NICE National Institute for Health and Care Excellence

NICE guidance

Adalimumab for treating moderate to severe hidradenitis suppurativa

Technology appraisal guidance
Published: 22 June 2016

www.nice.org.uk/guidance/ta392

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 Adalimumab is recommended, within its marketing authorisation, as an option for treating active moderate to severe hidradenitis suppurativa in adults whose disease has not responded to conventional systemic therapy. The drug is recommended only if the company provides it at the price agreed in the patient access scheme.

1.2 Assess the response to adalimumab after 12 weeks of treatment, and only continue if there is clear evidence of response, defined as:

- a reduction of 25% or more in the total abscess and inflammatory nodule count and
- no increase in abscesses and draining fistulas.

2 The technology

2.1 Adalimumab (Humira, AbbVie) is an antibody that inhibits tumour necrosis factor (TNF). It is given by subcutaneous injection. Adalimumab has a marketing authorisation in the UK for treating active moderate to severe hidradenitis suppurativa (acne inversa) in adult patients with an inadequate response to conventional systemic hidradenitis suppurativa therapy. The summary of product characteristics suggests that 'continued therapy beyond 12 weeks should be carefully reconsidered in a patient with no improvement within this time period'. This statement is clarified in the European Public Assessment Report (EPAR), which states that continued benefit of adalimumab was observed in anyone with a partial response or higher, defined as at least a 25% reduction in abscess and inflammatory nodule (AN) count with or without an increase in abscesses or draining fistulas from baseline. The summary of product characteristics also recommends that the benefit and risk of continued long-term treatment should be evaluated periodically.

2.2 The summary of product characteristics lists the following very common (affecting 1 in 10 people or more) adverse reactions for adalimumab: respiratory tract infections; low white blood cell count; low red blood cell count; increased blood lipids; headache; abdominal pain; nausea and vomiting; rash; musculoskeletal pain; injection site reactions; and increased plasma levels of liver enzymes. For full details of adverse reactions and contraindications, see the summary of product characteristics.

2.3 Adalimumab costs £352.14 for a 40-mg prefilled pen or syringe and for a 40-mg/0.8-ml vial (BNF, December 2015). The recommended dose of adalimumab for people with hidradenitis suppurativa is 160 mg on day 1 (given as 4 injections in 1 day or as 2 injections each day for 2 consecutive days), 80 mg on day 15 (given as 2 injections in 1 day), and a single 40-mg injection every week from week 4 onwards. Antibiotics may be continued during treatment with adalimumab, if necessary. The company has agreed a patient access scheme with the Department of Health. The company will provide adalimumab at a fixed price of £284.00 for the 40-mg prefilled pen or syringe for the hidradenitis suppurativa indication only. The Department of Health considered that this patient access scheme does not constitute an excessive administrative burden on the NHS. The

annual cost of treatment with adalimumab is estimated at £15,336, based on the dosing regimen recommended in the summary of product characteristics.

3 Evidence

The appraisal committee considered evidence submitted by AbbVie and a review of this submission by the evidence review group (ERG). See the committee papers for full details of the evidence.

Clinical effectiveness

3.1 The pivotal clinical evidence for treating hidradenitis suppurativa with adalimumab came from 2 randomised double-blind phase 3 trials (PIONEER I, n=307, and PIONEER II, n=326). The PIONEER trials compared adalimumab with placebo in adults who had been diagnosed with moderate to severe hidradenitis suppurativa at least 1 year earlier and who were intolerant to, or whose disease had not responded to, oral antibiotics. Moderate to severe disease was defined as people with Hurley stage 2 or 3 hidradenitis suppurativa in at least 1 affected anatomic region, and a total abscess and inflammatory nodule (AN) count greater than 3. Neither of the trials recruited people from the UK. Treatment with oral or topical antibiotics during the trial was allowed in PIONEER II but not in PIONEER I. Extensive surgical procedures were not allowed, but incision and drainage of lesions or corticosteroid injections directly into lesions were allowed. Supportive care interventions (such as tobacco cessation or weight-control counselling) were not given to anyone in the trials.

3.2 The primary end point in the PIONEER trials was the proportion of people with a Hidradenitis Suppurativa Clinical Response (HiSCR) at week 12. HiSCR is defined as at least a 50% reduction in the total AN count, with no increase in abscesses or draining fistulas. The secondary outcomes were: the proportion of people with Hurley stage 2 disease who had an AN count of 0, 1 or 2 at week 12; the proportion of people who had a 30% or more reduction, and at least 1 unit reduction, in the Patient's Global Assessment of Skin Pain from baseline to week 12; and change in the Modified Sartorius Score from baseline to week 12. EuroQol (EQ-5D) data were only collected in PIONEER II. Other health-related quality-of-life instruments used in the PIONEER studies included the Short Form-36 Health Status Survey (SF-36; PIONEER I only), Dermatology Life Quality Index (DLQI), and Hidradenitis Suppurativa Quality of Life (HSQOL).

3.3 Both trials included 2 study periods and an open-label extension study:

- Period A (12 weeks 'induction'): people were randomised to adalimumab 40 mg every week or placebo.
- Period B (24 weeks 'maintenance'): people who had adalimumab 40 mg every week in period A were re-randomised to have either adalimumab 40 mg every week, adalimumab 40 mg every other week or placebo. In PIONEER I, people who had placebo in period A were re-randomised to adalimumab 40 mg every week, whereas in PIONEER II people who had placebo in period A stayed on placebo for period B.

  Eligibility for period B depended on clinical response at the end of period A. People who had a clinical response (HiSCR) at week 12 were enrolled in period B until the end of week 36, but were excluded from the study if their condition stopped responding to treatment. People who did not have an HiSCR response at week 12 were enrolled in period B until week 16; if the severity of their hidradenitis suppurativa worsened or did not improve after week 16 they were excluded from the study. The open-label extension study included people who had completed PIONEER I or II and who:

- had an HiSCR response at the end of period B
- had an HiSCR response at the start of period B then experienced loss of response or
- did not have an HiSCR response at the start of period B, then experienced worsening or absence of improvement on or after week 16.

3.4 The company indicated that baseline characteristics were generally similar in the different arms of the trials. But, people in PIONEER I had more severe disease than those in PIONEER II. The average duration of hidradenitis suppurativa in the trials was about 11.5 years.

