National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Adalimumab for treating moderate to severe hidradenitis suppurativa

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

Comment 1: the draft remit

Section	Consultee/ Commentator	Comments	Action
Appropriateness	AbbVie	HS is a chronic debilitating disease with no established treatment pathway or licensed medical therapies. Patients suffer from this painful disease and go through years of misdiagnosis and are cycled through a variety of interventions without relief. AbbVie considers therefore, it is important to appraise this topic and ensure that there is an effective licensed treatment available for these patients.	Comment noted. NICE aims to provide guidance to the NHS within 6 months of the date when the marketing authorisation for a technology is granted.
	British Association of Dermatologists & Cochrane Skin Group (BAD)	Very appropriate - hidradenitis suppurativa (HS) is a difficult condition to treat and can cause large quality of life impairment. Adalimumab can be an effective treatment option.	Comment noted.
Wording	AbbVie	The wording of the remit is appropriate.	Comment noted. No actions required.

Section	Consultee/ Commentator	Comments	Action
	BAD	Yes.	Comment noted. No actions required.
Timing Issues	AbbVie	Given that (a) the abscesses and inflammatory nodules of HS cause pain and malodour, and may culminate in scar formation; (b) there are no approved medical therapies for HS and more specifically no approved treatments for abscesses and inflammatory nodules; (c) HS has a clear and substantial negative impact on quality of life, work productivity and activities of daily living and (d) surgical and laser therapies can be associated with significant post-procedure morbidity, recurrence and uncertain long-term disease control, AbbVie highlights that there is a significant unmet medical need for therapies to treat this condition. HS patients are waiting for an effective treatment to be made available so it is important for guidance to be available in close proximity to time of marketing authorisation.	Comment noted. NICE aims to provide guidance to the NHS within 6 months of the date when the marketing authorisation for a technology is granted.
	BAD	The proposed appraisal is timely because there is large inequality in access to adalimumab for HS.	Comment noted. NICE aims to provide guidance to the NHS within 6 months of the date when the marketing authorisation for a technology is granted.
Additional comments on the draft remit	AbbVie	-	Comment noted.
	BAD	-	Comment noted.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments	Action
Background information	AbbVie	It is stated in the background information that: "HS affects around 1 in 600 people in England. There are approximately 90,000 people with HS in England" HS prevalence in industrialised countries has been estimated to be 1%. In the two most frequently cited references for prevalence rates, the 1-year prevalence of symptomatic HS, including mild to severe disease, was estimated to be 0.97% in France and 1.0% in Copenhagen County, Denmark. Two recent studies of the prevalence of HS in large, US-based patient groups suggest that the diagnosed prevalence of HS in the US is approximately 0.05%.	Thank you for your comment. The estimation of the population of people with HS in England is based on the Oxford Textbook of Medicine (5 ed.) 2013 Chapter: Sebaceous and sweat gland disorders.
		It is also stated in the background information that: *"Surgery may be considered for people with chronic HS to remove the apocrine glands in the affected areas of skin although the disease can reoccur after surgery"* Current medical treatments are driven primarily by expert opinion and isolated case reports or series and are frequently ineffective, obliging patients to undergo surgery to remove the sinus tracts, scars, and draining fistulas that are the permanent sequelae of past inflammation. The physical and psycho-social morbidity associated with en bloc excision of scarred axillary, inguinal, or groin skin is substantial and can include wound contractures resulting in limitations in range of motion and keloid formation. Wound healing after HS surgery can be lengthy and result in substantial burden in terms of NHS and non-NHS costs such as lost work productivity. In addition, a considerable percentage of these patients who undergo surgical treatment for their HS experience disease persistence due to inadequate removal of involved tissue at the surgical site or due to the presence of disease at sites other than where surgery has been performed. Extensive surgery causes great disability in severe cases, leading to lack of mobility and work productivity loss, impeding patients' ability to have a normal	During the Scoping Workshop consultees suggested that adalimumab would replace surgery in some instances. In order to ensure the list of comparators is complete, surgery has therefore been included.

