NICE National Institute for Health and Care Excellence

NICE guidance

Cetuximab for treating recurrent or metastatic squamous cell cancer of the head and neck

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.

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This guidance replaces TA172.

1 Recommendations

1.1 Cetuximab in combination with platinum-based chemotherapy is recommended as an option for treating recurrent or metastatic squamous cell cancer of the head and neck in adults only:

- if the cancer started in the oral cavity and
- when the company provides the drug in line with the commercial access agreement with NHS England.

1.2 These recommendations are not intended to affect treatment with cetuximab that was started within the NHS before this guidance was published. People having treatment outside these recommendations 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.

2 Information about cetuximab

Description of the technology

2.1 Cetuximab (Erbitux; Merck) is a recombinant monoclonal antibody that blocks human epidermal growth factor receptor (EGFR). It inhibits the proliferation of cells that depend on EGFR activation for growth.

Marketing authorisation

2.2 Cetuximab has a UK marketing authorisation 'for the treatment of patients with squamous cell cancer of the head and neck... in combination with platinum-based chemotherapy for recurrent and/or metastatic disease'.

Adverse reactions

2.3 Very common adverse reactions with cetuximab include skin reactions, which occur in more than 80% of patients, and low blood magnesium levels, mild or moderate infusion-related reactions (such as fever, chills, nausea, vomiting, headache, dizziness or shortness of breath), inflammation of the lining of the digestive tract, and raised liver enzymes, which all occur in 10% or more of patients. Common side effects (occurring in 1% or more and less than 10% of patients) include severe infusion-related reactions (including anaphylactic reactions), dehydration, low blood calcium levels, anorexia, headache, conjunctivitis, fatigue, diarrhoea, nausea and vomiting. Cetuximab in combination with platinum-based chemotherapy may increase the frequency of severe leukopenia or severe neutropenia, and this may lead to a higher rate of infectious complications than platinum-based chemotherapy alone. For full details of adverse reactions and contraindications, see the summary of product characteristics.

Recommended dose and schedule

2.4 Cetuximab is administered intravenously. It is used in combination with platinum-based chemotherapy followed by cetuximab as maintenance therapy until disease progression. The initial loading dose is 400 mg/m^2 body surface area (BSA) given at a rate not exceeding 5 mg/minute. Subsequent weekly maintenance doses are 250 mg/m^2 BSA each.

Price

2.5 The list price of cetuximab is £178.10 for a 5-mg/ml 20-ml vial and £890.50 for a 5-mg/ml 100-ml vial (excluding VAT; British national formulary [BNF] online, accessed February 2017). Assuming that vials are not shared among patients, a person with a BSA of 1.75 m^2 would have 7 vials per loading dose and 5 vials per maintenance dose, equating to a cost of £1,246.70 for the loading dose and £890.50 for each maintenance dose.

The pricing arrangement considered during guidance development was one in which the company (Merck) had agreed a patient access scheme with the Department of Health. This scheme would have provided a simple discount to the list price of cetuximab with the discount applied at the point of purchase or invoice. The Department of Health considered that this patient access scheme would not constitute an excessive administrative burden on the NHS. This has now been replaced by a commercial access agreement between the company and NHS England, which incorporates this same simple discount applied at the point of purchase or invoice of all cetuximab but also includes additional and separate commercial arrangements. The financial terms of the agreement are commercial in confidence.

3 Evidence

3.1 The appraisal committee considered evidence submitted by Merck and a review of this submission by the evidence review group. This appraisal was a Cancer Drugs Fund reconsideration of NICE's technology appraisal guidance on cetuximab for the treatment of recurrent and/or metastatic squamous cell cancer of the head and neck (SCCHN). Sections 4.2 to 4.11 reflect the committee's consideration of the evidence submitted in the original appraisal. Sections 4.12 to 4.24 reflect the committee's considerations of the evidence submitted for the Cancer Drugs Fund reconsideration. The company focused on the subgroup of patients with oral cavity cancer from the EXTREME trial, and cost-effectiveness analyses using a patient access scheme that provides cetuximab at a reduced cost. After consultation, the company submitted additional 5-year follow-up data for this subgroup of patients, and a revised patient access scheme with a further discount. The level of discount is commercial in confidence.