3.5 More people treated with adalimumab had an HiSCR response than those having placebo; these differences were statistically significant in both PIONEER trials (table 1). The differences between adalimumab and placebo were statistically significant for all secondary outcomes at week 12 in PIONEER II (showing a benefit in favour of adalimumab), but none of the differences were significant at

week 12 in PIONEER I. Pre-planned analyses showed that a consistent treatment effect was seen across most subgroups, with a few exceptions in subgroups with small sample sizes.

Table 1 Primary outcomes at week 12 for adalimumab 40 mg every week compared with placebo, from phase 3 randomised controlled trials

PIONEER I	**Adalimumab (n=153)** • People with clinical response, 64 (41.8%) **Placebo (n=154)** • People with clinical response, 40 (26.0%)	**Difference (95% confidence interval [CI])** • 15.9% (5.3% to 26.5%), p=0.003
PIONEER II	**Adalimumab (n=163)** • People with clinical response, 96 (58.9%) **Placebo (n=163)** • People with clinical response, 45 (27.6%)	**Difference (95% CI)** • 31.5% (20.7% to 42.2%), p<0.001

3.6 The company stated that the benefits seen with adalimumab at 12 weeks continued up to 36 weeks (period B) in the PIONEER studies. The company provided an interim analysis of the primary end point from the open-label extension study, noting that patient numbers were small. A post hoc analysis of pooled data from the PIONEER studies and the open-label extension study showed that the continued benefit of adalimumab was seen in people with a partial HiSCR response (defined as at least a 25% reduction in the total AN count with or without an increase in abscess count or draining fistula count), as well as people with a complete clinical response.

3.7 In PIONEER I and II, adalimumab was associated with significant improvements from baseline in health-related quality of life after 12 weeks of treatment.

Adalimumab was associated with larger improvements from baseline than placebo; these differences were statistically significant, as measured by the EQ-5D, the physical components of SF-36, DLQI and the HSQOL. The difference between adalimumab and placebo in the mental component of the SF-36 was not significant.

3.8 The company reported that the most common adverse events with adalimumab were worsening of hidradenitis suppurativa, nasopharyngitis and headache. These were usually mild to moderately severe. The company noted that during the first 12 weeks of both PIONEER studies, adverse events and treatment discontinuation caused by adverse events were less common in people treated with adalimumab than in people treated with placebo. The company reported that the open-label extension study did not identify any new safety risks for adalimumab.

Cost effectiveness

3.9 The company provided a Markov model to assess the cost effectiveness of adalimumab compared with supportive care. The company stated that it was not appropriate to compare adalimumab with any active pharmacological agents, because adalimumab would be used after all conventional systemic treatments (including antibiotics, dapsone, retinoids and immunomodulators). The company based the efficacy data for adalimumab on pooled data from the PIONEER trials (using an integrated arm-based summary). Efficacy data for supportive care were based on the placebo arms in the PIONEER clinical trials.

3.10 The model used a lifetime horizon, with a cycle length of 4 weeks (except for the first 2 cycles, which were each 2 weeks). All patients entered the model in the non-response health state and then transitioned between health states based on the responses of their disease to treatment and the natural mortality rate. Four of the health states were defined according to varying levels of HiSCR response:

- high response: 75% or greater reduction in AN count with no increase in abscess count or draining fistula count
- response: 50% to 74% reduction in total AN count with no increase in abscess

count or draining fistula count

- partial response: 25% or greater reduction in total AN count with or without an increase in abscess count or draining fistula count
- non-response: less than 25% reduction in total AN count
- death.

The high response and response health states together make up the complete HiSCR response. People in the partial response and non-response health states would have been classified as 'HiSCR non-responders' in the PIONEER trials. The company provided several justifications for splitting the HiSCR into 4 health states:

- There was a statistically significant difference in the EQ-5D utility values (collected in PIONEER II) between the high response and response health states (p=0.036), and between the partial response and non-response health states (p=0.034).
- The difference in the response rates between adalimumab and placebo were statistically significant across 3 of the 4 response health states.
- Resource use differed across the 4 health states.
- A post hoc analysis of the PIONEER studies identified a population in which continued treatment with adalimumab could be beneficial (that is, people with a partial response or higher).

3.11 The level of HiSCR response at 12 weeks determined whether patients continued having adalimumab; people who had at least a partial response continued treatment. For patients who continued having adalimumab, there was an ongoing chance of stopping treatment at any time point:

- Weeks 12 to 36: The company used rates from the PIONEER studies, based on people who had a response at 12 weeks, to estimate 4-week discontinuation rates for the model. The company applied the same discontinuation rate to everyone having adalimumab, regardless of their response state.

- Long-term discontinuation (beyond 36 weeks): The company used data from the open-label extension study to estimate discontinuation rates specific to each response state. The company's application of discontinuation rates aimed to reflect its assumption that people in the non-response health state at 36 weeks would continue treatment for an additional 12 weeks, not stopping until 48 weeks, based on clinical advice and guidance in the adalimumab summary of product characteristics.

  People who stopped adalimumab treatment (at either 12 weeks or later) were assumed to move on to supportive care.

3.12 The company estimated the transition probabilities between health states for the first 36 weeks of treatment using the distribution of people across the 4 response health states in the PIONEER clinical trials. The company imputed missing values using the same method specified in the clinical trial protocol for analysis of the primary end point (non-responder imputation). To extrapolate data beyond what was available from clinical trials (that is, beyond 36 weeks), the company used separate generalised logit models from different sources depending on the treatment:

- For people who continued having adalimumab, the company used data from the open-label extension study and imputed missing values using last observation carried forward.
- For people who stopped adalimumab treatment, the company used data from period B of the PIONEER I and PIONEER II trials (weeks 12 to 36) and missing values were imputed using non-responder imputation.
- For people having supportive care, the company used data from period B of the PIONEER II trial (weeks 12 to 36) and missing values were imputed using non-responder imputation.

3.13 The company assigned utility values to each health state in the model using EQ-5D data collected in the PIONEER II clinical trial (table 2). The model did not incorporate reductions in utility values (disutilities) from treatment-related adverse events. The company stated that this was likely to have a minimal effect on the results because the adverse-event rates were similar between people who had adalimumab and people who had placebo in the PIONEER clinical trials.

