NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Appraisal consultation document

Adalimumab for treating moderate to severe hidradenitis suppurativa

The Department of Health has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using adalimumab for treating moderate to severe hidradenitis suppurativa 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 (see section 8) and the public. This document should be read along with the evidence base (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?

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 determination (FAD).
- Subject to any appeal by consultees, the FAD may be used as the basis for NICE's guidance on using adalimumab 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: 11 March 2016

Second appraisal committee meeting: 23 March 2016

Details of membership of the Appraisal Committee are given in section 7, and a list of the sources of evidence used in the preparation of this document is given in section 8.

1 Recommendations

1.1 The committee is minded not to recommend adalimumab within its marketing authorisation for treating moderate to severe hidradenitis suppurativa in people whose disease has not responded to conventional therapy.

1.2 The committee recommends that NICE requests further analyses from the company, as described in 1.3–1.6. This information should be made available for the second appraisal committee meeting.

1.3 The information should include a formal meta-analysis of the PIONEER I and II trials. Either meta-analyses of individual patient data or, if this is not feasible, full justification and a formal meta-analysis based on aggregate data. The analysis should include:

- the primary and secondary outcomes common to the trials
- outcomes used in the cost-effectiveness analysis
- subgroup analyses based on the resulting pooled data.

1.4 A revised base-case deterministic and probabilistic cost-effectiveness analysis of adalimumab compared with supportive care should be provided, incorporating:

- the results of a formal meta-analysis of the PIONEER trials
- the committee's preferred assumption about treatment continuation for people in the non-response health state at 36 weeks or later (see section 4.8).

1.5 Three alternative scenario analyses, applied to the revised base case, should also be provided, in which:

- Partial response is defined as 25% to 50% reduction in the total abscess and inflammatory nodule (AN) count and no increase in abscesses and draining fistulas.
- Transition probabilities beyond week 36 are based on the PIONEER trials instead of the open-label extension study, and missing data are handled consistently.
- Both assumptions above are combined.

1.6 The Committee also requires further clarification of the following:

- Calculation of utility values (table 47 of the company submission). Include the number of patients used to inform the utility values, the percentage of responses at 12 and 36 weeks, and patient characteristics (Hurley stage, AN count, abscess and draining fistulae count, Modified Sartorius Score and Dermatology Life Quality Index). Provide this information separately for high response, response, partial response and non-response.
- How resource use estimates were generated for each level of Hidradenitis Suppurativa Clinical Response (HiSCR). Provide:
  - results for each relevant physician survey question (including number of respondents, mean, range and standard deviation)
  - an explanation of how the responses were combined
  - an explanation of how the figures in table 51 of the company submission were derived.
- How data were selected from the open-label extension study to inform the transition probabilities in the cost-effectiveness analysis. Why were data from only weeks 0, 12 and 24 used? How many observations were used at each time point?
- How the model was validated. Present the data in table 58 of the company submission by arm and provide a comparison of the model's quality-adjusted life-year predictions by arm at 12 weeks and 36 weeks with those seen in the clinical trial.

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 (British national formulary, accessed 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. If adalimumab had been recommended, the NHS would have paid a fixed price for each prefilled pen or syringe of adalimumab, with the fixed price applying to the hidradenitis suppurativa indication only. The Department of Health considered that this patient access scheme would not constitute an excessive administrative burden on the NHS.

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 III 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 II or III 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 endpoint 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 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 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 III randomised controlled trials

Trial	Intervention	People with clinical response, n (%)	Difference (95% CI)	p value
PIONEER I	Adalimumab (n=153)	64 (41.8%)	15.9% (5.3% to 26.5%)	0.003
	Placebo (n=154)	40 (26.0%)		
PIONEER II	Adalimumab (n=163)	96 (58.9%)	31.5% (20.7% to 42.2%)	<0.001
	Placebo (n=163)	45 (27.6%)		
Abbreviations: CI, confidence interval; n, number.				

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 endpoint 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 stopping 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: 50–74% 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:

- 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 12–36: The company used rates from the PIONEER studies, based on people who had a response at 12 weeks, to estimate 4-week stopping rates for the model. The company applied the same stopping 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 studies to estimate discontinuation rates specific to each response state (table 2). 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.

