NICE National Institute for Health and Care Excellence

NICE guidance

Trastuzumab deruxtecan for treating HER2-positive unresectable or metastatic breast cancer after 2 or more anti-HER2 therapies

Technology appraisal guidance
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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 for use within the Cancer Drugs Fund as an option for treating HER2-positive unresectable or metastatic breast cancer in adults after 2 or more anti-HER2 therapies. It is recommended only if the conditions in the managed access agreement 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

Current treatment for HER2-positive unresectable or metastatic breast cancer includes anti-HER2 therapies. After 2 or more anti-HER2 therapies, standard care is chemotherapy (such as capecitabine, vinorelbine or eribulin). Trastuzumab deruxtecan is an anti-HER2 therapy that would be used after 2 or more anti-HER2 therapies.

Clinical trial evidence is limited. There is a trial of trastuzumab deruxtecan on its own, which means it is not directly compared with any other treatments. Indirect comparisons of trastuzumab deruxtecan with chemotherapy suggest that it may increase how long before disease progresses and how long people live. However, how much longer people live is uncertain because there are differences between trials included in the indirect comparisons, and the final data from the trial of trastuzumab deruxtecan on its own is not available yet. Because of this, the estimates of cost effectiveness are very uncertain and trastuzumab deruxtecan cannot be recommended for routine use in the NHS.

Trastuzumab deruxtecan could be cost effective if further data shows that people live longer with treatment. Another ongoing trial is directly comparing trastuzumab deruxtecan with anti-HER2 therapies plus chemotherapy. Data from the trials of trastuzumab deruxtecan and from NHS practice would help address the uncertainty about clinical effectiveness. Trastuzumab deruxtecan is therefore recommended for use in the Cancer Drugs Fund.

2 Information about trastuzumab deruxtecan

Marketing authorisation indication

2.1 Trastuzumab deruxtecan (Enhertu, Daiichi-Sankyo) has a marketing authorisation as 'monotherapy for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received two 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.

Price

2.3 The company's list price is £1,455 per vial containing 100 mg powder for concentrate for solution for infusion (company's submission). The average cost of a course of treatment at list price is £117,857.55.

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 appraisal committee considered evidence submitted by Daiichi-Sankyo, a review of this submission by the evidence review group (ERG) and responses from stakeholders. Ahead of technical engagement, the company submitted new data based on the latest data cut from the trial (June 2020). The evidence and results presented at the committee meeting were based on this data cut. See the committee papers for full details of the evidence.

Clinical need and treatment pathway

HER2-positive unresectable or metastatic breast cancer has a high disease burden

3.1 Some breast cancer cells have higher levels of a protein called 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. Patient experts explained that being diagnosed with unresectable or metastatic breast cancer is extremely difficult for people and their family and friends. It can cause considerable anxiety and fear, with the uncertainty being the hardest part for many people. These feelings can negatively affect mental health. People with unresectable or metastatic breast cancer must organise their lives around hospital appointments, which constrains 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.

There is a need for anti-HER2 therapies after second-line treatment

3.2 Clinical experts explained that people with HER2-positive unresectable

or metastatic breast cancer that has progressed after 2 or more anti-HER2 therapies have a high symptom burden and their disease is resistant to the previous lines of therapy. First-line treatment of HER2-positive unresectable or metastatic breast cancer includes anti-HER2 therapies pertuzumab with trastuzumab and docetaxel, or trastuzumab with paclitaxel (see NICE's technology appraisal guidance on pertuzumab with trastuzumab and docetaxel for treating HER2-positive breast cancer and trastuzumab for the treatment of advanced breast cancer). Trastuzumab emtansine is an anti-HER2 therapy used as second-line treatment (see NICE's technology appraisal guidance on trastuzumab emtansine for treating HER2-positive advanced breast cancer after trastuzumab and a taxane). The committee noted that, although some trusts may offer third-line anti-HER2 therapy, this is not available across the NHS and cannot be considered standard care. Instead, standard care for people whose disease has progressed on or after 2 anti-HER2 therapies is non-targeted chemotherapy, including capecitabine, vinorelbine, or eribulin (see NICE's guideline on advanced breast cancer: diagnosis and treatment and NICE's technology appraisal guidance on eribulin for treating locally advanced or metastatic breast cancer after 2 or more chemotherapy regimens). Patient experts explained that chemotherapy has limited efficacy and can cause side effects that are typically more severe than with anti-HER2 therapies. People having chemotherapy may also experience worse quality of life. Therefore, people want to avoid having chemotherapies for as long as possible. Patient experts highlighted the need for treatments that can extend survival with acceptable tolerability and quality of life. The committee concluded that that there is an unmet need for anti-HER2 treatment after second-line treatment.

