NICE National Institute for Health and Care Excellence

NICE guidance

# Trastuzumab deruxtecan for treating HER2-positive unresectable or metastatic breast cancer after 1 or more anti-HER2 treatments

Technology appraisal guidance
Published: 1 February 2023

www.nice.org.uk/guidance/ta862

# Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

# Contents

# 1 Recommendations

1.1 Trastuzumab deruxtecan is recommended with managed access as an option for treating HER2-positive unresectable or metastatic breast cancer after 1 or more anti-HER2 treatments in adults. It is only recommended if the conditions in the managed access agreement for trastuzumab deruxtecan are followed.

1.2 This recommendation is not intended to affect treatment with trastuzumab deruxtecan that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

**Why the committee made these recommendations**

Standard treatment for HER2-positive unresectable or metastatic breast cancer includes anti-HER2 treatments. After first-line treatment with trastuzumab and a taxane, standard treatment is trastuzumab emtansine. Trastuzumab deruxtecan would be an alternative anti-HER2 treatment after trastuzumab and a taxane.

Clinical trial evidence shows that trastuzumab deruxtecan increases how long people have before their cancer gets worse compared with trastuzumab emtansine.

There is not enough evidence yet to show if people live longer with trastuzumab deruxtecan compared with trastuzumab emtansine because the clinical trial is still ongoing. This means the cost-effectiveness estimates are highly uncertain and trastuzumab deruxtecan cannot be recommended for routine use in the NHS.

Trastuzumab deruxtecan could be cost effective if further evidence shows that people live longer with treatment. Evidence from the trial and from NHS practice could help address the uncertainty about how long people live. So, trastuzumab deruxtecan is recommended for use with managed access.

# 2 Information about trastuzumab deruxtecan

## Marketing authorisation indication

2.1 Trastuzumab deruxtecan (Enhertu, Daiichi Sankyo) 'as monotherapy is indicated for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received one or more prior anti-HER2-based regimens'.

## Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for trastuzumab deruxtecan.

## Price

2.3 The list price for trastuzumab deruxtecan is £1,455 per vial containing 100 mg powder for concentrate for solution for infusion (excluding VAT; BNF online accessed October 2022).

2.4 The company has a commercial arrangement. This makes trastuzumab deruxtecan available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

# 3 Committee discussion

The evaluation committee considered evidence submitted by Daiichi Sankyo, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the committee papers for full details of the evidence.

# The condition

## Details of the condition

3.1 Some breast cancer cells have higher levels of a protein called human epidermal growth factor receptor 2 (HER2) on their surface which stimulates them to grow. This is known as HER2-positive breast cancer and around 1 in 5 unresectable or metastatic breast cancers are HER2-positive. The patient experts explained that being diagnosed with unresectable or metastatic breast cancer is extremely difficult for people and their family and friends. Many people feel uncertain, upset, and anxious, which can negatively affect mental health. People with unresectable or metastatic breast cancer have to organise their lives around hospital appointments and scans, which can constrain their everyday activities. There is no cure for unresectable or metastatic breast cancer. Treatment aims to stop progression of the disease, extend life, and maintain or improve quality of life for as long as possible. Treatment is continued for as long as it works. The committee concluded that there is a high disease burden for people with HER2-positive unresectable or metastatic breast cancer.

# Clinical management

## Clinical need

3.2 Clinical and patient experts explained that people with HER2-positive unresectable or metastatic breast cancer who have had treatment with trastuzumab and a taxane have a high symptom burden. There is an unmet need for treatments that control disease progression, extend life,

and have an acceptable safety profile. First-line treatment of HER2-positive unresectable or metastatic breast cancer includes the anti-HER2 treatments pertuzumab and trastuzumab with docetaxel (see NICE's technology appraisal guidance on pertuzumab with trastuzumab and docetaxel for treating HER2-positive breast cancer), or trastuzumab with paclitaxel (see NICE's technology appraisal guidance on trastuzumab for the treatment of advanced breast cancer). Trastuzumab emtansine is an anti-HER2 treatment used at second line (see NICE's technology appraisal guidance on trastuzumab emtansine for treating HER2-positive advanced breast cancer after trastuzumab and a taxane). Non-targeted chemotherapy can also be used at second line (see NICE's guideline on advanced breast cancer: diagnosis and treatment) but the clinical experts confirmed that trastuzumab emtansine is the current standard treatment. Patient and clinical experts explained that new treatments with improved outcomes are needed. Patient experts highlighted the need for new treatments with acceptable tolerability that can extend how long people live and improve quality of life. The committee concluded that that there is an unmet need for alternative anti-HER2 treatments after 1 or more anti-HER2 treatments.