Table 2 Stopping rates for adalimumab after 12 weeks

	Annual rate	**4-week rate**
Maintenance period (weeks 12–36)		
All states	20.48%	1.75%
Maintenance period (after week 36)		
High response, response or partial response	7.47%	0.60%
Non-response	44.99%	4.49%

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 endpoint (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 12–36) 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 12–36) 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 3). 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 3 EQ-5D derived utility values in the company model (using data from weeks 12 and 36)

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

[a] 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 fixed price agreed by the Department of Health in the patient access scheme for adalimumab in hidradenitis suppurativa. 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 base-case deterministic cost-effectiveness analysis showed that adalimumab was more costly and more effective than supportive care, resulting in an incremental cost-effectiveness ratio (ICER) of £15,182 per quality-adjusted life year (QALY) gained when the discount in the patient access scheme was applied to the price of adalimumab (table 4). Results from the probabilistic sensitivity analysis indicated that there was a 58% probability of adalimumab being cost-effective if the maximum acceptable ICER was £20,000 per QALY gained, and an 80% probability if the maximum acceptable ICER was £30,000 per QALY gained.

Table 4 The company's base-case incremental cost-effectiveness analysis results (using adalimumab PAS price and including PAS operational costs)

Scenario	Total cost	Total QALY	Incremental cost	Incremental QALY	ICER
Deterministic analysis					
Supportive care	£128,541	11.61			
Adalimumab	£143,683	12.61	£15,142	1.00	£15,182
Probabilistic analysis					
Supportive care	£128,784	11.61			
Adalimumab	£145,256	12.63	£16,471	1.02	£16,162
Abbreviations: ICER, incremental cost-effectiveness ratio; PAS, patient access scheme; QALY, quality-adjusted life year					

3.17 The company did one-way deterministic sensitivity analyses around the 95% confidence interval values of key model parameters. The results indicated that the 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.

3.18 Across all but 1 of the company's scenario analyses, the ICER for adalimumab compared with supportive care remained below £30,000 per QALY gained and in most scenarios the ICER was below £20,000 per QALY gained (using the patient access scheme price for adalimumab). The ICER for adalimumab was greater than £20,000 per QALY gained, compared with supportive care, in the following scenarios:

- time horizon shortened to 20 years or 30 years
- data from PIONEER I excluded (model used only PIONEER II)
- different imputation rule for missing data.

The ICER for adalimumab was greater than £30,000 per QALY gained, compared with supportive care, in the scenario in which people whose disease was not responding to treatment after week 36 did not continue treatment for 12 weeks – an annual stopping rate was applied based on the open-label extension study.

Key issues

3.19 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

performed a formal meta-analysis of the PIONEER trials. The ERG considered that the company's method of pooling data from trials, to inform the transition probabilities in the model, was inappropriate.

3.20 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.

3.21 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 inpatient surgical admissions, which were a key cost driver in the company's model.

3.22 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 endpoint 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.

3.23 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.

3.24 The ERG identified an error in the way that the company had implemented long-term stopping rates (beyond week 36) in the model; the ERG did not consider the company's method to be mathematically correct. The ERG explained that the impact of the company's approach is that people stop adalimumab more quickly than the rate seen in the open-label extension study, thereby substantially reducing the total adalimumab treatment costs and improving its cost effectiveness when compared with supportive care. The ERG suggested that the mathematically correct approach would be to incorporate memory into the model by using additional health states (tunnel states).

3.25 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 were 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.

3.26 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 (for example, people have an average of 2 wide excisions over their lifetime), which suggested that the company overestimated the mean cost of inpatient surgical admissions in the model, for both the supportive care and adalimumab groups. The ERG was also concerned that the company had not included costs of other pharmacological therapies taken during the trial.

3.27 The ERG applied its preferred assumptions to the company model to address its methodological concerns. The ERG produced an alternative base case, including:

- correction of minor model errors
- incorporation of tunnel states, for people whose disease does not respond to adalimumab after 36 weeks (for whom treatment is continued for an additional 12 weeks)
- alternative assumptions about the costs of surgical procedures.

In the ERG's alternative base case (including the patient access scheme for adalimumab), adalimumab produced a deterministic ICER of £28,555 and a probabilistic ICER of £29,725 per QALY gained compared with

supportive care. The ERG did further analyses to explore the effect of excluding PIONEER I data (adalimumab produced a deterministic ICER of £36,372 per QALY gained, compared with supportive care) or assuming:

- Alternative transition probabilities beyond week 36 (adalimumab produced a deterministic ICER of £25,610–£28,110 per QALY gained compared with supportive care):
  - using transition probabilities derived from the open-label extension study, but excluding the use of last-observation-carried-forward imputation
  - using transition probabilities based on weeks 12–36 of the PIONEER trials.
- People with partial response or no response at 12 weeks stopped treatment (adalimumab produced a deterministic ICER of £23,341 per QALY gained, compared with supportive care).
- That there were no differences in costs or health benefits according to level of response (adalimumab produced a deterministic ICER of £40,923 per QALY gained compared with supportive care).