Section	Consultee/ Commentator	Comments	Action
		functional life.	
	BAD	Recommend omit the comment about HS lesions causing excessive sweating. The prevalence of HS remains an estimate and about 1% of European adults is probably the figure used most often, based on questionnaire studies. It is unproven whether there are differences in prevalence between people of different ethnicities. Current treatment includes topical antibiotics and antiseptics and oral antibiotics such as the tetracycline group and a combination of clindamycin and rifampicin. Short courses of oral flucloxacillin or erythromycin may be prescribed for disease flares but may not shorten the duration of transient skin boils. Other medical treatments include acitretin, dapsone, and immunosuppressants such as ciclosporin. Surgical options range from incision and drainage of abscesses, to excision of individual lesions, de-roofing of sinus tracts or wide local excision of an entire involved region of skin. In addition to the current treatments outlined above, infliximab is considered when standard therapies have failed. There is a minor inaccuracy in the definition of the cause - HS is caused by blocked hair follicles adjacent to apocrine glands as opposed to blocked apocrine glands adjacent to hair follicles.	Thank you for this comment. The list of comparators has been amended following the Scoping Workshop.
The technology/ intervention	AbbVie	The technology is accurately described.	Comment noted. No actions required.
	BAD	Yes, however we will need clarity about the proposed dose of adalimumab, which will have important cost and efficacy implications.	Comment noted. No actions required.

Section	Consultee/ Commentator	Comments	Action
Population	AbbVie	The population is accurately described (moderate to severe HS patients). There are several types of classification schemes that can be applied; all of which have limitations. Hidradenitis suppurativa can be divided into the following three severity classifications (Hurley staging): •Stage I: abscess formation, single or multiple without sinus tracts and scarring. •Stage II: recurrent abscesses with sinus tracts and scarring; single or multiple widely separated lesions. •Stage III: diffuse or almost diffuse involvement or multiple interconnected tracts and abscesses. Further, modified Sartorius score and Physician's Global Assessment (PGA) have been proposed to assess severity of HS. While these various methods exist, there is not one tool to assess severity that is widely used in clinical practice. In addition, the current severity measures do not assess treatment response and therefore are not appropriate for gauging treatment success.	Comment noted. No actions required.
	BAD	Yes.	Comment noted.
Comparators	AbbVie	It is worth specifying in the Comparators section of the table that no drugs are currently licensed for the treatment of HS. There are no head to head trials of adalimumab with other agents, because there are no licensed treatments for HS. Best alternative care is difficult to define given the absence of trial data for treatments in HS. Prior to the AbbVie HS clinical programme, the only randomised placebo-controlled study of HS meeting its primary endpoint was with the use of	Thank you for this comment, the list of comparators has been amended following the Scoping Workshop.

Section	Consultee/ Commentator	Comments	Action
		topical clindamycin in a small single centre study. Therefore the current evolving treatment algorithm is based on expert opinion and isolated case reports or case series. Since there are no robust data and no approved products for HS, treatments vary widely and are not well characterised. These include medical treatments (e.g., systemic combination therapy with clindamycin and rifampicin, tetracyclines including doxycycline and minocycline, intralesional triamcinolone, systemic cyclosporine, anti-androgen treatment in women, systemic dapsone, systemic retinoids, and metformin). Evaluating the efficacy of these interventions is not possible because their use is described in open-label, frequently retrospective case series and case reports, with typically short -term follow-up and varying eligibility criteria. Retrospective studies of oral clindamycin and rifampicin have not provided definitive evidence to establish the optimal duration of therapy.	
	BAD	The comparators currently listed do not comprise standard treatments used in the NHS; the comparators should be: 1. antibiotics such as tetracyclines or the clindamycin & rifampicin combination 2. acitretin (for males and non-fertile females) 3. dapsone 4. wide local excision surgery (in those who have disease mainly localised to a single site) 5. ciclosporin 6. antiandrogens 7. infliximab (althought not a standard treatment) We do not feel that high-dose oral steroids would be used frequently enough to be a comparator.	Thank you for this comment, the list of comparators has been amended following the Scoping Workshop.
Outcomes	AbbVie	AbbVie adopted the Hidradenitis Suppurativa Clinical Response (HiSCR) as a method to assess clinical response in HS patients treated with adalimumab in	Thank you for your comment, during the