Table 2 EQ-5D derived utility values in the company model (using data from weeks 12 and 36)

Model health state	Utility value	95% confidence interval
High response	0.782	0.746 to 0.816; p=0.036
Response	0.718	0.667 to 0.766; p=0.036
Partial response	0.576	0.512 to 0.639; p=0.034
Non-response	0.482	0.402 to 0.542; p=0.034

p values reflect the significant differences in utility values between the high response and response health states, and the difference between the partial and non-response states.

3.14 The company included the following costs in its model:

- treatment costs
- adverse-event-related costs, for adverse events with an incidence of 5% or more in the PIONEER trials
- resource-use costs, assigned to each health state independent of the treatment, for inpatient stays, outpatient visits, visits to wound-care (each divided into surgery related and non-surgery related) and emergency department visits
- one-off set-up costs (£0.70 per patient) and ongoing operational costs (£8.21 per 4-week cycle) associated with the patient access scheme.

3.15 Adalimumab costs were based on the discounted price agreed by the Department of Health in the patient access scheme for adalimumab in hidradenitis suppurativa (see section 2.3). The company did not include any drug costs for supportive care because it considered that any of the conventional treatments taken by people having supportive care would also be taken, less often, by people having adalimumab. The company estimated resource use based on the results of a survey of 40 physicians who treat people with moderate to severe hidradenitis suppurativa in the UK, and obtained costs associated with each type of resource use from NHS reference costs 2013/14.

3.16 The company's original base-case deterministic cost-effectiveness analysis

showed that adalimumab was more costly and more effective than supportive care. The results of the company's one-way deterministic sensitivity analyses showed that the incremental cost-effectiveness ratio (ICER) was sensitive to the assumptions about:

- long-term transition probabilities (after week 36)
- number and cost of hospital admissions, specifically the surgery-related hospital admissions, especially in the non-response health state
- utility values for partial and non-response health states.

The company stated that the ICER was relatively robust to any other changes in model inputs.

Key issues

3.17 The ERG noted that the benefit with adalimumab was greater in PIONEER II than PIONEER I for the primary and secondary outcomes, possibly because PIONEER II patients had less severe disease than people in PIONEER I. The ERG was concerned that the company had not done a formal meta-analysis of the PIONEER trials, and considered that the company's method of pooling data from trials, to inform the transition probabilities in the model, was inappropriate.

3.18 The ERG noted that although the differences between the improvements associated with adalimumab and the improvements with placebo were statistically significant for some health-related quality-of-life outcomes, they did not always exceed the minimum clinically important difference for the instrument. For example, the difference in change from baseline between adalimumab and placebo on the DLQI was 2.5 in PIONEER I ($p<0.001$) and 2.8 in PIONEER II ($p<0.001$); the minimum clinically important difference for the DLQI is 4.

3.19 The ERG had concerns about the company's assertion that adalimumab may delay or reduce the need for surgery, because it was not substantiated by empirical evidence. Based on a post hoc analysis of pooled data from the PIONEER studies, the company stated that a greater proportion of people who had adalimumab, compared with placebo, experienced improvement of both

draining fistulas (33% compared with 19%; p<0.001) and non-draining fistulas (15% compared with 9%; p=0.017). The ERG was unclear whether this reduction in minor procedures fully reflected an overall reduction in surgery, particularly surgical-inpatient admissions, which were a key cost driver in the company's model.

3.20 Given that the HiSCR is a dichotomous outcome (that is, either a clinical response or not), the ERG had concerns about the company's decision to model 4 health states according to the different levels of HiSCR response. The ERG questioned whether the company's assumption that people continued treatment if their disease had a partial response or higher reflects what would happen in clinical practice; it suggested that this assumption, and the decision to model 4 response states, was not consistent with the primary end point in the adalimumab trials or the validation study of the HiSCR measure by Kimball (2014). The ERG was also concerned that dividing the efficacy data across 4, rather than 2, health states resulted in small sample sizes for the calculation of some transition probabilities, which could be considered as a structural uncertainty.

3.21 The ERG had concerns about the company using 1 source to model the benefits of treatment (the clinical trials) and another source to model the resource use needed to get these benefits (the physician survey), and was unsure about the appropriateness of specifying resource use according to different levels of HiSCR response.

3.22 The ERG had concerns about the uncertainty in transition probability estimates beyond week 12, attributed to the small sample sizes in the maintenance period of the trials. The ERG also questioned the robustness of long-term transition probabilities in the company model (beyond week 36), because the company calculated them using data from the open-label extension study. The ERG was concerned because these data:

- were immature
- might have produced optimistic estimates of treatment effect because of the company's method for imputing missing data
- included people who did not reflect the modelled population
- introduced a risk of bias and confounding in the model.

3.23 The ERG's main concern about costs in the model related to the estimation of surgical-inpatient admissions, because this was a key cost driver in the model. The ERG agreed that the company's modelled estimate of total lifetime surgeries for people having supportive care (33.87 procedures) was reasonable, and that the length of stay associated with a wide excision (5.1 days) was appropriate, but considered that not all procedures would involve wide excisions or inpatient stays. Based on clinical advice, the ERG generated alternative estimates and assumptions, which suggested that the company overestimated the mean cost of surgical-inpatient admissions in the model, for both the supportive care and adalimumab groups. The company applied a cost of £5,488.32 to each inpatient admission. The ERG's alternative assumptions resulted in an estimated mean cost of £1,525.74 per surgical-inpatient procedure, which the ERG used as the unit cost for all surgical-inpatient admissions in the model, based on the following assumptions:

- 67% of all inpatient surgeries are intermediate procedures done in a day case setting (based on the company's retrospective study using Hospital Episode Statistics data)
- 6% of surgeries are wide excisions, meaning people have an average of 2 wide excisions over their lifetime
- the remaining 27% of surgeries are an equal mix of planned and unplanned intermediate procedures with an average stay of 2 days
- a wide excision costs £5,488, a day case intermediate procedure costs £943, and an intermediate procedure needing admission costs £2,103.

The ERG was also concerned that the company had not included costs of other pharmacological therapies taken during the trial.

New evidence submitted by the company after consultation

3.24 The company, in response to consultation, responded to all the committee's requests described in the appraisal consultation document.