## Comparator

3.3 The clinical experts confirmed that current standard care in the NHS for people with untreated HER2-positive unresectable or metastatic breast cancer is trastuzumab and a taxane and that for second-line treatment current standard care is trastuzumab emtansine (see section 3.2). The committee concluded that trastuzumab emtansine is the relevant comparator for trastuzumab deruxtecan.

# Clinical evidence

## Data source

3.4 The clinical evidence was based on DESTINY-Breast03, a phase 3, open-label, randomised controlled trial for people with HER2-positive unresectable or metastatic breast cancer previously treated with trastuzumab and a taxane. The trial was done in 169 centres in 15

countries, with a low number of people included from England. The EAG considered that this resulted in some uncertainty about how generalisable the DESTINY-Breast03 results are to UK clinical practice. The clinical experts highlighted that the DESTINY-Breast03 trial included people from different family backgrounds, including Asian and Black family backgrounds. The clinical experts confirmed that DESTINY-Breast03 is generalisable to UK clinical practice. The committee concluded that, although there were low numbers of people in the trial from England, DESTINY-Breast03 is generalisable to UK clinical practice.

## Subsequent treatments

3.5 In its submission, the company explained that the proportion of people who had subsequent treatments in DESTINY-Breast03 was higher than would be expected in NHS clinical practice based on its clinical expert opinion (the exact proportions are confidential and cannot be reported here). So, it assumed the proportion of people having subsequent treatments to be 66.7% in both the trastuzumab deruxtecan and trastuzumab emtansine arms, based on clinical expert opinion. In response to technical engagement, the company highlighted that its base case value is conservative, given that the same value is applied to both treatment arms. The EAG considered that there is uncertainty associated with clinical expert opinion but agreed the proportion of people having subsequent treatments should be 66.7% for both arms in the model. The committee acknowledged the uncertainty but concluded that an assumption that 66.7% of people would have subsequent treatments in both arms was acceptable for decision making.

3.6 In its submission, the company used the same subsequent treatments from the trastuzumab deruxtecan arm and the trastuzumab emtansine arm of DESTINY-Breast03 in its base case. The EAG considered that the subsequent treatment distributions from DESTINY-Breast03 may not be reflective of the subsequent treatments used in NHS clinical practice. It considered that the subsequent treatments in the European subgroup in DESTINY-Breast03 may be more applicable to NHS clinical practice. But it noted that the sample size for this subgroup is small and so is associated with uncertainty. In its response to technical engagement, the

company provided 3 scenario analyses using different subsequent treatments based on: the European subgroup in DESTINY-Breast03; UK clinical expert opinion; and the pooled subsequent treatment distribution from DESTINY-Breast03. It noted these scenarios had a very small impact on the cost-effectiveness estimates and so it maintained its original base case using the subsequent treatment distributions directly from DESTINY-Breast03. The EAG noted that using the scenario analyses provided by the company resulted in minor differences in the cost-effectiveness estimates. But each scenario was associated with uncertainty, and so it used the same estimates as in the company base case. The committee recognised the uncertainty, but it was satisfied that the various scenario analyses had a minor effect on the cost-effectiveness estimates. It concluded that using subsequent treatment distributions from DESTINY-Breast03 was acceptable for decision making.

## Clinical effectiveness

3.7 The primary endpoint of DESTINY-Breast03 is progression-free survival, and overall survival is a secondary endpoint. At the May 2021 data cut-off, median progression-free survival by blinded independent central review was not reached in the trastuzumab deruxtecan arm compared with 6.8 months in the trastuzumab emtansine arm. The hazard ratio was 0.28 ($p<0.001$), showing trastuzumab deruxtecan was associated with a statistically significant improvement in progression-free survival compared with trastuzumab emtansine. Median overall survival was not reached in either arm. The median follow up was 16.2 months in the trastuzumab deruxtecan arm and 15.3 months in the trastuzumab emtansine arm. The clinical experts commented that it is rare for a treatment for metastatic breast cancer to demonstrate such a favourable hazard ratio for progression-free survival, and they would expect this to translate into an overall survival benefit. The committee concluded that based on the interim trial data, trastuzumab deruxtecan could be considered a promising treatment for people with HER2-positive unresectable or metastatic breast cancer after 1 or more anti-HER2 treatments but that the evidence on long-term outcomes is limited.