Section	Consultee/ Commentator	Comments	Action
		the phase III clinical trials (PIONEER I & II). The HiSCR is defined as a ≥ 50% reduction in inflammatory lesion count (sum of abscesses and inflammatory nodules, AN), and no increase in abscesses or draining fistulas when compared with baseline. The HiSCR has been validated as a measure of treatment response in a publication, where its reliability, convergent validity, responsiveness and meaningfulness to patients were demonstrated. Consideration should be given to how the distressing symptoms related to the odour of the condition and its social impact are captured in quality of life assessment as this will not necessarily be captured in the domains included in the EQ-5D Improvements in work productivity for those of working age that are active in the labour force or improvements in ability to carry out normal daily activities for those not active in the labour force are useful outcome measures that should be added. It should be acknowledged that patients with long-standing disease may have already left the labour force due to their condition so the impact of treatment on activities of daily living may be as important as the impact on paid work productivity. Clinical outcomes such as outcomes influencing quality of life such as depression are not considered, and their omission will result in failure to capture the full benefits of adalimumab. The social impact of HS is a major determinant of quality of life that needs to be assessed.	Scoping workshop attendees discussed whether there are other relevant outcomes which should be considered and are not listed currently in the draft scope. They concluded that the list of outcomes is appropriate, but it is important to capture the mental burden of the disease, particularly relating to the distressing symptoms. It was discussed that these elements should be captured through the health related quality of life measures that were captured in the trial.
	BAD	We recommend the outcomes list should include patient-reported outcome emasures (PROMS): 1. quality of life 2. pain score	Thank you for your comment. During the Scoping workshop attendees discussed

Section	Consultee/ Commentator	Comments	Action
		3. patient global assessment As well as clinician-reported outcome measures: 1. disease severity (e.g. physician global assessment / Sartorius score) 2. response to treatment, e.g. HiSCR 3. adverse effects	whether there are other relevant outcomes which should be considered and are not listed currently in the draft scope. It was considered that the list of outcomes is appropriate.
Economic analysis	AbbVie	It will be important to take a lifetime perspective to ensure all important costs and benefits are captured in the economic evaluation. However, natural history of HS for patients with moderate to severe disease has not been well-characterised. The economic evaluation should also be conducted from the societal perspective, to capture the impact of HS disease on work productivity losses and other societal costs. The impact on patient out-of-pocket costs should also be captured as patients may resort to buying their own bandages and replacement clothes.	Thank you for your comments. No changes necessary to the scope.
	BAD	Will be greatly influenced by the dosing schedule for adalimumab. Short-term outcomes should be measured at 12-16 weeks, longer-term outcomes at one year.	Comment noted, no actions required.
Equality and Diversity	AbbVie	HS creates a substantial burden of disease, particularly in those patients with more severe disease. Mean Dermatology Life Quality Index [DLQI] is much higher (worse) in HS patients compared to other skin diseases. People suffering from moderate to severe HS are isolated, as the disease can be associated with social stigma and can cause people to withdraw from usual daily activities. Moderate to severe HS patients may be classified as disabled	Comments noted.

Section	Consultee/ Commentator	Comments	Action
		due to the level of functional impairment caused by the condition.	
	BAD	Fine.	Comment noted.
Innovation	AbbVie	Adalimumab should be considered a step-change innovation in the treatment of HS and will have a significant and substantial impact on patient's quality of life, as it is anticipated to be the first treatment for HS licensed for the indication. Work productivity impact is not included in the QALY calculation. Withdrawal from usual activities including work or other daily activities could lead to social exclusion which can have a detrimental effect on mental health. It may be important to consider the impact of adalimumab treatment on comorbidities in HS. A case-control study in the US by Shlyankevich et al. found that HS patients had a high comorbidity burden. In this study 52.5% of HS patients had an ICD-9 code for arthropathies compared to 3% of control subjects. Case reports have suggested that Crohn's disease may also be a comorbidity in some HS patients. There are no data available showing improvements in Crohn's disease or arthropathies with adalimumab use specifically in HS patients. However, adalimumab is licensed for treatment of some of these conditions as outlined in the current licensed indications section in comment 4 below.	Comments noted. No changes to the scope required.
	BAD	Adalimumab has proven helpful in a group of patients with severe HS, unresponsive to other treatments. Wide local excision surgery of an affected region may provide a good outcome with low chance of recurrence but this is not practical for patients with multiple affected skin regions. In these patients with severe disease, adalimumab is a valuable treatment option.	Comment noted. No changes to the scope required.
Other	AbbVie	-	Comment noted.

