</p> <p>Guidance on the use of trastuzumab for the treatment of advanced breast cancer (2002) NICE technology appraisal guidance TA34</p> <p>Appraisals in development (including suspended appraisals)</p>

	<p>Pertuzumab–trastuzumab with chemotherapy for treating HER2-positive breast cancer [ID2724] In development [GID-TA10592] Expected publication date: TBC</p> <p>Related Guidelines:</p> <p>‘Advanced breast cancer: diagnosis and treatment (2009) NICE guideline CG81 last updated August 2017</p> <p>Early and locally advanced breast cancer (update) (2018) NICE guideline. NG101.</p> <p>Related Quality Standards:</p> <p>Breast cancer (2011, updated 2016) NICE quality standard QS12</p>
Related National Policy	<p>The NHS Long Term Plan (2019) NHS Long Term Plan</p> <p>NHS England (2023) Manual for prescribed specialist services (2023/2024) Specialist cancer services (adults) Chapter 105</p> <p>Department of Health and Social Care (2016) NHS outcomes framework 2016 to 2017</p> <p>NHS Digital (2022) NHS Outcomes Framework England, March 2022 Annual Publication</p>

References

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