## Long-term treatment effects

3.8 The overall survival data from the DESTINY-Breast03 study is immature. The median overall survival for both the trastuzumab deruxtecan and trastuzumab emtansine arms could not be estimated from the number of deaths at the May 2021 data cut-off. The clinical experts commented that they would expect the significant benefit in progression-free survival for trastuzumab deruxtecan to translate into a long-term survival benefit (see section 3.7). The company commented that progression-free survival is a good surrogate for overall survival. It said that trastuzumab deruxtecan was associated with a numerically lower risk of death compared with trastuzumab emtansine at the May 2021 data cut-off, with a hazard ratio of 0.55 (95% confidence interval 0.36 to 0.86). So, it assumed a long-term survival benefit for trastuzumab deruxtecan compared with trastuzumab emtansine in its base case. The EAG noted that because of the small number of deaths in the trastuzumab deruxtecan arm of DESTINY-Breast03, there is a high level of uncertainty associated with assuming a long-term survival benefit. The committee accepted that it is unlikely that there is no overall survival benefit at all compared with trastuzumab emtansine. But, because the data is immature, it concluded the size of any overall survival benefit for trastuzumab deruxtecan was highly uncertain, resulting in significant uncertainty in the clinical-effectiveness and cost-effectiveness estimates.

## Adverse events

3.9 The committee noted that trastuzumab deruxtecan is associated with side effects, including interstitial lung disease (ILD). The clinical experts confirmed that trastuzumab deruxtecan is associated with side effects that need careful management. But they explained that trastuzumab deruxtecan is available in the NHS for HER2-positive unresectable or metastatic breast cancer at a later line in the treatment pathway. This means there is experience of using trastuzumab deruxtecan in the NHS and clinicians can effectively monitor and manage side effects, including ILD. The clinical experts advised that there is clinical enthusiasm to use trastuzumab deruxtecan at an earlier line in the treatment pathway for people with HER2-positive unresectable or metastatic breast cancer. The

patient experts commented that side effects do occur with trastuzumab deruxtecan and they can result in dose reductions, which make the side effects more manageable. But they explained that people will accept the side effects of trastuzumab deruxtecan given the benefit it may bring in reducing both tumour volume and symptoms. The committee concluded that trastuzumab deruxtecan is associated with side effects, which may impact on quality of life, but these are manageable for most people.

# Cost-effectiveness evidence

## Company's modelling approach

3.10 The company submitted a partitioned survival model to estimate the cost effectiveness of trastuzumab deruxtecan compared with trastuzumab emtansine. It has 3 health states: progression-free survival, progressed disease, and death. The committee considered that the partitioned survival model is a standard approach to estimate cost effectiveness of cancer drugs and is suitable for decision making.

## Progression-free survival

3.11 The company fitted independent Weibull models to Kaplan–Meier curves to estimate progression-free survival in both arms. The EAG noted that the progression-free survival estimates from DESTINY-Breast03 that were used to inform long-term extrapolations of progression-free survival in the economic model were associated with uncertainty because the data was immature. The EAG acknowledged that alternative extrapolations of the data only have a small effect on the cost-effectiveness estimates. The committee concluded that the company's approach to estimating progression-free survival was appropriate.

## Long-term overall survival

3.12 In its submission, the company assumed a long-term survival benefit for trastuzumab deruxtecan compared with trastuzumab emtansine (see sections 3.7 and 3.8). In its base case, the company extrapolated overall survival beyond the end of the trial follow-up period using parametric