Relevant comparators for trastuzumab deruxtecan include capecitabine, vinorelbine and eribulin

3.3 Current standard care in the NHS for people with HER2-positive unresectable or metastatic breast cancer that has progressed after 2 or more anti-HER2 therapies is non-targeted chemotherapy, including capecitabine, vinorelbine, or eribulin. Eribulin is recommended for treating locally advanced or metastatic breast cancer after 2 or more chemotherapy regimens (which may include an anthracycline or a

taxane, and capecitabine; see NICE's technology appraisal guidance on eribulin). The clinical experts explained that, in practice, capecitabine or vinorelbine is mostly used as third-line treatment and eribulin is more likely to be used as fourth-line treatment. They confirmed that trastuzumab deruxtecan would replace capecitabine, vinorelbine and eribulin. The committee concluded that capecitabine, vinorelbine and eribulin are all relevant comparators for trastuzumab deruxtecan.

Clinical evidence

DESTINY-Breast01 is generalisable to UK clinical practice

3.4 The clinical evidence was based on DESTINY-Breast01, a single-arm trial for people with HER2-positive unresectable or metastatic breast cancer previously treated with trastuzumab emtansine. Clinical experts explained that DESTINY-Breast01 is representative of patients in the NHS in terms of characteristics and previous treatment. The committee noted that most people in the trial had 3 or more previous therapies (median 6, range 2 to 24, excluding hormone therapy) and so had more previous treatments than people in the NHS. Clinical experts explained that in people who have had more previous treatments, disease is usually less likely to respond to the next line of treatment. Therefore, trastuzumab deruxtecan efficacy could be higher in the NHS than in the trial. This is supported by a subgroup analysis from DESTINY-Breast01 (see section 3.5). The committee concluded that DESTINY-Breast01 is broadly generalisable to clinical practice in the UK.

Preliminary data for trastuzumab deruxtecan is limited but promising

3.5 The primary end point of DESTINY-Breast01 is overall response rate, while overall survival and progression-free survival are secondary endpoints. At the June 2020 data cut-off, overall response rate for trastuzumab deruxtecan was 61.4%. The preliminary median overall survival was 24.6 months (95% confidence interval [CI] 23.1 to not evaluable). Median progression-free survival was 19.4 months (95% CI 14.1 to not evaluable). The median follow up was 20.5 months. However,

data was immature, with only 35% maturity for overall survival analysis, and a high amount of censoring. The clinical experts explained that although it was a single-arm trial with immature data, the observed results suggested a promising efficacy. They noted an overall response rate of 61.4% in a population who have had a lot of previous treatments, such as in DESTINY-Breast01, which is much higher than with other available therapies. They explained that response to treatment is usually better with earlier lines of therapy and decreases with subsequent lines of therapy. The pre-specified subgroup analysis from the DESTINY-Breast01 trial showed that overall response rate was higher in people who only had 2 previous lines of treatment (76% [95% CI 50% to 93%]), compared with those who had 3 or more previous lines of treatment (59% [95% CI 51% to 67%]). However, this analysis was based on a small number of patients (17 people in the group who had only 2 previous lines) so it is highly uncertain. Clinical experts also explained that in DESTINY-Breast01, only 21.7% of people had disease response to previous treatment with trastuzumab emtansine. This suggests that a high response rate to trastuzumab deruxtecan is unlikely to be because of patient selection. The clinical experts described randomised controlled trials in people with HER2-positive metastatic breast cancer who have had at least 2 previous anti-HER2 therapies (TH3RESA, SOPHIA, NALA, HER2CLIMB). These trials used more intensive treatments as the control arms (chemotherapy plus anti-HER2 therapy) than chemotherapy alone. This means the efficacy of these control arms is likely to be the same as or higher than for chemotherapy alone. Median progression-free survival in the control arms was between 3.3 months and 5.6 months, and median overall survival between 15.8 months and 19.8 months. This is lower than the lower bound of the confidence interval for overall survival (23.1 months) for trastuzumab deruxtecan from DESTINY-Breast01. The committee concluded that the preliminary data for trastuzumab deruxtecan suggests a promising efficacy but is limited for decision making.