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 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 approved medical treatments until adalimumab received its marketing authorisation. The committee noted the survey done by the company, 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; 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, because surgery only treats 1 area at a time, the disease worsens in other areas of the body and repeat surgery and ongoing pharmacological treatment are needed. 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, 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 the validation study for the HiSCR-defined response to treatment 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 treatment success. 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 an adequate response to treatment. The committee concluded that it is appropriate to use the HiSCR and patient-reported outcomes. The committee accepted how treatment failure would be defined in clinical practice using the HiSCR, DLQI and pain VAS.

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 endpoint 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 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 the 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 justification 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 based on the dichotomous primary endpoint in the trials, because it reflected the clinical management of hidradenitis suppurativa with respect to how treatment success is defined. The committee discussed the company model'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 the drug 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. The committee also had some concerns about other assumptions and inputs (see sections 4.8–4.12) and would have liked to see more detail on how the company validated the model results.

4.8 The committee discussed the company's assumption 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 committee heard from the evidence review group (ERG) that the company's application of this assumption in the model was mathematically incorrect. Both the company and the committee agreed that the ERG's inclusion of tunnel states in the model was more appropriate than the company's approach. However, 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 receiving 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).

4.9 The committee discussed the company's application of clinical trial data in the 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 and may have introduced bias in the analysis. The committee was also concerned that the transition probabilities from weeks 12–36 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.

4.10 The committee considered the company's extrapolation of long-term data in the model, beyond week 36. The committee heard the ERG's 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 would have liked to see a more detailed explanation of how the company used the open-label study data to calculate the transition probabilities. 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.

4.11 The committee discussed the utility values in the company 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. The committee would have liked to see more information on how the company calculated the utility values, including the number of patients used to inform the calculations for each level of response. The committee

concluded that the utility estimates generated uncertainty in the model, because they came from only 1 trial, but it was 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. It was aware that the company had estimated these 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, and would have liked to see how the company analysed the survey results. 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 that the ERG agreed with the company's estimate of total lifetime surgeries for the supportive care arm (33.87 surgeries). The committee also heard that the ERG considered, based on clinical advice, that 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 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. The clinical experts suggested that the ERG's alternative assumptions about surgical procedures may have underestimated the costs, but could not present any alternative estimates. The clinical experts also disagreed with the company's assumption that adalimumab reduced the number of inpatient admissions compared with supportive care; stating that there is no clinical evidence to support this. The committee was unclear whether adalimumab would reduce the need for surgery. 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.

4.13 The committee attempted to identify the most plausible incremental cost-effectiveness ratio (ICER) for adalimumab compared with supportive care. The committee preferred the resource use assumptions in the ERG's alternative base case, and agreed with the ERG's minor model corrections. The ERG's alternative base case produced a probabilistic ICER including the patient access scheme for adalimumab of about £29,700 per QALY gained compared with supportive care. However, the committee recognised that the true ICER might be lower than this, if people whose disease was not responding to treatment after 36 weeks stopped treatment immediately (see section 4.8). Given the other uncertainties in the model, the committee then considered the ERG's exploratory analyses. It noted that the ERG's alternative calculation of transition probabilities beyond week 36 (in which extrapolation was based on data from the PIONEER trials and missing data were handled consistently) did not have a material effect on the ICER. But, it noted that the ICER for adalimumab increased to about £36,400 per QALY gained compared with supportive care (based on a deterministic analysis) when the efficacy data from PIONEER I data were excluded. The committee considered that this was counter-intuitive because the benefit with adalimumab was smaller in PIONEER I than in PIONEER II. This supported the committee's concerns about the company's inconsistent use of data sources instead of a meta-analysis, which contributed to the structural uncertainties in the model. The committee did not consider it appropriate to exclude data from one of the pivotal studies, but neither did it consider it appropriate to base its decision on inappropriately pooled data as in the company and ERG base case; it would have preferred to see a model based on a formal meta-analysis of the PIONEER studies (see section 4.9). The committee concluded that the ICER for adalimumab

may lie within the range of £29,000 to £36,000 per QALY gained, but could be above or below this range. Given that these ICERs were associated with substantial uncertainties (see sections 4.9–4.13) and did not include all of its preferred assumptions, the committee was minded not to recommend adalimumab for treating moderate to severe hidradenitis suppurativa in people whose disease has not responded to conventional therapy. The committee recommends that NICE requests further analyses from the company, as specified in sections 1.2–1.6 which should be made available for the second appraisal committee meeting.