3.25 The company submitted revised deterministic and probabilistic cost-effectiveness analyses (table 3). The revised model compared adalimumab with supportive care and incorporated the following changes to the base-case analysis:

- clinical estimates were based on the results of a formal meta-analysis of the PIONEER trials instead of the integrated arm-based summary
- people stopped treatment if their disease was not responding after 36 weeks, rather than continuing for an additional 12 weeks.

To apply the results of the network meta-analysis to the model, the company used a different approach for the transition probabilities in weeks 12 to 36. The company considered weeks 12 to 36 as a single transition instead of dividing weeks 12 to 36 into 6 cycles of 4 weeks, as it had done in its original submission. The company explained that the patient numbers were too small to estimate reliable transition probabilities for the additional 4-weekly time points during this period.

Table 3 Company's revised base-case incremental cost-effectiveness analysis results (using adalimumab patient access scheme price)

Scenario	Total cost	Total quality-adjusted life year (QALY)	Incremental cost	Incremental QALY	Incremental cost-effectiveness ratio
Deterministic analysis (random effects model) Supportive care	£128,647	11.63	–	–	–
Deterministic analysis Adalimumab	£140,342	12.58	£11,695	0.95	£12,336
Probabilistic analysis (random effects model) Supportive care	£129,062	11.64	–	–	–
Probabilistic analysis Adalimumab	£142,407	12.61	£13,345	0.98	£13,676

3.26 The company also provided the results of 3 scenario analyses (table 4), applied

to the revised base case as requested in the appraisal consultation document:

- Scenario 1: Partial response was defined as 25% to 50% reduction in the total AN count and no increase in abscesses and draining fistulas.
- Scenario 2: Transition probabilities beyond week 36 were based on the PIONEER trials instead of the open-label extension study, and missing data were handled consistently.
- Scenario 3: Assumptions for scenarios 1 and 2 were combined.

The definitions of health states in the company's revised base-case analysis were unchanged from its original model (see section 3.10). The definitions of partial response and non-response were amended in line with the committee's preferred assumptions in the scenario analyses only. The company did not include the committee's preferred assumptions about the cost of surgical-inpatient procedures in either the revised base case or the scenario analyses; the assumptions were unchanged from the company's original model (see section 3.23 and section 4.12).

Table 4 Company's scenario analyses, applied to the revised base case (deterministic analysis, random effects model, using adalimumab patient access scheme price)

Scenario	Total cost	Total quality-adjusted life year (QALY)	Incremental cost	Incremental QALY	Incremental cost-effectiveness ratio
Scenario 1 (new definition of partial responders) Supportive care	£125,243	11.86	–	–	–
Scenario 1 Adalimumab	£130,225	12.51	£4,982	0.65	£7,646
Scenario 2 (transition probabilities beyond week 36 from PIONEER instead of open-label extension) Supportive care	£128,647	11.63	–	–	–
Scenario 2 Adalimumab	£130,247	12.39	£1,599	0.76	£2,098

Scenario	Total cost	Total quality-adjusted life year (QALY)	Incremental cost	Incremental QALY	Incremental cost-effectiveness ratio
Scenario 3 (scenarios 1 and 2 combined) Supportive care	£125,243	11.86	–	–	–
Scenario 3 Adalimumab	£126,373	12.43	£1,131	0.57	£2,002

3.27 The company also provided the results of a formal network meta-analysis of the primary and secondary outcomes from the 2 PIONEER trials, for the overall population as well as subgroups. The company used a different method for this meta-analysis, compared with the meta-analysis of outcomes used in the model, because of the difference in the way the HiSCR outcome was reported:

- the primary end point of the trials was dichotomous: response or no response
- the model divided the HiSCR into 4 categories according to the level of response: high response, response, partial response or no response.

  The results of the meta-analysis suggested that the likelihood of an HiSCR response was about 3 times greater for people having adalimumab compared with people having placebo.

Key issues

3.28 The ERG reviewed the new evidence submitted by the company in response to consultation on the appraisal consultation document. The ERG was broadly satisfied with the company's methods for the network meta-analysis of outcomes used in the model, and although the ERG highlighted a few issues with the company's methods, it considered the network meta-analysis was fit for purpose. The ERG was able to replicate the results from the company's revised base-case and scenario analyses.

3.29 The ERG suggested that the results of the company's revised base-case model were unreliable for the following reasons:

- The company applied the 4-week discontinuation rate (1.75%) to the 24-week fifth cycle.
- The company did not use the committee's preferred assumptions about the cost of surgical-inpatient procedures.
- The company applied the transition probabilities from the network meta-analysis to weeks 0 to 36 of the model, but used data from its original arm-based summary for transition probabilities beyond week 36. The ERG noted that this issue applies only to people who have stopped adalimumab treatment, because transition probabilities for people continuing adalimumab were based on the open-label extension study. In reviewing the company's revised base case, the ERG considered that data from the network meta-analysis may not be preferable beyond week 36, because the relevant patient group is not randomised. The ERG also identified another issue, which was that the company's approach to long-term transition probabilities resulted in a better prognosis for people who had adalimumab, but stopped treatment, compared with people who had never had the drug. The ERG did not consider this to be clinically realistic.

3.30 The ERG addressed the issues with the company's revised base case in its exploratory analyses (table 5); all exploratory analyses used the corrected discontinuation rate for the fifth cycle (10.04%). In scenarios 2 to 5, the company's assumption that adalimumab reduces the number of surgical-inpatient admissions compared with supportive care was maintained, but the mean cost of surgical-inpatient admissions was varied based on the following responses to the appraisal consultation document:

- The company suggested that the ERG overestimated the proportion of inpatient surgeries done in a day case setting, because the ERG misinterpreted the Hospital Episode Statistics data. The company suggested that only 49% of inpatient surgeries, rather than 67%, are done in a day-case setting.
- A professional group suggested that a patient might have 3 to 4 wide excisions in their lifetime.

  In scenario 6, the ERG assumed that surgical procedures were the same

regardless of treatment and set the costs of surgical-inpatient admissions to zero. In scenarios 7 to 9, the ERG assumed that there was no difference in prognosis beyond week 36 between people who previously had adalimumab and those who had never had the drug, and applied different costs for surgical-inpatient admissions.