Trastuzumab deruxtecan is likely to improve clinical outcomes, including overall survival, but the size of effect is uncertain

3.6 Because DESTINY-Breast01 is a single-arm trial, there is no evidence for the efficacy of trastuzumab deruxtecan directly compared with other

treatments. The company therefore did unanchored matching-adjusted indirect comparisons (MAIC) of trastuzumab deruxtecan compared with capecitabine, vinorelbine and eribulin. The MAIC results showed that trastuzumab deruxtecan was associated with improved overall response rate, progression-free survival and overall survival compared with the comparators, but there were major limitations. The committee understood that for an unanchored indirect comparison such as MAIC, population adjustment methods should adjust for all effect modifiers and prognostic variables. But important factors such as HER2 status and previous anti-HER2 therapy could not be adjusted for, because all patients in DESTINY-Breast01 had HER2-positive disease and previous anti-HER2 therapy. In the eribulin trial (Cortes 2011) used in the comparison, not all patients had HER2-positive disease or 2 or more previous lines of anti-HER2 therapy. The company explained that eribulin is not an anti-HER2 therapy, so additional data is unlikely to become available for the HER2-positive subgroup. The capecitabine trial (EGF100151 study) was done in a HER2-positive population who had at least 1 previous line of anti-HER2 therapy. The ERG explained that this study was more relevant to the population of this appraisal, but there was still some uncertainty in the MAIC of trastuzumab deruxtecan compared with capecitabine. This is because the capecitabine trial was done in a population who had at least 1 previous anti-HER2 therapy. Also, the analysis only included patients who did not cross over to combination therapy (lapatinib plus capecitabine) after their disease had progressed on capecitabine, which may have introduced selection bias. The vinorelbine (KCSG BR11-16) trial was done in a population that matched the DESTINY-Breast01 population. However, clinical experts explained that it was a small study done in South Korea, so the generalisability to UK clinical practice was unclear. The committee understood that the comparative efficacy of trastuzumab deruxtecan was difficult to assess. This was because the trials available for the comparators were quite old and not representative of the latest developments in metastatic breast cancer. The clinical experts mentioned that more meaningful comparisons could be done using control arms from more recent trials for anti-HER2 therapies, even though they do not represent current NHS practice (see section 3.5). The committee concluded that the company's MAIC has limitations, and the results are uncertain. It also concluded that trastuzumab deruxtecan is likely to improve clinical outcomes, including

overall survival, compared with eribulin, capecitabine and vinorelbine. But the size of this effect is uncertain.

Trastuzumab deruxtecan has an acceptable safety profile

3.7 The committee noted that trastuzumab deruxtecan was associated with a relatively high rate of interstitial lung disease (ILD). The clinical experts explained that close monitoring for signs and symptoms of ILD is needed and that, when treated early and adequately, ILD usually resolves without any long-term issues. Also, the clinical experts explained that other treatments approved by NICE can also cause ILD, and clinical teams have experience to manage it adequately. The committee noted that non-targeted chemotherapies have higher rates of grade 3 to 4 adverse events that have a negative effect on patients' quality of life. Also, adverse effects of chemotherapies are a key concern for patients (see section 3.2). The clinical experts also explained that adverse events rates usually increase or stay steady across treatment lines, so trastuzumab deruxtecan is not expected to be tolerated less if it is used as third-line treatment in NHS clinical practice. The committee concluded that trastuzumab deruxtecan is associated with side effects, but its safety profile was acceptable.

