NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Appraisal consultation document

Dupilumab for treating severe asthma with type 2 inflammation

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using dupilumab in the NHS in England. The appraisal committee has considered the evidence submitted by the company and the views of non-company consultees and commentators, clinical experts and patient experts.

This document has been prepared for consultation with the consultees. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the consultees and commentators for this appraisal and the public. This document should be read along with the evidence (see the committee papers).

The appraisal committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

Issue date: May 2021

Note that this document is not NICE's final guidance on this technology. The recommendations in section 1 may change after consultation.

After consultation:

- The appraisal committee will meet again to consider the evidence, this appraisal consultation document and comments from the consultees.
- At that meeting, the committee will also consider comments made by people who are not consultees.
- After considering these comments, the committee will prepare the final appraisal document.
- Subject to any appeal by consultees, the final appraisal document may be used as the basis for NICE's guidance on using dupilumab in the NHS in England.

For further details, see NICE's guide to the processes of technology appraisal.

The key dates for this appraisal are:

Closing date for comments: 28 May 2021

Third appraisal committee meeting: 9 September 2021

Details of membership of the appraisal committee are given in section 5

1 Recommendations

1.1 Dupilumab as add-on maintenance therapy is not recommended, within its marketing authorisation, for treating severe asthma with type 2 inflammation that is inadequately controlled in people aged 12 years and over, despite maintenance therapy with high-dose inhaled corticosteroids and another maintenance treatment.

1.2 This recommendation is not intended to affect treatment with dupilumab 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

Severe asthma is usually treated with inhaled corticosteroids plus another drug, such as a long-acting beta-agonist. Oral corticosteroids may also be needed to prevent exacerbations (asthma attacks), but they cause long-term side effects. These treatments may not work well enough for severe asthma with type 2 inflammation, which can be difficult to control. Some people who have another type of severe asthma called eosinophilic asthma can have mepolizumab, reslizumab or benralizumab. These drugs, like dupilumab, are biological agents but work in a different way.

Clinical trial results show that having dupilumab plus standard asthma treatment reduces exacerbations and the use of oral corticosteroids more than placebo in people with severe asthma with type 2 inflammation. There are no trials directly comparing dupilumab with mepolizumab, reslizumab or benralizumab. Comparing these drugs indirectly suggests a reduction in asthma exacerbations with dupilumab but no difference in other asthma symptoms.

The company's population of people with type 2 inflammation is not suitable for considering the cost effectiveness of dupilumab compared with standard care. This

is because it combines people eligible for biologicals (mepolizumab, reslizumab or benralizumab) with people not eligible for biologicals who can only be offered standard care. The cost-effectiveness estimates for dupilumab vary depending on whether people are eligible for mepolizumab, reslizumab or benralizumab, and what their individual treatment options are. Regardless, the cost-effectiveness estimates for dupilumab are higher than what NICE usually considers a cost-effective use of NHS resources. Dupilumab cannot be recommended for treating inadequately controlled severe asthma with type 2 inflammation.

2 Information about dupilumab

Marketing authorisation indication

2.1 Dupilumab (Dupixent, Sanofi) has a marketing authorisation 'in adults and adolescents 12 years and older as an add-on maintenance treatment for severe asthma with type 2 inflammation characterised by raised blood eosinophils and/or raised FeNO [fractional exhaled nitric oxide]…who are inadequately controlled with high dose ICS [inhaled corticosteroid] plus another medicinal product for maintenance treatment'. The definition of type 2 inflammation is as in the Global Initiative for Asthma guideline.

Dosage in the marketing authorisation

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

Price

2.3 The list price of dupilumab is £1,264.89 for 2 prefilled syringes of either the 200 mg per 1.44 ml or 300 mg per 2 ml dose (excluding VAT; British National Formulary online accessed November 2020).

2.4 The company has a commercial arrangement. This makes dupilumab available to the NHS for all indications with a discount and it would have also applied to this indication if the technology had been recommended. 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 (section 5) considered evidence submitted by Sanofi Genzyme, a review of this submission by the evidence review group (ERG), NICE's technical report, and responses from stakeholders. See the committee papers for full details of the evidence.