survival models. The log-logistic model provided the best statistical fit to the DESTINY-Breast03 trial data. But the company chose the generalised gamma curve for its base case based on clinical expert opinion. The EAG noted that there is considerable uncertainty in the company's predicted survival for trastuzumab deruxtecan. The company's extrapolated overall survival curve for trastuzumab deruxtecan relies on the assumption that the trend in overall survival seen within the trial will continue beyond the follow-up period. The EAG considered this an uncertain assumption given the immature survival data in DESTINY-Breast03. It recognised that there is some separation of the overall survival curves between trastuzumab deruxtecan and trastuzumab emtansine. But it commented that there is insufficient evidence to prove a long-term difference in overall survival between them, in particular, if there is a continued benefit during disease progression after treatment has stopped. It commented that there is no survival data post-progression, meaning that it is not clear if there is a treatment effect after disease progression. In its base case, the EAG preferred an assumption that there is no survival benefit after progression. Instead, it used the estimated overall survival from the company's base case for the first 2 years and then adjusted the overall survival beyond 2 years. It used 2 years as the point to adjust overall survival because only 24 people were still in the trastuzumab deruxtecan arm of the trial by 2 years. This method consisted of increasing the mortality hazard ratio according to the implied progression-free survival mortality rate that was derived from the generalised gamma overall survival curve fitted for trastuzumab deruxtecan. The EAG assumed no difference in effectiveness between trastuzumab deruxtecan and trastuzumab emtansine in the progressed disease state beyond 2 years. At technical engagement, the company provided an alternative methodology incorporating further long-term data. Data was replicated from the trastuzumab emtansine arm of the EMILIA study, which compared trastuzumab emtansine with lapatinib and capecitabine. It had a median follow up of 47.8 months. Parametric survival models were fitted to the replicated data to inform the trastuzumab emtansine overall survival. The hazard ratio from DESTINY-Breast03 was then applied to this curve to inform the trastuzumab deruxtecan overall survival. This alternative method resulted in similar cost-effectiveness estimates to the company's base case. The committee noted that only a small number of deaths occurred during the follow-up period of DESTINY-Breast03. So,

the long-term extrapolation of overall survival for trastuzumab deruxtecan is highly uncertain, with no data currently available to inform which extrapolation method is most appropriate. The committee concluded that the modelling of overall survival was highly uncertain and further data collection was needed to inform overall survival with trastuzumab deruxtecan.

## Utility values

3.13 In its submission, the company noted that the number of post-progression observations from DESTINY-Breast03 were limited. It also highlighted that post-progression utility values taken directly from the trial were implausibly high in comparison to previously accepted progressed disease utility values within the same population, based on clinical opinion. So, it used utility values which were derived from coefficients of the mixed model analysis from Lloyd et al. (2006). The company assumed that people who progress while on trastuzumab deruxtecan would have a better quality of life compared with those who progress while on trastuzumab emtansine. This is because of improved response rates and improved disease control. The EAG raised concerns about using Lloyd et al. (2006) to calculate coefficients for the utility values weighted by responder and non-responder from the DESTINY-Breast03 trial. It noted Lloyd et al. (2006) does not provide any evidence for difference in utility values for people who have progressed after responding to initial treatment. It provides evidence for people who currently respond to treatment before progression. The EAG commented it could not find any evidence for a difference in utility values after progression. At technical engagement, the company provided scenario analyses as an alternative to assuming a utility benefit for trastuzumab deruxtecan across the entire progressed disease state. Instead, the difference in utility lasts for 4 or 6 months after progression, then the same utility value is assumed for both trastuzumab deruxtecan and trastuzumab emtansine. The committee noted the company's rationale that people on trastuzumab deruxtecan would have a higher quality of life post-progression than people on trastuzumab emtansine because of improved response rates and disease control. But the committee considered that there is no direct trial evidence to support such a utility benefit. It concluded that there was no direct evidence of a utility benefit

post-progression and that post-progression utility values should be independent of previous treatment.

## Vial sharing

3.14 In its submission, the company assumed that vial sharing is available in some UK centres. In its base case, the company assumed 50% vial sharing in line with the assumptions accepted in NICE's technology appraisal guidance on sacituzumab govitecan for treating unresectable triple-negative advanced breast cancer after 2 or more therapies and NICE's technology appraisal guidance on trastuzumab deruxtecan for treating HER2-positive unresectable or metastatic breast cancer after 2 or more anti-HER2 therapies. The EAG commented that 50% vial sharing could be an overestimate and that if vial sharing is carried out it is unlikely there would be perfect allocation of each dose. So, it preferred to use 10% vial sharing in its base case. The NHS England Cancer Drugs Fund clinical lead confirmed that vial sharing is encouraged by NHS England and that they expected vial sharing to occur regularly for trastuzumab deruxtecan because of dose banding, in which individual doses are rounded up or down. They commented that they would expect vial sharing to occur in at least 50% of cases. The committee concluded that vial sharing should be assumed to occur in 50% of cases.