Cost-effectiveness evidence

The company's economic model is suitable for decision making

3.8 The company submitted a partitioned survival model to estimate the cost effectiveness of trastuzumab deruxtecan compared with eribulin, capecitabine and vinorelbine. It had 4 health states: progression-free on treatment, progression-free off treatment, progressed, and death. The committee considered that the partitioned survival model is a standard approach to estimate the cost effectiveness of cancer drugs and is suitable for decision making.

The company's modelling of progression-free survival and time to stopping treatment for comparators is uncertain

3.9 In the model, progression-free survival and time to stopping treatment for trastuzumab deruxtecan are extrapolated from DESTINY-Breast01 trial data. The company used the hazard ratios from the MAIC to derive progression-free survival for comparators. The MAIC results were uncertain because some important characteristics could not be adjusted for (see section 3.6). Time to stopping treatment was not available in the studies of comparators, so the company assumed it was the same as progression-free survival. The committee concluded that the modelling of progression-free survival and time to stopping treatment for comparators was uncertain. This was because of the uncertainty in the indirect treatment comparison and using proxy data for time to stopping treatment for comparators.

The company's modelling of overall survival for trastuzumab deruxtecan relies on data from another treatment and is highly uncertain

3.10 In the economic model, overall survival is one of the key drivers of the results. The company explained that overall survival data from DESTINY-Breast01 is too immature to extrapolate and provide robust long-term overall survival estimates. Therefore, the company used an alternative approach in its base case. It modelled overall survival for trastuzumab deruxtecan by applying a hazard ratio for trastuzumab deruxtecan relative to trastuzumab emtansine to an extrapolated survival curve for trastuzumab emtansine. The hazard ratio was calculated for trastuzumab deruxtecan based on DESTINY-Breast01 (June 2020 data cut, censored at 20.5 months) relative to trastuzumab emtansine based on TH3RESA. This was calculated using the Cox proportional hazards model in a naive comparison; that is, without adjusting for differences between the populations in the 2 trials. This hazard ratio was then applied to the overall survival curve of trastuzumab emtansine in TH3RESA, extrapolated using the generalised gamma function. The company's approach was based on clinical opinion that the shape of the curve for trastuzumab deruxtecan will be similar to trastuzumab emtansine. This is because both are HER2-antibody drug conjugates,

where a HER2-antibody is linked to a cytotoxic agent that is released after binding to HER2 on the surface of cancer cells. The company used DESTINY-Breast01 overall survival data censored at 20.5 months because it considered that the small number of events after this timepoint made the data uninformative. It chose the generalised gamma to extrapolate overall survival of TH3RESA. This was based on clinical opinion that it gave more plausible survival estimates, and better reflected the observed overall survival shape of other anti-HER2 therapies, than other survival functions. The committee noted that this modelling approach gave an optimistic estimate of overall survival at 20 months (75%), compared with overall survival observed in the DESTINY-Breast01 trial at the same timepoint (70%). It also noted that it would have been useful to have clinical opinion on the expected hazards for death over time, to help select the most appropriate function to extrapolate overall survival. The company also presented:

- Secondary analysis using uncensored DESTINY-Breast01 overall survival data to calculate the hazard ratio for trastuzumab deruxtecan compared with trastuzumab emtansine (the hazard ratio was higher than in the base case).

- Exploratory analysis in response to technical engagement, directly extrapolating overall survival data from DESTINY-Breast01 trial (June 2020 data cut, censored at 20.5 months). The company used an average of the Weibull and exponential curves. This was based on clinical expert opinion that the Weibull curve was implausibly low and exponential curve was implausibly high.