New treatment option

An additional treatment option that lowers the risk of exacerbations and may reduce the need for oral corticosteroids would be welcome

3.1 Severe asthma is a distressing and socially isolating condition. The patient expert explained that exacerbations can happen without warning, be life threatening, cause fear and result in hospitalisation. People are often unable to work or start a family, and may need help with day-to-day activities because of their symptoms. The clinical expert explained that, in addition to optimised inhaled treatment, standard treatment for severe asthma is oral systemic corticosteroids or, if the patient has eosinophilic asthma and depending on the blood eosinophil count, NICE recommended interleukin-5 inhibitors biologicals benralizumab, mepolizumab and reslizumab. Dupilumab is the only licensed treatment for severe asthma with type 2 inflammation. Although asthma can respond to systemic corticosteroids, the treatment can be associated with long-term complications (such as diabetes mellitus, weight gain, bone loss, immunosuppression and a negative effect on mental health). The patient expert explained that patients would welcome treatment options that replace the need for corticosteroids. The clinical expert explained that a blood eosinophil count and fractional exhaled nitric oxide (FeNO) are used to help define subtypes of severe asthma and help predict the people with severe asthma who are at highest risk of a future exacerbation. In people with severe asthma with type 2 inflammation, their condition does not

respond to interleukin-5 inhibitors but can respond to interleukin-13 inhibitors such as dupilumab. The committee concluded that there is a need for new treatments with a different mode of action for people with severe asthma with type 2 inflammation whose asthma does not respond with current standard care, and for people not eligible for current NICE recommended biologicals.

Clinical management

Severe asthma with type 2 inflammation is a subtype of asthma

3.2 Severe asthma with type 2 inflammation is associated with allergy, higher risk of exacerbations, hospitalisation, dependency on oral corticosteroids and increased risk of dying. The Global Initiative for Asthma (GINA) guideline on difficult to treat severe asthma (2019) lists 5 criteria in its definition of severe asthma with type 2 inflammation that are prognostics markers:

- a blood eosinophil count of 150 cells per microlitre or more
- FeNO of 20 parts per billion or more
- sputum eosinophils of 2% or more
- asthma that is clinically allergen driven
- the need for maintenance oral corticosteroids.

GINA suggests that 1 or more criterion can be used to make a diagnosis. The clinical expert explained that raised blood eosinophils and FeNO are risk predictors for future exacerbations. That is, the higher these biomarkers, the more likely you are to have an exacerbation. The committee concluded that this subtype of severe asthma exists.

Blood eosinophil count and FeNO are common biomarkers for diagnosis

3.3 The clinical expert explained that blood eosinophil counts and FeNO levels are routinely measured in clinical practice. They also explained that, while blood eosinophils counts are raised in both eosinophilic asthma and

asthma with type 2 inflammation, raised FeNO is more specific to type 2 inflammation. The committee noted the response of stakeholders during technical engagement that a blood eosinophil count of 150 cells per microlitre or more, FeNO of 20 parts per billion or more, or both, could be used for identifying people with type 2 inflammation. The committee acknowledged the complexity of diagnosing asthma subtypes, and the potential for overlap or misclassification between them, despite the use of blood eosinophil counts and FeNO levels.

Dupilumab as add-on treatment is an option for managing uncontrolled severe asthma with type 2 inflammation

3.4 The clinical expert explained that treatment for asthma in clinical practice follows the NICE guideline on diagnosis, monitoring and chronic asthma management and the GINA 2019 guideline (which includes the use of biologicals). If the asthma is still uncontrolled despite optimised inhaled therapy that includes corticosteroids, then low-dose oral corticosteroids or biologicals are added. The clinical and patient experts explained that biologicals are preferred over oral corticosteroids because they have fewer debilitating side effects. The choice of biological depends on the subtype of asthma. For severe eosinophilic asthma, according to NICE technology appraisal guidance for benralizumab, mepolizumab and reslizumab, the treatment of choice depends on the blood eosinophil count (300 cells per microlitre or more, or 400 cells per microlitre or more) and the number of exacerbations (3 or 4, or more) or the use of systemic corticosteroids. Omalizumab is another biological used for treating severe persistent allergic asthma. However, it is not used for eosinophilic asthma (see section 3.6). There are currently no NICE recommended biologicals for treating severe asthma with type 2 inflammation. The committee concluded that dupilumab as add-on treatment is an option for managing uncontrolled severe asthma with type 2 inflammation.