3.2 See the committee papers for full details of the Cancer Drugs Fund reconsideration evidence, and the history for full details of the evidence used in NICE's original technology appraisal guidance on cetuximab for the treatment of recurrent and/or metastatic SCCHN.

4 Committee discussion

4.1 The appraisal committee reviewed the data available on the clinical and cost effectiveness of cetuximab, having considered evidence on the nature of recurrent or metastatic squamous cell cancer of the head and neck (SCCHN) and the value placed on the benefits of cetuximab by people with the condition, those who represent them, and clinical experts. It also took into account the effective use of NHS resources.

Clinical effectiveness (NICE technology appraisal guidance 172)

4.2 The committee reviewed the evidence available on the clinical effectiveness of cetuximab as presented in the company's submission and the evidence review group's (ERG's) report. It noted that there was only 1 relevant randomised controlled trial that compared cetuximab plus platinum-based chemotherapy with chemotherapy alone in patients with recurrent or metastatic SCCHN (the EXTREME trial). The committee noted that few of the patients included in the clinical trial were from the UK although many were from other European countries. It was also aware of the ERG's concern that the patients in the trial appeared younger and fitter, on the basis of a higher Karnofsky performance status (KPS), than patients in UK clinical practice. Therefore, there was some uncertainty about whether the benefits of cetuximab would be seen in patients with this condition in the UK. Additionally, the committee heard from the clinical experts that most patients presenting with recurrent or metastatic SCCHN in the UK were older and had poorer general health than those recruited to the trial. However, patients for whom platinum-based chemotherapy would be considered appropriate were more likely to be of a similar age and performance status to those in the EXTREME trial. Overall, the committee accepted the evidence from the clinical experts that the results of the EXTREME trial would be applicable to the UK population.

4.3 The committee discussed the reported results from the clinical trial. It noted that the company had presented results for the total population of the trial and for a

number of pre-planned subgroups. It noted the statistically significant improvement in overall survival associated with cetuximab in the total population represented in the trial. The committee was aware that, in the pre-planned subgroup analyses, only tumour location showed a significant interaction with treatment, suggesting greater effectiveness in tumours in the oral cavity. The committee heard from the clinical experts that patients with tumours in the oral cavity have a relatively favourable prognosis compared with the average prognosis for recurrent or metastatic SCCHN. The experts were not aware of any biological reason for cetuximab to be more clinically effective in oral cavity tumours. The committee accepted that the trial showed the efficacy of cetuximab plus platinum-based chemotherapy in patients with recurrent or metastatic SCCHN, but it was not persuaded that the evidence supported using the subgroup estimate for clinical effectiveness in the economic model.

4.4 The committee reviewed the additional cost-effectiveness analyses submitted by the company for additional subgroups based on age (younger than 65 years) and KPS (KPS of 90 or more and KPS of 80 or more). It was aware that the pre-planned subgroup analyses in the clinical study presented results for patients with a KPS of 80 or more (rather than 90 or more) and for patients who were younger than 65 years, but subgroups combining age and KPS were not included. The committee noted the concerns raised by the ERG about the validity of the modelled overall survival gains for the additional subgroup and whether the number of patients included was sufficient to provide robust evidence of efficacy. It was therefore not persuaded that the evidence provided by the company supported the predicted life years gained for the combined age and KPS subgroup. On this basis, the committee concluded that the estimates of cost effectiveness for the subgroup of patients who were younger than 65 years with a KPS of 90 or more could not be considered reliable.

4.5 The committee discussed the adverse effects of cetuximab treatment. It noted that the incidence of severe adverse events in the cetuximab plus platinum-based chemotherapy group and the platinum-based chemotherapy only group were generally similar with the exception of acne and acneiform dermatitis, which were reported only for the cetuximab plus platinum-based chemotherapy group. The clinical experts and a patient expert advised the committee that the adverse events reported for the trial were consistent with those seen in clinical practice when cetuximab had been used for locally advanced SCCHN and colorectal

cancer.