4.14 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 heard 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 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 noted that surgery-related disutilities were not included in the model, but given that there is no evidence to show that adalimumab reduces the need for surgery, it did not consider this to be an added benefit of adalimumab. The committee concluded that adalimumab addresses an unmet need in an extremely burdensome condition, and may provide additional gains in health-related quality of life over those already included in the QALY calculations.

4.15 The committee considered whether its preliminary 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.

4.16 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.

Summary of appraisal committee's key conclusions

TAXXX	**Appraisal title: adalimumab for treating moderate to severe hidradenitis suppurativa**	**Section**
Key conclusion		
The committee is minded not to recommend adalimumab within its marketing authorisation for treating moderate to severe hidradenitis suppurativa in people whose disease has not responded to conventional therapy.		1.1, 1.2-1.6, 4.13

The committee concluded that the incremental cost-effectiveness ratio (ICER) for adalimumab may lie within the range of £29,000 to £36,000 per quality-adjusted life year (QALY) gained compared with supportive care, but given that these ICERs were associated with substantial uncertainties and did not include all of its preferred assumptions, the committee was minded not to recommend adalimumab. The committee recommends that NICE requests further analyses from the company, which should be made available for the second Appraisal committee meeting.		
Current practice		
Clinical need of patients, including the availability of alternative treatments	Hidradenitis suppurativa has a significant physical and psychosocial impact and puts a strain on intimate physical relationships, family life and work, causing many people to lose their jobs and develop depression. The most commonly used treatments are topical and oral antibiotics. In addition to pharmacological treatment, repeated and extensive surgeries are needed throughout a person's lifetime, which results in painful scarring. There is no standard of care and none of the current treatments offer effective long-term disease control.	4.1, 4.2, 4.14
The technology		
Proposed benefits of the technology How innovative is the technology in its	Adalimumab is the only medical treatment with a marketing authorisation for hidradenitis suppurativa. A range of other treatments are used to manage hidradenitis suppurativa, but not all of the treatments are supported by	4.2, 4.5, 4.6, 4.14

potential to make a significant and substantial impact on health-related benefits?	robust evidence in this indication, and no treatments offer effective long-term disease control. Based on clinical trial data, adalimumab provides significant benefits compared with placebo, in the short term. Adalimumab also has a statistically significant and clinically meaningful positive effect on health-related quality of life.	
What is the position of the treatment in the pathway of care for the condition?	Adalimumab is positioned after all other conventional treatment options (including tetracycline, clindamycin with rifampicin, acitretin, isotretinoin, dapsone and ciclosporin).	4.2
Adverse reactions	The most common adverse events with adalimumab in clinical trials of people with hidradenitis suppurativa were worsening of the condition, nasopharyngitis and headache. These were usually mild to moderately severe.	3.8
Evidence for clinical effectiveness		
Availability, nature and quality of evidence	The pivotal clinical evidence for treating hidradenitis suppurativa with adalimumab came from 2 randomised placebo-controlled double-blind phase III trials (PIONEER I and PIONEER II) in adults with moderate to severe hidradenitis suppurativa who were intolerant to, or whose disease had not responded to, oral antibiotics. An open-label	3.1, 4.5

	extension study provided data up to 72 weeks.	
Relevance to general clinical practice in the NHS	People in PIONEER I had more severe disease than those in PIONEER II. This may have been the cause of the different treatment effect across the trials: the benefit with adalimumab was greater in PIONEER II than PIONEER I for the primary and secondary outcomes. The committee concluded that the trials were generalisable to UK clinical practice.	3.4, 4.5
Uncertainties generated by the evidence	The company gave contradictory views on whether the PIONEER trials had similar or heterogeneous baseline characteristics. The committee would have preferred the company to do a formal random effects meta-analysis of the PIONEER trials. The open-label extension study of adalimumab only had data up to 72 weeks, and full data were only available for 26% of enrolled patients.	4.5, 4.9
Are there any clinically relevant subgroups for which there is evidence of differential effectiveness?	No.	-
Estimate of the size of the clinical	More people treated with adalimumab had an Hidradenitis Suppurativa Clinical Response	3.5, 4.5