Populations

It is challenging to define which populations should be used for decision making

3.5 There are several subgroups to consider when deciding which population to use for decision making. At the first appraisal committee meeting, the committee considered whether the population would need to have a raised eosinophil count, raised FeNO or both based on the 'and/or' wording in the marketing authorisation and GINA recommendations for these biomarkers. The committee also acknowledged that there are subgroups on or off maintenance oral corticosteroids, or both (mixed proportions on and off oral corticosteroids), and populations eligible or not eligible for biologicals. In addition, it acknowledged the overlap between the populations in the marketing authorisation, trials and company decision problem at the first appraisal committee meeting:

- The marketing authorisation population is broad, consisting of people with uncontrolled severe asthma with type 2 inflammation on high-dose inhaled corticosteroids plus 1 maintenance treatment and with a blood eosinophil count and FeNO as described by GINA.
- The clinical trials (DRI12544, QUEST and VENTURE) recruited people with 1 or more exacerbation in the previous year and no restrictions on blood eosinophils and FeNO.

3.6 The company's updated decision problem (base case) was in a subpopulation of people who are not eligible for biologicals or who did not respond to biological therapy,based on a posthoc analysis of the QUEST data. They were people aged 12 and older, with blood eosinophils counts of 150 cells per microlitre or more and a fractional exhaled nitric oxide of 25 or more, who have had at least 4 exacerbations in the previous 12 months and who are not eligible for biologicals or did not respond to biological therapy and will be referred to as the updated population hereafter. The company considered that this narrower population represented people with highest unmet need

and can be split into 3 subgroups: adolescents who are aged 12 to 17, adults who are not eligible for biologicals (blood eosinophil count 150 to 299) and adults who previously received biologicals but did not respond (blood eosinophil count of 300 and more). The committee noted that the comparator for the updated population is standard care and other biologicals were only recommended in adults in NICE guidance. The committee concluded that the updated population was suitable for decision making.

Comparators

Standard care is the appropriate comparator in the updated population

3.7 The clinical trial populations included people with differing severity of asthma (defined by eosinophil level and the number of exacerbations in the previous year). These populations therefore included people who would be offered different treatment options in the NHS:

- People with a blood eosinophil count of 300 cells per microlitre or more, who have had at least 4 exacerbations in the previous 12 months or who are taking oral corticosteroids, can have mepolizumab or benralizumab.
- People with a blood eosinophil count of 400 cells per microlitre or more, who have had at least 3 exacerbations in the previous 12 months, can have reslizumab or benralizumab.
- People not eligible for biologicals (defined below) are offered standard care:
  - a blood eosinophil count of between 150 and 299 cells per microlitre and 4 or more exacerbations (not eligible for mepolizumab or benralizumab)
  - a blood eosinophil count of between 150 and 399 cells per microlitre and 3 or more exacerbations (not eligible for reslizumab or benralizumab)

  - a blood eosinophil count of less than 150 cells per microlitre and FeNO of 25 parts per billion or more (not eligible for any other biological)
- People who did not respond to biological therapy are offered standard care

  The committee concluded that standard care was an appropriate comparator in the company's updated population, that is people not eligible for biologicals or those who did not respond to biological therapy.

Clinical evidence

The evidence on clinical effectiveness is relevant to NHS clinical practice

3.8 The company's clinical evidence came from 3 randomised-controlled trials, DRI12544, QUEST and VENTURE. These compared dupilumab with placebo in people aged 12 years and over (except DRI12544, which only included people aged 18 years or over) with persistent asthma who had 1 or more exacerbations in the previous year. None of the trials had restrictions on blood eosinophils or FeNO. DRI12544 and QUEST included people with moderate-to-severe asthma not on maintenance oral corticosteroids. VENTURE included people with severe corticosteroid-dependent asthma (on maintenance corticosteroids). The 3 trials were conducted globally, and QUEST was the only trial that included people from the UK. The trial populations were based on use of moderate-to-high doses of inhaled corticosteroids. This was because they included people from countries like the US and Japan, where the clinical expert stated that there is reluctance to use high-dose inhaled corticosteroids. The committee concluded that there were some caveats, but that all 3 trials included were relevant to NHS clinical practice.