Table 5 ERG's exploratory cost-effectiveness analyses, to address issues with the company's revised base case (using adalimumab patient access scheme price)

Evidence review group (ERG) scenario	Deterministic incremental cost-effectiveness ratio (ICER) compared with supportive care, £ per quality-adjusted life year (QALY)	Probabilistic ICER compared with supportive care, £ per QALY
1: Corrected discontinuation rate for cycle 5.	£10,770	Not reported (NR)
2: ERG's original mean surgery cost estimate (£1,525.74); 2 wide excisions, 67% inpatient procedures done in a day setting.	£19,816	NR
3: Increased mean cost of surgery (£1,738.73); 2 wide excisions, 49% inpatient procedures in a day setting.	£19,330	NR
4: Increased mean cost of surgery (£1,838.69); 3 wide excisions, 49% inpatient procedures in a day setting.	£19,101	NR
5: Increased mean cost of surgery (£1,938.65); 4 wide excisions, 49% inpatient procedures in a day setting.	£18,873	£20,196
6: No difference in surgical procedures between people having adalimumab and people having supportive care; costs set to zero.	£23,299	£24,769
7: Same transition probabilities beyond week 36 for people stopping adalimumab and people having supportive care; with ERG's original mean surgery cost estimate (£1,525.74).	£27,701	NR

Evidence review group (ERG) scenario	Deterministic incremental cost-effectiveness ratio (ICER) compared with supportive care, £ per quality-adjusted life year (QALY)	Probabilistic ICER compared with supportive care, £ per QALY
8: Same transition probabilities beyond week 36 for people stopping adalimumab and those having supportive care, with most favourable ERG estimate for mean surgery cost (£1,938.65).	£26,763	£28,525
9: Same transition probabilities beyond week 36 for people stopping adalimumab and those having supportive care, with least favourable ERG estimate for mean surgery cost (costs set to zero).	£31,167	£33,231

All ERG scenarios were based on the company's random-effects network meta-analysis and included the corrected discontinuation rate for cycle 5.

3.31 The ERG was concerned about the company's scenario analyses. In the first scenario analysis, the company used different transition probabilities taken from separate network meta-analyses based on the new definition of partial response. But the ERG noted that the company did not change other model parameters that would be affected by the new definition, such as utility values, adalimumab discontinuation caused by adverse events, and costs for the partial response and non-response health states. The ERG highlighted that in the company's second scenario analysis, in which long-term transition probabilities were based on weeks 12 to 36 of the PIONEER trials instead of the open-label extension study, the company did not use the new transition probabilities estimated from the network meta-analysis done at the request of the committee. Instead, the company applied the transition probabilities for weeks 12 to 36 from its original model to all patients in the model, which the committee had expressed concerns about in the first appraisal meeting (see section 4.9).

4 Committee discussion

The appraisal committee reviewed the data available on the clinical and cost effectiveness of adalimumab, having considered evidence on the nature of hidradenitis suppurativa and the value placed on the benefits of adalimumab by people with the condition, those who represent them, and clinical experts. It also took into account the effective use of NHS resources.

Clinical management

4.1 The committee noted that hidradenitis suppurativa is a chronic inflammatory skin disorder characterised by recurrent painful boils – caused by blocked hair follicles – in areas with apocrine sweat glands, such as the groin and armpits. The committee was aware of consultation comments that symptoms may reduce after the menopause, but heard from the patient experts that symptom patterns differ from person to person. The patient experts explained that hidradenitis suppurativa has a substantial effect on every aspect of their quality of life. Patients can have as many as 30 active, open abscesses in 1 area at the same time, and the pain associated with this can be so severe that they are unable to climb stairs, do housework or look after their children. The committee was aware that patient-expert submissions stated that simply walking and moving in general becomes painful. The committee heard from the clinical and patient experts that this puts a strain on intimate physical relationships, family life and work, causing many people to lose their jobs and develop clinical depression. The patient experts reported that the clinical community lacks awareness of hidradenitis suppurativa and does not appreciate the severity of the condition. They expressed frustration at the many years it took to get a correct diagnosis, and highlighted the lack of available support. The clinical experts noted that people with hidradenitis suppurativa will have repeated and extensive surgeries over their lifetime, which is burdensome. The patient experts explained that it may take months to recover from surgery and return to work, and that the procedures result in painful scarring, which affects quality of life even when the disease is under control. The clinical experts noted that scarring, which is not a feature of other skin conditions such as psoriasis, is associated with its own comorbidities. They also emphasised the substantial psychological burden of the disease and

noted that hidradenitis suppurativa is associated with increased mortality, which can be a result of physical complications such as sepsis, or people taking their own lives. The committee concluded hidradenitis suppurativa has a significant physical and psychosocial impact, which can be underestimated.

4.2 The committee discussed the clinical management of hidradenitis suppurativa. It was aware that there is no standard of care and no NICE guidance; there were no medical treatments specifically licensed for hidradenitis suppurativa until adalimumab received its marketing authorisation. The committee noted the results of a survey of the UK Dermatology Trials Network and British Association of Dermatologists, presented in the company submission, which showed that the most commonly used treatments in the UK – after topical antibiotics – are oral antibiotics; first tetracycline, and then a combination of clindamycin and rifampicin. The third, fourth, fifth and sixth most commonly used interventions in the survey were acitretin, isotretinoin, dapsone and ciclosporin respectively; the choice of treatment depends on individual patient characteristics. The committee noted the company statement that if the condition has not responded to these treatments, tumour necrosis factor (TNF)-inhibitors, including adalimumab and infliximab, are used in the UK. The clinical experts agreed that the survey results accurately reflected the treatment options for hidradenitis suppurativa and that TNF-inhibitors are only considered if the disease is not responding to other conventional treatments. However, they noted that not all of the treatments are supported by robust evidence in this indication. The committee heard from the clinical experts that surgery is done throughout a person's lifetime. The patient experts noted that repeat surgery and ongoing pharmacological treatment are needed because surgery only treats 1 area at a time. The committee concluded that it was appropriate for the company to position adalimumab after all other conventional treatment options.

4.3 The committee questioned whether infliximab would be an appropriate comparator for adalimumab. The clinical experts explained that, although infliximab is used to treat hidradenitis suppurativa, infliximab does not have a marketing authorisation for this indication and the evidence base is very limited; there is only 1 trial of infliximab in hidradenitis suppurativa and the trial population was very small. They explained that access to biologic treatments for hidradenitis suppurativa is restricted and funding is based on individual funding requests. Therefore, the committee did not consider infliximab to be an appropriate

comparator for adalimumab because it is not established practice. The committee concluded that supportive care was the most appropriate comparator for adalimumab.