effectiveness including strength of supporting evidence	(HiSCR) response than those having placebo; these differences were statistically significant in both PIONEER trials. 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. Data from the open-label extension study were immature. The committee concluded that adalimumab provided significant benefits compared with placebo, but that these had not been shown over the long term.	
Evidence for cost effectiveness		
Availability and nature of evidence	The company provided a Markov model to assess the cost effectiveness of adalimumab compared with supportive care. 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. The model used a lifetime horizon with 5 health states including death. The 4 other health states were defined according to varying levels of HiSCR response (high response, response, partial response and non-response).	3.9, 3.10, 4.7
Uncertainties around	The company's application of clinical trial data	4.4,

and plausibility of assumptions and inputs in the economic model	in the model created uncertainty and may have introduced bias in the model, because the company did not do a formal random effects meta-analysis of the PIONEER trials. The long-term transition probabilities in the company's model were based on a very small sample of data from the open-label extension study, which introduced a risk of bias and confounding in 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. The committee agreed with the company's assumption that someone with at least a 25% reduction in abscess and inflammatory nodule (AN) count would continue treatment beyond 12 weeks. However, the committee concluded that it was not appropriate to assume that people would continue receiving treatment if the number of abscesses or draining fistulas had increased. The committee disagreed with the company's assumption that people whose disease was not responding to treatment at 36 weeks would continue adalimumab treatment for another 12 weeks. The utility estimates generated uncertainty in	4.7–4.13

	the model, because they came from only 1 trial, but the committee was satisfied with the company's approach given that the estimates came directly from trial-based EQ-5D data. The company overestimated resource use costs for supportive care and adalimumab in its model, and the committee concluded that the true values were closer to the evidence review group's (ERG's) estimates. There was no clinical evidence to support the company's assumption that adalimumab reduced the number of inpatient admissions compared with supportive care. Given that the benefit with adalimumab was greater in PIONEER II than PIONEER I, it was counter-intuitive for the ICER to increase when PIONEER I data were excluded. This supported the committee's concerns about the structural uncertainties in the model.	
Incorporation of health-related quality-of-life benefits and utility values Have any potential significant and substantial health-related benefits been	Improvements in the psychological burden of hidradenitis suppurativa may not be captured in the QALY calculations, because there is a time lag between reducing disease activity and seeing a benefit on patient-reported outcomes. The benefits associated with reducing the wound-care regimen needed during active disease were also not captured in the model.	4.5, 4.14

identified that were not included in the economic model, and how have they been considered?	The committee concluded that adalimumab addresses an unmet need in an extremely burdensome condition, and may provide additional gains in health-related quality of life over those already included in the QALY calculations.	
Are there specific groups of people for whom the technology is particularly cost effective?	No.	-
What are the key drivers of cost effectiveness?	The cost of surgical-inpatient admissions.	3.21, 3.26, 4.12
Most likely cost-effectiveness estimate (given as an ICER)	The committee preferred the resource use assumptions in the ERG's alternative base case, which produced a probabilistic ICER including the patient access scheme for adalimumab of about £29,700 per QALY gained compared with supportive care. The true ICER might be lower than this, if people whose disease was not responding to treatment after 36 weeks stopped treatment immediately. The committee considered the ERG's exploratory analyses and concluded that the ICER for adalimumab may lie within the range of £29,000 to £36,000 per QALY gained compared with supportive care, but could be above or below this range. Given	4.13

	that these ICERs were associated with substantial uncertainties and did not include all of the its preferred assumptions, the committee was minded not to recommend adalimumab.	
Additional factors taken into account		
Patient access schemes (PPRS)	The company has agreed a patient access scheme with the Department of Health. If adalimumab had been recommended, the NHS would have paid a fixed price for each prefilled pen or syringe of adalimumab, with the fixed price applying to the hidradenitis suppurativa indication only. The Department of Health considered that this patient access scheme would not constitute an excessive administrative burden on the NHS.	2.3
End-of-life considerations	Not applicable	-
Equalities considerations and social value judgements	The committee agreed that, because all people would be affected equally by its recommendations, there was no unfairness to any group protected under the Equality Act 2010.	4.15

5 Related NICE guidance

There is no related guidance for this technology.

6 Proposed date for review of guidance

6.1 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.