Dupilumab is more clinically effective than standard care in the clinical trial populations

3.9 All primary outcomes were reported for the intention-to-treat population in all 3 trials. In QUEST, the first coprimary outcome was annualised rate of severe exacerbations. There was a 47.7% (95% confidence interval [CI] 33.8% to 58.7%, p<0.0001) lower rate of severe exacerbations in the dupilumab group compared with placebo. Change from baseline in the forced expiratory volume in 1 second (FEV1) at 12 weeks was the second coprimary outcomes in QUEST and the primary outcome in DRI12544. There was an increase in FEV1 at 12 weeks when dupilumab was compared with placebo in DRI12544 (least squares [LS] mean difference 0.14 litre, 95% CI 0.08 to 0.19, p<0.0001) and QUEST (LS mean difference 0.20 litre, 95% CI 0.11 to 0.28, p<0.0001). In VENTURE, the primary outcome was the percentage reduction in oral corticosteroid dose from baseline. There was a greater reduction in oral corticosteroid use with dupilumab compared with placebo (LS mean difference 28 mg, 95% CI 16 to 41, p<0.0001) at 24 weeks. The proportion of people with treatment-related adverse events was similar within each trial between those having dupilumab and placebo. In DRI12544 and QUEST, the proportion of people with any treatment-related adverse events ranged from 74.7% to 84.1%. In VENTURE, a smaller proportion experienced any treatment-related adverse events (64.5% and 62.1% in the placebo and dupilumab arms respectively). The committee concluded that dupilumab was more clinically effective than standard care in the clinical trial populations and is a relatively safe treatment.

The clinical effectiveness estimates for dupilumab are uncertain in the company's updated population

3.10 The company's decision-problem subgroup analyses at the first appraisal committee meeting focused on the annualised rate of severe exacerbations for the posthoc population (that is, people with a blood eosinophil count of 150 cells per microlitre or more, FeNO of 25 parts per

billion or more and 3 or more exacerbations in the previous year) from QUEST and VENTURE. Dupilumab reduced the rate of severe exacerbations when compared with placebo within this subpopulation in QUEST and VENTURE, although in small posthoc subgroups with 101 and 152 people respectively. There were improvements in the placebo groups for the primary outcomes of these trials. This was possibly because of regression to the mean and the placebo effect. The committee concluded that dupilumab is clinically effective and safe as an addition to standard care in people with a blood eosinophil count of at least 150 cells per microlitre or FeNO of 25 parts per billion or more and 3 or more exacerbations in the previous year who may or may not be taking maintenance oral corticosteroids. However, there were very limited evidence clinical efficacy data provided for the company's updated population because of small number of patients in the QUEST trial corresponding to each subgroup. The committee concluded that the clinical effectiveness of dupilumab in the company's updated base case was highly uncertain.

The company's economic model

The model structure is appropriate for decision making

3.11 The company submitted a 4-state Markov model comparing dupilumab with standard care in people with severe asthma and type 2 inflammation. The model consisted of 4 live health states: uncontrolled asthma; controlled asthma; moderate exacerbation; and severe exacerbation. In addition, the model included states for asthma-related deaths and death from other causes. Response to treatment was defined as a 50% or greater reduction in the annual exacerbation rate, which was assessed at 52 weeks. People whose asthma responded continued on dupilumab and those whose did not transferred to standard care. The company derived the efficacy and clinical parameters in the model from the QUEST clinical trial. The committee concluded that the model structure was appropriate for decision making.