# Severity

## QALY weighting

3.15 In its submission, the company provided evidence that HER2-positive unresectable or metastatic breast cancer after 1 or more anti-HER2 treatments is a severe condition. The severity modifier allows the committee to give more weight to health benefits in the most severe conditions. The company provided absolute and proportional quality-adjusted life year (QALY) shortfall estimates in line with NICE's health technology evaluations manual. Absolute QALY shortfall is the future health that is lost by people living with a condition, including quality and length of life, compared with the expected future health of people living without the condition, over their remaining lifetimes. Proportional QALY

shortfall represents the proportion of future health that is lost by people living with the condition, including quality and length of life. To estimate the absolute and proportional QALY shortfalls, the company provided the QALYs of people without the condition over their remaining lifetime, based on the characteristics of people in the trial and the QALYs of people with the condition on current standard care. The company estimated that people with these characteristics without HER2-positive unresectable or metastatic breast cancer would be expected to have remaining lifetime QALYs of 14.63. It used the Measuring and Valuing Health Study EQ-5D-3L value set and health state profiles from 2012 and 2014 Health Survey for England data. The EAG estimated the expected remaining lifetime QALYs to be 14.33 using Hernández-Alava et al. (2017) EQ-5D-5L to EQ-5D-3L mapping with health state profiles from Health Survey for England data for 2017 to 2018. The company's model estimated the expected remaining lifetime QALYs for people with the condition who have trastuzumab emtansine after trastuzumab and a taxane, by cross-walking EQ-5D-5L to EQ-5D-3L using the van Hout algorithm. This resulted in values for absolute QALY shortfall of 12 or above. The proportional QALY shortfall was estimated at less than 0.85. The company considered that the 1.2 QALY weight should apply (the exact QALYs, and the absolute and proportional QALY shortfalls are confidential so cannot be reported here). The EAG preferred to cross-walk EQ-5D-5L to EQ-5D-3L using the Hernández-Alava et al. (2017) algorithm which resulted in values for absolute QALY shortfall of less than 12 and a proportional QALY shortfall of less than 0.85. So, the EAG base case suggested that a severity QALY weighting does not apply (the exact QALYs, and the absolute and proportional QALY shortfalls, are confidential so cannot be reported here). The committee discussed the methods used by the company and the EAG to estimate the remaining lifetime QALYs for the general population and for people living with the condition. It noted NICE's position statement on the use of the EQ-5D-5L value set and was also aware that NICE's health technology evaluations manual states a preference for Hernández-Alava et al. (2017), as used by the ERG to cross-walk EQ-5D-5L to EQ-5D-3L. It considered there was high uncertainty around the methods used to estimate the remaining lifetime QALYs for the general population and for people living with the condition. The committee noted that the modifier for disease severity was not convincingly met but recognised that there were plausible cost-

effectiveness estimates below £30,000 per QALY gained when the QALY weight was not applied and when the 1.2 QALY weight was applied. The committee concluded that it is uncertain whether the modifier for disease severity was convincingly met, but recognised it was met in some scenarios.

# Cost-effectiveness estimates

## Company and EAG cost-effectiveness estimates

3.16 Because of confidential discounts for trastuzumab deruxtecan, trastuzumab emtansine and subsequent treatments, the cost-effectiveness results are commercial in confidence and cannot be reported here. The committee preferred an analysis that included:

- 66.7% of people having subsequent treatments in both arms
- the distributions of subsequent treatments from DESTINY-Breast03
- treatment-independent post-progression utility values
- vial sharing in 50% of cases.

The committee recalled the uncertainty in how the survival benefit of trastuzumab deruxtecan was modelled and that further data collection was needed to inform overall survival with trastuzumab deruxtecan (see section 3.8 and section 3.11). Using the committee's preferred assumptions and the company's preferred overall survival extrapolation resulted in an incremental cost-effectiveness ratio (ICER) above £30,000 per QALY gained. But the committee noted that using the committee's preferred assumptions with different methods of extrapolating overall survival resulted in ICERs below £30,000 per QALY gained. The committee considered these scenarios were plausible but uncertain. Using the committee's preferred assumptions and the EAG's preferred overall survival extrapolation, which assumed no long-term survival benefit for trastuzumab deruxtecan, resulted in an ICER that was above £30,000 per QALY gained. The committee agreed that this ICER is not implausible, because of the high degree of uncertainty of the long-term overall survival benefit of trastuzumab deruxtecan compared with trastuzumab

emtansine. This is mainly related to the immaturity of the overall survival data. The committee recognised that the evidence base was immature and the most plausible cost-effectiveness estimates for trastuzumab deruxtecan are highly uncertain. It concluded that with the available data, the most plausible ICER had not been proven to be within the range usually considered a cost-effective use of resources, even when the severity modifier was applied. So, it concluded that trastuzumab deruxtecan could not be recommended for routine commissioning.