Gary McVeigh
Chair, appraisal committee
February 2016

7 Appraisal committee members, guideline representatives and NICE project team

Appraisal committee members

The appraisal committees are standing advisory committees of NICE. Members are appointed for a 3-year term. A list of the committee members who took part in the discussions for this appraisal appears below. There are 4 appraisal committees, each with a chair and vice chair. Each appraisal committee meets once a month, except in December when there are no meetings. Each committee considers its own list of technologies, and ongoing topics are not moved between committees.

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.

Professor Gary McVeigh (Chair)

Professor of Cardiovascular Medicine, Queen's University Belfast and Consultant Physician, Belfast City Hospital

Dr Lindsay Smith (Vice Chair)

GP, West Coker Surgery, Somerset

Dr Aomesh Bhatt

Regulatory and Medical Affairs Director Europe and North America, Reckitt Benckiser

Dr Andrew Black

GP, Mortimer Medical Practice, Herefordshire

Professor David Bowen

Consultant Haematologist, Leeds Teaching Hospitals NHS Trust

Dr Ian Campbell

Honorary Consultant Physician, Llandough Hospital, Cardiff

Ms Tracey Cole

Lay Member

Dr Ian Davidson

Lecturer in Rehabilitation, University of Manchester

Professor Simon Dixon

Professor of Health Economics, University of Sheffield

Mrs Susan Dutton

Senior Medical Statistician, Oxford Clinical Trials Research Unit

Dr Alexander Dyker

Consultant Physician, Wolfson Unit of Clinical Pharmacology, University of Newcastle

Mrs Gillian Ells

Prescribing Advisor – Commissioning, NHS Hastings and Rother and NHS East Sussex Downs and Weald

Professor Paula Ghaneh

Professor and Honorary Consultant Surgeon, University of Liverpool

Dr Susan Griffin

Research Fellow, Centre for Health Economics, University of York

Professor Carol Haigh

Professor in Nursing, Manchester Metropolitan University

Professor John Henderson

Professor of Paediatric Respiratory Medicine, University of Bristol and Bristol Royal Hospital for Children

Dr Malcolm Oswald

Lay Member

Dr Paula Parvulescu

Consultant in Public Health Medicine, Liverpool City Council

Dr Mohit Sharma

Consultant in Public Health, Public Health England

Dr Murray Smith

Associate Professor in Social Research in Medicines and Health, University of Nottingham

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.

Sophie Laurenson

Technical Lead

Sally Doss

Technical Adviser

Kate Moore

Project Manager

8 Sources of evidence considered by the committee

A. The evidence review group (ERG) report for this appraisal was prepared by School of Health and Related Research (ScHARR):

- Tappenden P, Carroll C, Stevens J, et al. Adalimumab for treating moderate to severe hidradenitis suppurativa: A Single Technology Appraisal, December 2015

B. The following organisations accepted the invitation to participate in this appraisal as consultees and commentators. They were invited to comment on the draft scope, the ERG report and the appraisal consultation document (ACD). Organisations listed in I were also invited to make written submissions. Organisations listed in II and III had the opportunity to make written submissions. Organisations listed in I, II and III also have the opportunity to appeal against the final appraisal determination.

I. Company:

- AbbVie

II. Professional/expert and patient/carer groups:

- Hidradentitis Suppurative Trust
- British Association of Dermatologists
- Royal College of Nursing
- Royal College of Physicians

III. Other consultees:

- Department of Health
- NHS England
- Welsh Government

IV. Commentator organisations (did not provide written evidence and without the right of appeal):

- Department of Health, Social Services and Public Safety for Northern Ireland

- Boehringer Ingelheim
- Janssen–Cilag
- Merck Sharp & Dohme Ltd

C. The following individuals were selected from clinical expert and patient expert nominations from the consultees and commentators. They gave their expert personal view on adalimumab by attending the initial committee discussion and providing a written statement to the committee. They are invited to comment on the ACD.

- Dr Anthony Bewley, Dermatology Consultant, nominated by AbbVie – clinical expert
- Dr John Ingram, Senior Lecturer and Consultant Dermatologist, nominated by British Association of Dermatologists – clinical expert
- Tara Burton, nominated by the Hidradentitis Suppurativa Trust – patient expert
- Ceri Harris, nominated by the Hidradentitis Suppurativa Trust – patient expert

E. Representatives from the following company attended committee meetings. They contributed only when asked by the committee chair to clarify specific issues and comment on factual accuracy.

- AbbVie