Clinical inputs to the model

The evidence for the company's updated population is limited and effectiveness estimates are based on assumptions

3.12 The committee noted that the company split the updated population into 3 subgroups: the adolescents who are aged 12 to 17, the adults who are not eligible for biologicals (blood eosinophil count 150 to 299) and adults who previously received biologicals but did not respond (blood eosinophil count of 300 and more). The committee noted that the clinical effectiveness evidence available for each of the subpopulations was limited because the number of patients included in the QUEST trial corresponding to each subgroup was small. The trial included 2 patients corresponding to the adolescent subgroup and 14 patients corresponding to the subgroup of adults who are not eligible to biologicals. The QUEST protocol excluded patients who had been on biologicals but 1 patient in the trial was included who had previously received a biological. The ERG noted that the estimates of transition probabilities for the company's updated population were highly uncertain, due to small sample sizes. The company assumed that clinical effectiveness was the same for each subgroup based on trial estimates for the overall company's updated population. The committee particularly considered the assumption of equal efficacy of dupilumab regardless of whether people had received prior biological therapy. The company provided clinical expert opinion that switching from other biologicals (interleukin-5 inhibitors: mepolizumab, reslizumab, benralizumab) to dupilumab (interleukin-4/13 inhibitor) was acceptable because the mechanisms of action were different enough. The committee was concerned about this assumption and considered that although it is plausible that people who did not respond to other biologicals could respond to dupilumab, assuming that the response rate would be as good as in people not eligible for other biologicals was optimistic. The committee considered this to be a key area of uncertainty and noted that it would have liked to see exploration of scenarios with a

range of alternative response rates for the group of adults who did not respond to biological therapy. The committee concluded that the effectiveness estimates in the company's updated population were highly uncertain.

The company's updated base case does not include a multiplier for long-term severe exacerbation rates

3.13 The committee noted that asthma-related mortality often drives cost effectiveness in asthma models. The annual severe exacerbation rate (2.39 exacerbations per year) in the placebo arm of the QUEST trial was lower than observed in clinical practice in the year before trial enrolment (4.46 exacerbations per year).The company's model after technical engagement used the exacerbation rates from QUEST and VENTURE in the first year of the model and increased the number of severe exacerbations in subsequent years for both dupilumab and standard care by applying a multiplier. The ERG considered the trial to be the best source of exacerbation data and did not include an exacerbation multiplier in its base case model which resulted in higher incremental cost effectiveness ratios (ICERs). The company provided evidence on severe exacerbation rates from 3 severe asthma cohorts: WATCH (Wessex Asthma Cohort of Difficult Asthma), U-BIOPRED (Unbiased BIOmarkers in PREDiction of respiratory disease outcomes) and the Sanofi Real World Evidence (RWE) study. It also accepted the committee and ERG's concerns about the uncertainty of using a multiplier. The exacerbation rates in the company's updated base case model were taken from the QUEST trial for the duration of the model without an exacerbation multiplier. The committee concluded that the updated base case without the exacerbation multiplier was appropriate.

Real world evidence is best source of data to inform the setting of treating severe exacerbations

3.14 The company assigned different mortality rates to severe exacerbations treated in hospital emergency care, inpatients and general practice. In the

QUEST trial 6.7% of severe exacerbations were treated in hospital (3.0% in emergency care, 3.7% in inpatients and 93.3% in general practice). The company originally based resource use associated with severe exacerbations on the UK Difficult Asthma Registry registry data (O'Neill 2015) with 26.5% (7.8% in emergency care, 18.7% in inpatients) and 74.0% in general practice) as a better estimate or resource use in the NHS. The ERG base-case model used the QUEST data for the setting of severe exacerbations. The clinical expert explained that the number of patients treated in hospital in clinical practice is likely to be higher than that seen in the trial because patients in trials are well monitored on optimised treatment, more motivated and have better adherence to treatment. The committee requested further exploration of different sources of data for the setting of treating exacerbations, to inform the model. The company submitted data on the setting of treating severe exacerbation rates from 3 different sources (WATCH, U-BIOPRED and the Sanofi RWE study). The Sanofi RWE study was based on case notes from severe asthma centres in the NHS, in which the definition of severe exacerbation was established to match the QUEST trial definition and was used in the company's updated model. The ERG considered the Sanofi RWE study to be of reasonable quality which produced consistent results with other sources. The committee concluded that the Sanofi RWE study on the setting of severe exacerbations was appropriate for use in the company's updated base case.