Cost effectiveness (NICE technology appraisal guidance 172)

4.6 The committee discussed the cost effectiveness of cetuximab plus platinum-based chemotherapy compared with platinum-based chemotherapy alone. It was aware that the incremental cost-effectiveness ratios (ICERs) presented by the company for the base-case and pre-planned subgroup analyses were substantially higher than those normally considered to be an acceptable use of NHS resources. In addition, the committee noted the concerns raised by the ERG about extrapolation of the trial results to estimate survival in the economic model, and the uncertainty about the number of patients available for analysis in each of the pre-planned subgroups. The committee noted the exploratory analyses done by the ERG using alternative assumptions and parameters in the economic model. The committee concluded that there remained considerable uncertainty around the results of the company's analyses, and that it was plausible that the true cost-effectiveness estimate for cetuximab plus platinum-based chemotherapy would be even higher than that presented by the company.

End-of-life considerations (NICE technology appraisal guidance 172)

4.7 The committee considered supplementary advice from NICE that should be taken into account when appraising treatments that may extend the life of patients with a short life expectancy, and that are licensed for indications that affect small numbers of people with incurable illnesses. For this advice to be applied, all the following criteria must be met:

- The treatment is indicated for patients with a short life expectancy, normally less than 24 months.
- There is sufficient evidence to indicate that the treatment offers an extension to life, normally of at least an additional 3 months, compared with current

NHS treatment.

- No alternative treatment with comparable benefits is available through the NHS.
- The treatment is licensed or otherwise indicated for small patient populations.

In addition, when taking these criteria into account, the committee must be persuaded that the estimates of the extension to life are robust and that the assumptions used in the reference case economic modelling are plausible, objective and robust.

4.8 The committee discussed whether cetuximab, in combination with platinum-based chemotherapy for the treatment of recurrent or metastatic SCCHN, fulfilled the criteria for consideration as a life-extending, end-of-life treatment. It considered the criteria only in relation to the estimate of overall survival for the cohort population because it did not consider the subgroup data to be robust (see sections 4.3 and 4.4). The committee noted from the EXTREME trial that life expectancy for patients treated with chemotherapy alone was unlikely to be more than 24 months and could be as low as 7 months. It observed that the trial data suggested that cetuximab plus platinum-based chemotherapy extended median survival by 2.7 months compared with platinum-based chemotherapy alone. The committee was concerned about the uncertainty associated with this estimate because of the wide confidence interval. It was also aware that the predicted life years gained from the economic modelling for this group was 0.187, reflecting a gain in overall survival of approximately 2.2 months. The committee therefore did not consider that this estimate of gain in overall survival was in keeping with the criteria relating to extension of life or that the addition of cetuximab represented a marked change from current treatment for SCCHN.

4.9 The committee also understood that an estimated 3,000 people in England and Wales are diagnosed with recurrent or metastatic SCCHN every year. However, based on the evidence from clinical experts, cetuximab plus platinum-based chemotherapy would be appropriate for only a small proportion of these patients (that is, those whose disease was unsuitable for local treatment and who were well enough to have platinum-based chemotherapy). However, the committee understood that it should take into account the cumulative population for each

product in considering the strength of any case, for justifying decisions which employ, in whole or part, the supplementary criteria for appraising life-extending, end-of-life treatments. It noted that cetuximab was licensed for a number of other indications involving much larger patient groups.

4.10 In summary, the committee was not persuaded that the use of cetuximab plus platinum-based chemotherapy fulfilled all the criteria to be considered as a life-extending, end-of-life treatment. It came to this conclusion taking into account the importance of supporting the development of innovative treatments licensed for small groups of patients who have an incurable illness.

4.11 The committee concluded that cetuximab, given in combination with platinum-based chemotherapy for the treatment of recurrent or metastatic SCCHN, could not be recommended as a cost-effective use of NHS resources. The committee noted that some people may be currently having cetuximab in combination with platinum-based chemotherapy for this indication, and recommended that these people should have the option to continue treatment until they and their clinician consider it appropriate to stop.

Cancer Drugs Fund reconsideration

4.12 This appraisal was a Cancer Drugs Fund reconsideration of NICE's technology appraisal guidance on cetuximab for the treatment of recurrent and/or metastatic squamous cell cancer of the head and neck. At its first reconsideration meeting, the committee considered the company's submission that:

- included only the oral cavity cancer subgroup
- included a patient access scheme that would have provided a simple discount to the list price of cetuximab (this scheme was subsequently replaced by a commercial access agreement between the company and NHS England [see 'price' in section 2 for more details])
- addressed some of the committee's preferred assumptions (see section 4.6).

The committee also considered the ERG's critique of the company's reconsideration submission and the ERG's exploratory analyses.