4.4 The committee considered how clinicians assess disease severity and response to treatment in people with hidradenitis suppurativa. The clinical experts considered that the Hidradenitis Suppurativa Clinical Response (HiSCR) is a reliable and reproducible tool, which has been validated for hidradenitis suppurativa and is relevant to clinical practice, but noted that the minimum clinically important difference has not yet been established. The clinical experts were aware that according to the validation study for the HiSCR measure, response to treatment was defined as a 50% reduction in total abscess and inflammatory nodule (AN) count, with no increase in abscesses or draining fistulas from baseline. However, the clinical experts considered that the 50% threshold was too high, and stated that a 25% reduction in AN count, provided there was no increase in abscesses or draining fistulas from baseline, would reflect a response to treatment. The clinical experts suggested that if the reduction in AN count was between 25% and 50%, they would continue with the existing treatment but may prescribe additional treatments to be taken at the same time (such as anti-inflammatories, retinoids and antibiotics) to improve response. The committee heard from the clinical experts that they would stop treatment if the reduction in AN count was lower than 25%, or if there was an increase in abscesses or draining fistulas. The clinical experts stated that it was important to also use patient-reported outcomes when monitoring people with hidradenitis suppurativa (in particular, the Dermatology Life Quality Index [DLQI], the pain visual analogue scale [VAS] and SF-36, even though they are not specific to this indication), because physician-reported and patient-reported scores do not always correlate. The clinical experts considered that the minimum clinically important difference on the DLQI is 4 points, but commented that, because some people with chronic skin conditions can develop coping mechanisms and so adjust to the effect of the disease, the DLQI may underestimate the beneficial effects of treatment. The clinical experts stated that a 50% reduction in baseline pain is usually considered to be clinically meaningful. The committee concluded that it is appropriate to use the HiSCR for assessing response to treatment, with supporting information provided by patient-reported outcomes. The committee accepted how treatment failure would be defined in clinical practice using the HiSCR.

Clinical effectiveness

4.5 The committee discussed the clinical evidence for adalimumab and noted that people treated with adalimumab were more likely to have a clinical response (the primary end point of the trials) than people treated with placebo. The committee recognised that the difference between adalimumab and placebo was significant. The committee was aware that the benefit with adalimumab was greater in PIONEER II than PIONEER I, possibly because PIONEER II patients appeared to have had less severe disease than people in PIONEER I, and had potentially had higher levels of systemic antibiotics. The company noted that only 19% of patients in PIONEER II took oral antibiotics during the trial. The committee noted that the company had not originally done a formal meta-analysis of the data and was concerned that the company had given contradictory views on whether the PIONEER trials had similar or heterogeneous baseline characteristics, but concluded that the trials were generalisable to UK clinical practice. The committee considered the open-label extension study of adalimumab and was concerned that it only had data up to 72 weeks, given that adalimumab may be used for many years, and that full data were only available for 26% of enrolled patients. The committee concluded that adalimumab provided significant benefits compared with placebo, but that these had not been shown over the long term.

4.6 The committee discussed the health-related quality-of-life benefits associated with adalimumab and understood that adalimumab was associated with significant improvements in health-related quality of life compared with placebo after 12 weeks, as measured by the EQ-5D in PIONEER II. The committee was aware that adalimumab showed a beneficial effect on the SF-36 (collected in PIONEER I) and DLQI (collected in both PIONEER trials) but noted that the difference between adalimumab and placebo was not significant for all components of the SF-36, and that the difference between arms in DLQI improvement at week 12 was not greater than the minimum clinically important difference. The committee discussed the mental component of the SF-36, acknowledging that the change from baseline was not significantly different between the trial arms. The clinical experts explained that they would not expect to see a change in psychological burden of a chronic disease after only 12 weeks of treatment. The committee considered that the DLQI may have underestimated the beneficial effects of adalimumab, based on the clinical experts' comments that people with chronic skin conditions can develop coping mechanisms, which

may result in lower DLQI scores than would be expected (indicating a better health-related quality of life; see section 4.4). The committee concluded that adalimumab had a statistically significant and clinically meaningful positive effect on health-related quality of life.

Cost effectiveness

4.7 The committee considered the structure of the company model and noted the company's justifications for modelling 4 health states according to the level of HiSCR response (see section 3.10). The committee considered it appropriate that the company had developed a more granular model than might have been expected given the dichotomous primary end point in the trials, because it reflected the how treatment success is defined in the clinical management of hidradenitis suppurativa. The committee was aware that response to treatment at 12 weeks determined whether people in the company's model continued having adalimumab, and understood that this reflected the marketing authorisation for adalimumab. The committee discussed the company's assumption that anyone with a partial response or higher at 12 weeks, defined as at least a 25% reduction in AN count with or without an increase in abscesses or draining fistulas from baseline, would continue adalimumab treatment. The clinical experts confirmed that it was reasonable to assume a 25% reduction in AN count would support treatment continuation (see section 4.4). However, they reiterated that if they saw an increase in abscesses or draining fistulas, which are very painful and troublesome complications indicating that adalimumab is not working, they would stop treatment. The committee concluded that the model structure was broadly appropriate for its decision making, but would have preferred to see a model in which people stopped adalimumab treatment if abscesses or draining fistulas increased from baseline. After a request by the appraisal committee in the appraisal consultation document, the company submitted a scenario analysis in which this assumption was applied, through redefining the partial response and non-response health states.

4.8 The committee discussed the company's assumption, in its original model, that people in the non-response health state at 36 weeks or later would continue treatment for an additional 12 weeks, and so would not stop treatment until 48 weeks. The clinical experts disagreed with the assumption that treatment

would be continued in people whose disease is not responding (see section 4.4), because this exposes people to a risk of adverse effects without giving any health benefits. The committee concluded that it was not appropriate to assume that people would continue having treatment if their disease is not responding to treatment (that is, if there is less than a 25% reduction in AN count, or an increase in abscesses or draining fistulas). In response to the appraisal consultation, the company submitted a revised base-case analysis in which people stopped treatment immediately if they were in the non-response health state at 36 weeks or later.