# Managed access

## Recommendation with managed access

3.17 Having concluded that trastuzumab deruxtecan could not be recommended for routine use, the committee then considered if it could be recommended with managed access for treating HER2-positive unresectable or metastatic breast cancer after 1 or more anti-HER2 treatments. The committee considered whether a recommendation with managed access could be made, and discussed that:

- There is plausible potential to satisfy the criteria for routine use:
  - the committee considered there are plausible ICERs below £30,000 per QALY both when the modifier for disease severity is applied and when it is not applied
  - the company's model is structurally robust for decision making (see section 3.10).
- The key uncertainties relate to overall survival, which is a key driver of the cost-effectiveness results.
- New evidence could address the clinical uncertainty:
  - data from DESTINY-Breast03 is immature because only a small percentage of those recruited had had an event by the May 2021 data cut-off. The trial is ongoing and further data could help reduce uncertainties around long-term progression-free survival and overall survival

  - the Systemic Anti-Cancer Therapy dataset could provide meaningful real-world data about time on treatment and overall survival for trastuzumab deruxtecan in the NHS.

- The company submitted a managed access proposal and expressed an interest in trastuzumab deruxtecan being considered for funding through managed access. The managed access feasibility assessment noted that trastuzumab deruxtecan would likely be eligible for use in the Cancer Drugs Fund.

  The committee considered that trastuzumab deruxtecan met the criteria to be considered for a recommendation with managed access. It recommended trastuzumab deruxtecan for use in managed access as an option for people with HER2-positive unresectable or metastatic breast cancer, after 1 or more anti-HER2 treatments, if the conditions in the managed access agreement are followed. When the guidance is next reviewed the company should use the committee's preferred assumptions (unless new evidence indicates otherwise) as set out in sections 3.4 to 3.15.

## Innovation

3.18 The company, patient experts and clinical experts considered trastuzumab deruxtecan to be innovative. They explained that it would be a step-change in improving clinical outcomes and managing HER2-positive unresectable or metastatic breast cancer after 1 or more anti-HER2 treatments. The committee considered whether trastuzumab deruxtecan was innovative. It did not identify additional benefits of trastuzumab deruxtecan not captured in the economic modelling. So, the committee concluded that all additional benefits of trastuzumab deruxtecan had already been taken into account.

# 4 Implementation

4.1 When NICE recommends a treatment as an option for use with managed access, NHS England will make it available according to the conditions in the managed access agreement. This means that, if a patient has HER2-positive unresectable or metastatic breast cancer after 1 or more anti-HER2 treatments and the doctor responsible for their care thinks that trastuzumab deruxtecan is the right treatment, it should be available for use, in line with NICE's recommendations and the criteria in the managed access agreement.

4.2 Chapter 2 of Appraisal and funding of cancer drugs from July 2016 (including the new Cancer Drugs Fund) – A new deal for patients, taxpayers and industry states that for those drugs with a draft recommendation for use in the Cancer Drugs Fund, interim funding will be available (from the overall Cancer Drugs Fund budget) from the point of marketing authorisation, or from release of positive draft guidance, whichever is later. Drugs that are recommended for use in the Cancer Drugs Fund will be funded in line with the terms of their managed access agreement, after the period of interim funding. The NHS England Cancer Drugs Fund list provides up-to-date information on all cancer treatments recommended by NICE since 2016. This includes whether they have received a marketing authorisation and been launched in the UK.

4.3 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance when the drug or treatment, or other technology, is approved for use with managed access. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, for use with managed access, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final draft guidance or agreement of a managed access agreement by the NHS in Wales, whichever is the later.

# 5 Evaluation committee members and NICE project team

## Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee A.

Committee members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

## Chair

**Jane Adam**
Chair, technology appraisal evaluation committee A

## NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser and a project manager.

**Nigel Gumbleton**
Technical lead

**Elizabeth Bell**
Technical adviser

**Jeremy Powell**
Project manager

ISBN: 978-1-4731-4992-2