4.13 At its second reconsideration meeting, the committee considered the company's responses to the appraisal consultation document, specifically:

- additional 5-year survival data for the oral cavity cancer subgroup from the EXTREME trial
- a new economic analysis based on the updated trial data
- a revised patient access scheme providing a further discount to that considered at the first meeting.

The committee also considered the ERG's critique of the company's responses to the appraisal consultation document and the ERG's exploratory analyses.

Cetuximab in the clinical management of head and neck cancer

4.14 The committee heard from the clinical experts that the EXTREME trial population represented patients who would be offered cetuximab plus platinum-based chemotherapy in the UK. The clinical experts also noted that the comparator used in the trial is the standard of care in the UK, although the clinical effectiveness of cisplatin plus fluorouracil was not studied in clinical trials before being introduced into clinical practice. The clinical experts stated that cetuximab is used according to the protocol described in the EXTREME trial in their clinics, and that they have seen similar outcomes to the trial. However, they noted that they were aware of other clinicians using different dosing protocols in the UK. At the second meeting, the Cancer Drugs Fund clinical lead provided anecdotal evidence that cetuximab is always given weekly with chemotherapy, but that it may be given every 1 or 2 weeks during the maintenance phase. If it is given every 2 weeks, the dose is doubled so that the overall cumulative dose remains the same. This regimen is not consistent with that set out in the summary of product characteristics for cetuximab. The committee heard from the company that there are no data available on the clinical effectiveness of this regimen in people with SCCHN, but that it is safe in people with colorectal cancer. The committee concluded that cetuximab should be appraised according to the regimen set out in the summary of product characteristics but it supported the potential advantages in studying different dosing regimens.

Subgroup analysis

4.15 The committee noted that the company had based its submission on a subgroup of patients with oral cavity cancer. It also noted that, in its earlier deliberations, it had not been persuaded that the estimate from the subgroup was sufficiently reliable for use in the economic model. The company argued that, in the EXTREME trial, these patients had a poorer prognosis and gained greater benefit from cetuximab than the overall population of the trial. It noted that at the 2-year cut-off in the trial, cetuximab increased median overall survival by 6.6 months in patients with tumours of the oral cavity compared with an increase of 2.7 months in the whole population of the trial. The results for median progression-free survival were also better in the oral cavity cancer subgroup than in the whole trial population (3.3 months compared with 2.3 months). However, the committee noted that the subgroup was small (n=88) compared with the whole trial population (n=442), adding to the uncertainty inherent when considering estimates of effectiveness based on subgroup data. The clinical experts at the meeting confirmed that, in the EXTREME trial, patients with tumours in the oral cavity had a poorer prognosis than people with tumours in other locations. They also confirmed that, before the EXTREME trial, no other treatments had been shown to be of benefit in clinical trials in this patient group. This suggested an unmet need in this patient group, who were often older and had comorbidities. However, the experts were not aware of a biological mechanism that could explain why cetuximab would differ in its relative effects between different tumour types. The committee also discussed the additional published evidence on epidermal growth factor receptor (EGFR) overexpression in SCCHN that the company had provided after consultation. The committee concluded that it was possible that cetuximab might have greater benefits in oral cavity tumours but that the evidence in support of this was limited.

Progression-free and overall survival from the EXTREME trial

4.16 The committee noted that the company's new model, submitted after consultation, used 5-year survival data from the oral cavity cancer subgroup of the EXTREME trial directly to estimate progression-free survival and overall survival in both trial arms (that is, it did not use any survival curve fitting). The committee noted that the difference in mean overall survival seen with cetuximab

after 5 years of follow-up was similar to the difference in median overall survival seen after 2 years. It also noted that the difference in mean progression-free survival after 5 years was increased compared with the median progression-free survival after 2 years. The ERG noted that only 1 patient in the cetuximab plus chemotherapy arm of EXTREME remained event free at 5-year follow-up. The ERG argued that this patient alone contributed substantially to the mean progression-free and overall survival benefit, and that this could influence the results in favour of cetuximab plus chemotherapy. The ERG had attempted to adjust the survival analyses to take into account the 'long tail' associated with patients who remained event free. Taking this adjustment into account, the ERG estimated slightly shorter progression-free and overall survival values. The company disputed this approach, arguing that this patient also contributed to cumulative costs as well as quality-adjusted life-year gains. The committee noted that although patients whose disease responds extremely well to treatment are not uncommon in clinical trials, the extraordinary response seen in this single patient added to the uncertainty in the estimates resulting from the oral cavity cancer subgroup.