  The ERG agreed with the company that the DESTINY-Breast01 overall survival data is still too immature to extrapolate and provide robust long-term overall survival estimates. It explained that company's base-case approach is not implausible but is highly uncertain. It did not identify any alternative approach to generate more robust analysis, because of evidence limitations. The clinical experts explained that it was difficult to predict the shape of the overall survival curve of trastuzumab deruxtecan in the long term, but that data available indicated considerable survival benefits. The committee noted the high uncertainty in the company's base-case approach for modelling overall survival for trastuzumab deruxtecan. This related to uncertainty in the hazard ratio for overall survival compared with trastuzumab emtansine and long-term extrapolations of overall survival. Therefore, the committee agreed to consider a range of scenario analyses presented by the ERG. These used alternative extrapolation curves for TH3RESA overall survival and, at the same time, varied the hazard ratio for overall survival with trastuzumab deruxtecan relative to trastuzumab emtansine. The committee concluded that the modelling of overall survival was highly uncertain and further data collection was needed to inform trastuzumab deruxtecan overall survival. It also concluded that, once more mature data is available, it would prefer the overall survival data for trastuzumab deruxtecan to be directly extrapolated without relying on data from another treatment.

The company's modelling of overall survival for comparators is a naive comparison

3.11 The company modelled the overall survival for comparators using the Kaplan–Meier data from comparator studies directly (Cortes 2011 for eribulin, EGF100151 for capecitabine and Sim 2019 for vinorelbine) rather than using MAIC results. It explained that this was based on clinical opinion that applying a hazard ratio from the MAIC may not be appropriate. This is because the shape of the overall survival curves is expected to differ between the comparators and trastuzumab

deruxtecan, for which a tail may be expected, as seen with other targeted therapies. The committee noted that this approach was a naive comparison; that is, it was not adjusted for differences in patient characteristics between the trials. But, the MAIC also had limitations. There were important differences between DESTINY-Breast01 and the trials of comparators (see section 3.6) and the committee understood that the direction of the uncertainty was unclear. Therefore, it was impossible to assess whether the relative overall survival with trastuzumab deruxtecan compared with its comparators was overestimated or underestimated in the model. The committee concluded that the relative overall survival benefit for trastuzumab deruxtecan compared with its comparators in the model was uncertain, because it was based on naive comparisons. It also concluded that evidence from a randomised controlled trial was needed to allow a more robust comparison. As a minimum, evidence from such a trial would allow an indirect treatment comparison using a connected network.

The company's utility values are broadly appropriate

3.12 Health-related quality-of-life data were not collected in the DESTINY-Breast01 trial, so the company used utility values from NICE's technology appraisal guidance for eribulin. The utility values for the 'progression-free on treatment' health state were calculated as a function of the overall response rate for each treatment. Overall response rates for comparators were derived from the MAIC, which was uncertain (see section 3.6). The committee noted that disutility was also applied for adverse events. The clinical expert confirmed that in metastatic breast cancer, there was a clear link between health-related quality of life and objective response rate, progression-free survival, and treatment-emergent adverse events. The committee concluded that the company's approach to utility values is broadly appropriate, but there may be some uncertainty related to limitations of the indirect treatment comparison.

End of life

Trastuzumab deruxtecan meets the end of life criteria

3.13 The committee considered the advice about life-extending treatments for people with a short life expectancy in NICE's guide to the methods of technology appraisal. Clinical experts explained that life expectancy after progressing on trastuzumab emtansine was less than 24 months. They also explained that the preliminary overall survival results from the DESTINY-Breast01 trial were promising, with the likely extension to life of at least 3 months. The ERG agreed that, based on the latest data cut from June 2020, an improvement in overall survival of at least 3 months was plausible. The clinical experts also noted that the end of life criteria were accepted in NICE's technology appraisal guidance on eribulin in third-line treatment and trastuzumab emtansine in second-line treatment. The committee agreed that although the size of the overall survival benefit compared with NHS clinical practice is uncertain, trastuzumab deruxtecan was likely to give an extension to life of at least 3 months. It concluded that, despite the uncertainty in the clinical evidence, trastuzumab deruxtecan likely meets the end of life criteria.