4.9 The committee discussed the company's application of clinical trial data in its original model. It considered that the company's use of an integrated arm-based summary to pool data from the 2 PIONEER trials, to inform the transition probabilities up to week 12 in the model, was inappropriate because it breaks the randomisation in the clinical trials and may have introduced bias in the analysis. The committee was also concerned that the transition probabilities from weeks 12 to 36 used different trial data depending on the treatment arm; the transition probabilities for the adalimumab arm came from pooled data, whereas only PIONEER II data were used for the supportive care arm. The company explained that this was a result of the clinical trial design (see section 3.3), but the committee was concerned that the approach created uncertainty and may have introduced bias in the model. The committee concluded that it would have preferred the company to do a formal random effects meta-analysis of both periods of the PIONEER trials to calculate the efficacy estimates in the model. In response to consultation, the company did a formal random effects meta-analysis of the 4 levels of HiSCR response from 2 PIONEER trials which was incorporated into the revised base case.

4.10 The committee considered the company's extrapolation of long-term data in its original base-case analysis, beyond week 36. The committee heard the evidence review group's (ERG) concerns that the long-term transition probabilities were not robust because they were based on a very small sample of data from the open-label extension study. The committee acknowledged that this could introduce a risk of bias and confounding in the model because of the study design and the inclusion of a select group of people who did not reflect the modelled population. The committee was also concerned that the company's use of different imputation methods (to account for missing data) for different arms of

the model had the potential to introduce bias into the model. The committee concluded that the long-term transition probabilities in the model would be more robust if extrapolation was based on data from the PIONEER trials and missing data were handled consistently. In response to consultation, the company submitted a scenario analysis in which long-term transition probabilities were based on weeks 12 to 36 of the PIONEER trials instead of the open-label extension study.

4.11 The committee discussed the utility values in the company's model. The committee was satisfied with the company's rationale for not including adverse-event-related disutilities in the model. The committee considered it appropriate to use trial-based EQ-5D data for utility values, in line with the NICE reference case, and agreed that the utility values for each health state seemed appropriate. However, the committee was concerned that the company had only used EQ-5D data from PIONEER II and had not used any quality-of-life data from PIONEER I in the model, particularly because the benefit of adalimumab was lower in PIONEER I. In response to consultation, the company gave more information about how it calculated the utility values, including the number of patients used to inform the calculations for each level of response. The committee was aware that few patients in PIONEER II completed the EQ-5D questionnaire at week 36, and noted an imbalance in the proportion of patients in each response category at this time point. The committee heard from the ERG that this could lead to bias in the utility values applied to the model, but the ERG was unsure of the size of the impact. The committee concluded that the utility estimates generated uncertainty in the model, but it was broadly satisfied with the company's approach given that the estimates came directly from trial-based EQ-5D data.

4.12 The committee understood that the cost of surgical-inpatient admissions was a key cost driver in the model, and noted that the company did not change its assumptions about surgical-inpatient admissions in the revised model submitted in response to consultation. The committee was aware that the company had estimated the cost of inpatient surgeries using an online survey in which physicians were asked to estimate resource use for each of the 4 HiSCR health states in the model, based on the average baseline characteristics of patients in the trial. The committee was concerned that this would have been extremely difficult for physicians to estimate. In addition, the committee did not consider it appropriate to estimate resource use based on the level of HiSCR response in the

absence of data from the clinical trials, because each health state would comprise patients with varying disease severity and different surgical needs. The committee heard from the ERG that it agreed with the company's estimate of total lifetime surgeries for the supportive care arm (33.87 surgeries). The ERG also considered that, based on clinical advice, it was not physically possible for a patient to have 34 wide excision procedures in their lifetime, as assumed by the company, and that most of these 34 procedures would be minor. The committee was aware that the ERG had estimated that someone with hidradenitis suppurativa would have 2 wide excisions in their lifetime. The clinical experts agreed that the company had overestimated the surgery-related resource use, and stated that most surgeries are minor procedures; wide excisions are less common. However, the clinical experts suggested that the ERG's alternative assumptions about surgical procedures may have underestimated the costs. The committee noted that comments received during consultation estimated that a patient might have 3 to 4 wide excisions in a lifetime; the ERG explored the impact of these new estimates on the incremental cost-effectiveness ratio (ICER). In the second appraisal committee meeting, the clinical experts suggested that the average number of wide excisions in a person's lifetime may exceed 4, based on research which shows that wide excisions are often associated with poor outcomes and disease recurrence, meaning that many people have repeated surgeries. The committee concluded that the company had overestimated resource-use costs for supportive care and adalimumab, and that the true values were closer to the ERG's estimates, but that the ERG may have underestimated the average cost of surgical-inpatient admissions in all of its exploratory analyses.

4.13 The committee discussed the company's assumption that adalimumab reduced the number of surgical-inpatient admissions compared with supportive care. The ERG and the clinical experts stated that there is no clinical evidence to support this assumption. However, the committee was aware of consultation comments suggesting that the disease control gained with adalimumab, combined with surgery, might lead to disease-freedom in some areas of the body and so reduce the need for major surgery in the long term. The committee noted clinical trial data showing that adalimumab reduces the number of minor surgeries, such as narrow margin excisions and incision and drainage procedures, and noted the consultation comments supporting this. The committee concluded that adalimumab reduces the need for some types of surgical procedure, but it could

not make any definite conclusions about adalimumab's effect on the need for surgical-inpatient admissions in the absence of robust evidence.

4.14 The committee discussed the company's revised base-case cost-effectiveness analysis and noted that the company included the 2 amendments requested by the committee in the appraisal consultation document, which were that:

- clinical estimates were based on the results of a formal meta-analysis of the PIONEER trials instead of the integrated arm-based summary
- people stopped treatment if their disease was not responding after 36 weeks, rather than continuing for an additional 12 weeks.