4.17 The ERG noted that the company had not supplied detailed clinical trial data in its response to consultation to allow for an analysis of survival after disease progression in the new model. However, the ERG was able to estimate the mean post-progression survival gain attributable to cetuximab plus chemotherapy from the difference between the mean overall survival and mean progression-free survival. This indicated that more than a third of the overall survival benefit may come after disease progression. The ERG believed that this is uncommon in trials of advanced cancer treatments with chemotherapy, in which the disease more often reverts to following the typical progressive disease trajectory, independent of the choice of previous treatment. The committee noted that at its first reconsideration meeting, the clinical experts had considered some survival gain after disease progression to be plausible because of the potential immune effects of cetuximab and a lower disease burden because of tumour response. However, the committee concluded that even if this were the case, the extent of survival gain after disease progression was uncertain.

Choice of utility values

4.18 The committee noted that after consultation, the company had estimated utilities based on quality-of-life data from the oral cavity cancer subgroup of the EXTREME trial, rather than the full trial population. It had, however, noted in the first committee meeting that the questionnaire used did not include a measure of adverse events. The data were converted to utilities using an algorithm. The company used the same utility estimates for both treatment arms in the post-progression health state, but different utility estimates for both treatment arms in the pre-progression health state. The ERG considered that the data from the EXTREME trial did not allow for reliable utility estimates for the 2 treatment arms. It stated that there was no justification for not using a common utility estimate for the pre-progression health state. The committee heard from the company that its quality-of-life questionnaire, on which its utility estimates were based, was not mandatory and was most likely to have omitted the most sick patients. When the ERG used a common utility value for both treatment arms, the ICER increased. The committee noted that, contrary to the implications of the company's utility values, adverse events were more frequent for patients having cetuximab than for those having standard therapy in the oral cavity subgroup. The committee concluded that the pre-progression utility value used by the company may have resulted in an ICER for cetuximab that was too low, and that it preferred the approach taken by the ERG.

Drug acquisition costs

4.19 The ERG identified an error in the method used to calculate drug costs in the company's new model, submitted after consultation. Correcting this error resulted in an increase in the number of vials used per patient session and a corresponding increase in the ICER. The company did not provide details of the body surface area (BSA) measurements from the oral cavity cancer subgroup in its response to consultation. It had previously considered that the mean BSA in EXTREME was lower than that of people with head and neck cancer in the UK. The ERG re-estimated the drug doses based on the mean value and the distribution seen in BSA in a UK audit of people with head and neck cancer. It also applied an adjustment for gender ratio based on the EXTREME trial. Cetuximab is available in 100-mg vials; these adjustments suggested that 7 to 8 vials are

needed for initial dosing, and 4 to 5 vials are needed for each subsequent dose. Adjusting for vial wastage also increased the drug costs by an estimated 11%. These adjustments resulted in a higher ICER for cetuximab than that in the company's base case. The committee concluded that the ERG's corrected calculation, including its adjustments, provided a better estimate of the costs of treatment for patients in the NHS.

Treatment administration costs

4.20 The committee noted the company has collected evidence in the UK that suggests cetuximab may be given less often in the maintenance phase than the standard weekly dosing regimen used in the EXTREME trial. However, the committee and ERG agreed that it is not clear how this is managed in terms of the total dose administered per cycle, the extent of this dosing in practise and how different regimens affect treatment outcomes. The ERG considered that it was not appropriate to model the patient survival outcomes reported in the EXTREME trial while also reducing treatment administration costs; this fails to consider how variations in treatment intensity and dose timing may affect treatment effectiveness. The committee noted that EXTREME is the only source of evidence relevant to the small subgroup being considered, and that the trial used weekly dosing. It agreed with the ERG that there was too much uncertainty attached to this deviation in dosing regimen to warrant its inclusion in the cost-effectiveness analysis, and that only the standard weekly dosing regimen should be included in the analysis.

Discounting

4.21 The committee noted that the company had not applied standard discounting to the new base case; the company explained that it did not consider this to be a major limitation, given the short time horizon of the model (5 years). The committee concluded that discounting should be applied to the revised base case, noting that this would have only a small effect on the ICER.