Cost-effectiveness estimates

Trastuzumab deruxtecan is not recommended for routine use in the NHS

3.14 The committee recalled the high uncertainty in how the relative efficacy of trastuzumab deruxtecan was modelled (see sections 3.9 to 3.12). The ERG did not identify any alternative approach to allow a more robust analysis, because of evidence limitations. The company's base-case fully incremental analysis produced an incremental cost-effectiveness ratio (ICER) of £47,230 per quality-adjusted life year (QALY) gained relative to capecitabine. The committee considered this ICER was plausible, but highly uncertain. Therefore, the committee considered a range of scenario analyses provided by the ERG. In these, the hazard ratio for overall survival for trastuzumab deruxtecan compared with trastuzumab

emtansine and overall survival extrapolation from the TH3RESA trial were varied at the same time (see section 3.10). This gave ICERs of up to £78,142 per QALY gained relative to capecitabine. The committee agreed that this ICER is not implausible, because of the high degree of uncertainty in the relative clinical benefit of trastuzumab deruxtecan compared with its comparators. This is mainly related to the immaturity of the overall survival data and the lack of comparative evidence. The committee concluded that the evidence base was immature and that the ICER could be higher than what NICE normally considers an acceptable use of NHS resources, even considering end of life criteria. Therefore, it concluded that trastuzumab deruxtecan could not be recommended for routine commissioning.

Cancer Drugs Fund

Trastuzumab deruxtecan meets the criteria for inclusion in the Cancer Drugs Fund

3.15 Having concluded that trastuzumab deruxtecan could not be recommended for routine use, the committee considered if it could be recommended within the Cancer Drugs Fund. The committee discussed the arrangements for the Cancer Drugs Fund agreed by NICE and NHS England in 2016, noting NICE's Cancer Drugs Fund methods guide (addendum). It noted that:

- The company expressed an interest in trastuzumab deruxtecan being considered for funding through the Cancer Drugs Fund.
- The company model is structurally robust for decision making (see section 3.8).
- Overall survival is a key driver of the cost-effectiveness results and the key source of uncertainty.
- Data from DESTINY-Breast01 is immature. This single-arm trial is still ongoing and further data could help reduce uncertainties around long-term progression-free survival and overall survival.

- Comparative evidence is currently not available. A randomised controlled trial, DESTINY-Breast02, is ongoing and will provide direct comparative evidence of trastuzumab deruxtecan compared with either trastuzumab plus capecitabine or lapatinib plus capecitabine (treatment is chosen by the investigator). These comparators are not used in NHS clinical practice, but data could be used to inform an indirect treatment comparison using a connected network.
- 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.
- Trastuzumab deruxtecan has plausible potential to be cost effective, considering end of life criteria (see sections 3.13 and 3.14) and a confidential patient access scheme (see section 2.4).

  The committee was satisfied that trastuzumab deruxtecan met the criteria for inclusion in the Cancer Drugs Fund. Therefore, it recommended trastuzumab deruxtecan for use within the Cancer Drugs Fund for people with HER2-positive unresectable or metastatic breast cancer, after 2 or more anti-HER2 therapies, 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 3.9 to 3.12.

Innovation

The model adequately captures the benefits of trastuzumab deruxtecan

3.16 The company, patients 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-postive unresectable or metastatic breast cancer after 2 or more anti-HER2 therapies. The committee concluded that trastuzumab deruxtecan had the potential to give significant benefits for patients, but these benefits have been adequately captured in the model.

4 Implementation

4.1 When NICE recommends a treatment as an option for use within the Cancer Drugs Fund, 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 2 or more anti-HER2 therapies 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 Cancer Drugs Fund criteria in the managed access agreement. Further information can be found in NHS England's Appraisal and funding of cancer drugs from July 2016 (including the new Cancer Drugs Fund) – A new deal for patients, taxpayers and industry.

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 and NHS Improvement 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 within the Cancer Drugs Fund. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, for use within the Cancer Drugs Fund, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal document or agreement of a managed access agreement by the NHS in Wales, whichever is the later.

5 Appraisal committee members and NICE project team

Appraisal 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 to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

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.

NICE project team

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

Rebecca Thomas and Caroline Bregman
Technical leads

Ewa Rupniewska
Technical adviser

Thomas Feist
Project manager

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Accreditation