Mortality estimates are uncertain and probably overestimated in the company economic model

3.15 The ERG explained that the original company model (using the confidential exacerbation multiplier) predicted 20% mortality over 10 years in the standard care arm. The committee questioned the clinical plausibility of this estimate because it seemed high compared with the approximate 1,300 asthma-related deaths a year in the UK. The higher death rate was a result of interaction between the exacerbation multiplier (see section 3.13) and using registry data to inform the setting of treating

exacerbations (see section 3.15). The committee noted that the model did not offer plausible estimates, and requested that any additional analyses presented by the company include 10-year mortality rates for dupilumab and standard care and show the flow of patients though different health states in the model for the purposes of model validation. Following the first committee meeting, the company conducted a literature search for UK asthma-related mortality data, but no further publications were retrieved. The committee noted that when the exacerbation multiplier was removed (in the updated company model, see section 3.14), 10-year mortality with standard care was reduced to 18%. The ERG considered that the mortality was probably still overestimated, but the plausibility of model survival projections was difficult to judge without UK data available. The ERG explained that the model predicted a mean age of deaths of 70 years with standard care (73 years with dupilumab), compared to an estimated life expectancy of 80 years with standard care in the benralizumab appraisal TA565. The committee was concerned that mortality could be overestimated because asthma-related mortality was one of the drivers of the model. The committee also noted that alternative methods had been used in the benralizumab appraisal, to adjust for high mortality. The committee concluded that the mortality rates were uncertain, and that alternative scenarios could be tested to explore the impact of the mortality on the ICER.

The company's base-case economic analysis

The company's updated base-case ICER is £35,968 per QALY gained for dupilumab compared with standard care in the proposed population

3.16 The company's base-case deterministic ICER for dupilumab compared with standard care is £35,968 per quality-adjusted life year (QALY) gained in the company's updated population. This included the confidential discount for dupilumab. The committee concluded that dupilumab does not represent a cost-effective use of resources, so could not be recommended for treating severe asthma with type 2 inflammation.

Other factors

Additional benefits in people with severe asthma and type 2 inflammation, and nasal polyps or atopic dermatitis, may not have been adequately captured

3.17 The committee recognised that there is an unmet need for people with severe asthma caused by type 2 inflammation. The committee also heard that dupilumab is effective in people with comorbidities (such as nasal polyps and atopic dermatitis). It concluded that these additional benefits of dupilumab had not been captured in the QALY calculation.

There are limited data available on dupilumab for young people

3.18 Dupilumab is licensed in people aged 12 years and over. The company provided a subgroup analyses for the subgroup of people aged 12-17 years. The committee noted that the QUEST trial only included 2 patients aged under 18 years meeting the criteria of the updated base case population. There is an unmet need in this population with uncontrolled severe asthma with type 2 inflammation. Current NICE recommended biologicals are licensed in adults for eosinophilic asthma only. Mepolizumab is currently the only other biological that is licensed for treating children aged 6 years or over for severe refractory eosinophilic asthma. However NICE's technology appraisal guidance on mepolizumab recommends it for use in adults. The committee concluded that there are limited data available for dupilumab in young people, and acknowledged this during decision making.

Conclusion

Dupilumab is not recommended for treating severe asthma with type 2 inflammation

3.19 The committee acknowledged that dupilumab is effective for preventing exacerbations in people with severe asthma with type 2 inflammation compared with standard care. However, the cost-effectiveness estimates

for dupilumab compared with standard care were higher than what NICE considers a cost-effective use of NHS resources. The committee identified several uncertainties in the modelling assumptions, particularly about mortality estimates and response rates in adults who did not respond to biological therapy. These uncertainties resulted in uncertainty about the true ICER. Therefore, the committee was unable to recommend dupilumab as a cost-effective treatment for use in the NHS for treating severe asthma with type 2 inflammation.

4 Proposed date for review of guidance

4.1 NICE proposes that the guidance on this technology is considered for review by the guidance executive 3 years after publication of the guidance. NICE welcomes comment on this proposed date. The guidance executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Sanjeev Patel
Chair, appraisal committee
April 2021

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 B.

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.

Shelly Patel, Caroline Bregman
Technical leads

Eleanor Donegan
Technical adviser

Joanne Ekeledo, Jeremy Powell, Shonagh D'Sylva
Project manager

ISBN: [to be added at publication]