End-of-life considerations

4.22 The committee considered the advice about life-extending treatments for people with a short life expectancy in NICE's final Cancer Drugs Fund technology appraisal process and methods. The committee noted that, at 5-year follow-up in EXTREME, the mean life expectancy of people with oral cavity cancer was less than 24 months. It also noted that the difference in mean survival was similar to the difference in median survival seen after 2 years (that is, 6.6 months). The committee was aware of the uncertainty surrounding the magnitude of the survival benefit because of the limited number of people included in the oral cavity cancer subgroup. Nonetheless, despite this uncertainty, the committee agreed that it was plausible that the survival benefit in the subgroup was larger than that in the whole population. It therefore concluded that all of the end-of-life criteria were met for people with oral cavity cancer treated with cetuximab.

Conclusions

4.23 The committee discussed the most plausible ICER for cetuximab plus platinum-based chemotherapy compared with platinum-based chemotherapy alone. To protect the level of discount, the ICERs including the patient access scheme were considered commercial in confidence and cannot be presented here. The committee went on to discuss the range of cost-effectiveness estimates. It highlighted that:

- There remained some uncertainty about the clinical-effectiveness evidence for cetuximab in oral cavity cancer, particularly because of the small subgroup size in the EXTREME trial (see section 4.15).
- The committee preferred common utility values, as used by the ERG (see section 4.18).
- It would have preferred drug costs to be estimated using the BSA values from the UK audit study, with adjustment for the gender ratio (see section 4.19).

  The committee assumed that the oral cavity subgroup data were accurate, and that cetuximab was indeed more effective in this subgroup. On this basis, it agreed that the most plausible ICER would need to be based on

correct estimates of drug costs and with common utilities for pre-progression health states in both arms of the model. The committee took into account the clinical- and cost-effectiveness evidence for cetuximab in patients with oral cavity cancer, including the discount in the revised patient access scheme. Using this, it concluded that the most plausible ICER for cetuximab plus platinum-based chemotherapy compared with platinum-based therapy alone was above the range that would normally be considered cost effective if the end-of-life criteria apply. In addition, the uncertainties around this estimate, principally arising from the reliability of the estimation of clinical effectiveness in the subgroup, were too great to allow it to recommended cetuximab for routine use.

4.24 Subsequent to the committee meeting, a commercial access agreement was negotiated with NHS England. This arrangement was sufficient to reduce the ICER so that cetuximab could be recommended as a cost-effective use of NHS resources for the treatment of cancer starting in the oral cavity.

Summary of appraisal committee's key conclusions

4.25 Cetuximab in combination with platinum-based chemotherapy is recommended as an option for treating recurrent or metastatic squamous cell cancer of the head and neck in adults only:

- if the cancer started in the oral cavity and
- when the company provides the drug at the prices agreed with NHS England in the commercial access agreement (section 1.1).

4.26 The committee discussed the most plausible incremental cost-effectiveness ratio (ICER) for cetuximab plus platinum-based chemotherapy compared with platinum-based chemotherapy alone. To protect the level of discount, the ICERs including the patient access scheme were considered commercial in confidence and cannot be presented here. Based on the clinical- and cost-effectiveness analyses, including the discount in the revised patient access scheme, the committee considered that the most plausible ICER for cetuximab plus platinum-based chemotherapy compared with platinum-based therapy alone was above

the range that would normally be considered cost effective if the end-of-life criteria apply and so could not recommend it for routine use. A subsequently negotiated commercial access agreement reduced this ICER to the extent that cetuximab could be recommended as a cost-effective use of NHS resources for the treatment of cancer starting in the oral cavity (sections 4.23 and 4.24).

5 Implementation

5.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.

5.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal determination.

5.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has oral cavity cancer and the doctor responsible for their care thinks that cetuximab is the right treatment, it should be available for use, in line with NICE's recommendations.

6 Appraisal committee members and NICE project team

Appraisal committee members

The technology appraisal committees are standing advisory committees of NICE. This topic was considered by members of the existing standing committees who have met to reconsider drugs funded by the Cancer Drugs Fund. The names of the members who attended are in the minutes of the appraisal committee meeting, which are posted on the NICE website.

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.

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.

TA172

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Cancer Drugs Fund reconsideration of TA172

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