The committee was aware that the company had applied the transition probabilities from the network meta-analysis to weeks 0 to 36 of the model, but beyond week 36 the company used data from its original arm-based summary for people who had stopped adalimumab. The committee heard from the ERG that it considered it appropriate not to use the network meta-analysis for people who stop treatment, because this patient group is not randomised. However, the ERG explained that the company's approach resulted in a better prognosis for people who previously had adalimumab but stopped treatment, compared with people who had never had adalimumab, and this assumption was applied to the lifetime horizon of the model. The committee discussed whether this difference was clinically plausible. It heard from clinical experts that adalimumab is unlikely to alter the natural history of the disease, but that people whose disease had responded at first to adalimumab may have some continued benefit after stopping treatment, such as a reduced psychological burden and less scarring. The patient experts supported this statement, explaining that any period of respite from the condition, even if the disease eventually stops responding to treatment, improves psychological wellbeing in the long term by providing hope that effective treatments exist. The committee concluded that there is no evidence that adalimumab affects the natural history of hidradenitis suppurativa, although it acknowledged that adalimumab may be associated with short-term improvements in psychological wellbeing after stopping treatment.

4.15 The committee was aware that the company's revised base case did not include

its preferred definitions of partial response and non-response and that this was addressed in one of the company's scenario analyses. The committee noted that redefining the response health states in line with its preferred assumptions reduced the ICER substantially (see section 3.26). However, the committee heard from the ERG that the results of this scenario analysis were not reliable because the company had not accounted for the impact of redefining partial response and non-response on all relevant model parameters, such as utility values, adalimumab discontinuation caused by adverse events, and costs for the partial response and non-response health states. The committee concluded that the results of the company's scenario analysis were unreliable.

4.16 The committee discussed the company's second scenario analysis provided in response to consultation, in which the transition probabilities beyond week 36 were based on the PIONEER trials instead of the open-label extension study. The committee heard from the ERG that the company did not use the new transition probabilities estimated from the network meta-analysis done at the request of the committee. Instead, the company applied the transition probabilities for weeks 12 to 36 from the integrated arm-based summary in its original model, which the committee had already concluded were not robust (see section 4.9). The committee concluded that the results of this scenario analysis were also unreliable.

4.17 The committee attempted to identify the most plausible ICER for adalimumab compared with supportive care. The committee considered that the resource-use assumptions in the ERG's new exploratory analyses, provided after consultation (see section 3.30), were more realistic than the assumptions in the company's revised base-case model. The committee also preferred the ERG's assumption that there is no lifelong difference in prognosis between people who previously had adalimumab and then stopped treatment, and those who had never had the drug. It agreed with the ERG's corrected discontinuation rate for cycle 5 (see section 3.29 and section 3.30). Based on the ERG's exploratory analyses, the committee concluded that the maximum possible ICER for adalimumab compared with supportive care was between £28,500 and £33,200 per quality-adjusted life year (QALY) gained (based on the probabilistic analysis). However, the committee considered that the most plausible ICER would be lower than this for several reasons. First, the ERG's assumption of an average of 4 wide excisions over a patient's lifetime may be an underestimate, and the committee understood that

the ICER reduced as the number of wide excisions increased. Second, the committee acknowledged that adalimumab may be associated with short-term improvements in psychological wellbeing after treatment is stopped, and so considered that the ERG's assumption about prognosis was possibly pessimistic and may have overestimated the ICER. The committee also considered that if its preferred definitions of partial response and non-response had been incorporated in the ERG's exploratory analyses the ICER would have reduced, because continued treatment in people for whom a drug is not effective would be minimised. Taking these factors into account, the committee was certain that the most plausible ICER for adalimumab compared with supportive care was below the ERG's estimate of £28,500 to £33,200 per QALY gained.

4.18 The committee heard from the patient experts that adalimumab was innovative in its potential to make a significant and substantial effect on health-related benefits. The committee understood that adalimumab is the only medical treatment with a marketing authorisation for hidradenitis suppurativa, and no other treatments offer effective long-term disease control. The committee considered whether any gains in health-related quality of life were excluded from the QALY calculations. It understood that improvements in the psychological burden of hidradenitis suppurativa may not be captured in the QALY calculations, given the clinical experts' view that there is a time lag between reducing disease activity and seeing a benefit on patient-reported outcomes (see section 4.6). The committee also heard from patient experts that adalimumab might give enough disease control to allow people to return to work, which has an important positive impact on psychological wellbeing and feelings of self-worth. The committee heard from clinical and patient experts that the benefits associated with reducing the wound-care regimen needed during active disease, such as the time spent on wound care and the effect on work and family life, as well as the cost of dressings, were not captured in the model. The committee concluded that adalimumab is an effective treatment option for an extremely burdensome condition and may provide additional gains in health-related quality of life over those already included in the QALY calculations. Although the committee could not quantify the additional benefits of adalimumab, it considered that they would reduce the ICER compared with best supportive care. Taking this into account, alongside the committee's certainty that the ICER for adalimumab compared with supportive care was below £28,500 per QALY gained (section 4.17), the committee concluded that adalimumab is a cost-effective use of NHS resources

in people with moderate to severe hidradenitis suppurativa whose disease has not responded adequately to conventional systemic therapy. The committee further concluded that the response to adalimumab treatment should be assessed after 12 weeks, in line with the marketing authorisation, and that treatment should only continue if there is clear evidence of response (defined as a reduction of 25% or more in the total abscess and inflammatory nodule count, with no increase in abscesses and draining fistulas; see section 4.7).

4.19 The committee considered whether its recommendations were associated with any issues related to the equality legislation and the requirement for fairness. The committee discussed comments from patient and professional organisations indicating that prevalence is greater in people of African family origin and in women, and some people with hidradenitis suppurativa have other disabilities; these characteristics are protected under the Equality Act 2010. The committee agreed that, because all people would be affected equally by its recommendations, there was no unfairness to any protected group.

4.20 The committee was aware of NICE's position statement on the Pharmaceutical Price Regulation Scheme (PPRS) 2014, and in particular the PPRS payment mechanism. It accepted the conclusion 'that the 2014 PPRS payment mechanism should not, as a matter of course, be regarded as a relevant consideration in its assessment of the cost effectiveness of branded medicines'. The committee heard nothing to suggest that there is any basis for taking a different view about the relevance of the PPRS to this appraisal. It therefore concluded that the PPRS payment mechanism was not relevant in considering the cost effectiveness of the technology in this appraisal.

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 integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation 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 guidance 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 draft guidance.

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 moderate to severe hidradenitis suppurativa and the healthcare professional responsible for their care thinks that adalimumab is the right treatment, it should be available for use, in line with NICE's recommendations.

6 Appraisal committee members, guideline representatives and NICE project team

Appraisal committee members

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

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.

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ISBN: 978-1-4731-1942-0