Section	Consultee/ Commentator	Comments	Action
considerations	BAD	-	Comment noted.
Questions for consultation	AbbVie	Trial data are currently very limited for standard of care for HS patients. Antibiotics may be considered for use as first line treatment, likely related to their anti-inflammatory properties rather than to their antibacterial effects. Other TNF- inhibitors are not licensed for use in HS. Surgery may be conducted but does not address the underlying condition and therefore disease symptoms can occur at other sites in the body. [redacted] Traditionally disease severity is assessed by Hurley stage and Sartorius score. However, the HiSCR is used for treatment response assessment in PIONEER I & II clinical trials with adalimumab vs. placebo.	Comment noted. No changes to the scope required.
	BAD	There is no evidence surrounding the efficacy of biosimilars in HS to date.	Comment noted. No actions required.
Additional comments on the draft scope	AbbVie	-	Comment noted.
	BAD	-	Comment noted.

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

GSK
Department of Health
Royal College of Pathologists

Response to consultee and commentator comments on the provisional matrix of consultees and commentators (pre-referral)

Version of matrix of consultees and commentators reviewed: Provisional matrix of consultees and commentators sent for consultation					
Summary of comments, action taken, and justification of action:					
	Proposal:	Proposal made by:		Action taken: Removed/Added/Not included/Noted	Justification:
1.	Remove Afiya Trust from the matrix of consultees and commentators	NICE Secretariat		Removed	The organisation is no longer actively engaging with NICE and was removed from the matrix under 'patient/carer groups'

2.	Remove Muslim Health Network from the matrix of consultees and commentators	NICE Secretariat		Removed	The organisation has disbanded and was removed from the matrix under 'patient/carer groups'
3.	Add British Contact Dermatitis Society to the matrix of consultees and commentators	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria and equalities commitments. Therefore the British Contact Dermatitis Society has been added to the matrix under 'professional groups'
4.	Add British Epidermo-Epidermiology Society to the matrix of consultees and commentators	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria and equalities commitments. Therefore the British Epidermo-Epidermiology Society has been added to the matrix under 'relevant research groups'

5.	Add Centre of Evidence Based Dermatology, University of Nottingham to the matrix of consultees and commentators	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria and equalities commitments. Therefore the Centre of Evidence Based Dermatology, University of Nottingham has been added to the matrix under 'relevant research groups'
6.	Remove Equalities National Council from the matrix of consultee and commentators	NICE Secretariat		Removed	The organisation's interests are not related to this appraisal topic. Therefore, the Equalities National Council were removed from the matrix under 'patient/carer groups'

7.	Remove Alcon UK Pharma from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Alcon UK Pharma has therefore been removed from the matrix under 'comparator companies'.
8.	Remove Amdipharm Mercury from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Amdipharm Mercury has therefore been removed from the matrix under 'comparator companies'.

9.	Remove Aspen Pharma Trading from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Aspen Pharma Trading has therefore been removed from the matrix under 'comparator companies'.
10.	Add AstraZeneca to the matrix of consultee and commentators	NICE Secretariat		Added	This organisation has a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). AstraZeneca has therefore been added to the matrix under 'comparator companies'

11.	Add Boehringer Ingelhein to the matrix of consultee and commentators	NICE Secretariat		Added	This organisation has a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Boehringer Ingelhein has therefore been added to the matrix under 'comparator companies'
12.	Add Crawford Healthcare to the matrix of consultee and commentators	NICE Secretariat		Added	This organisation has a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Crawford Healthcare has therefore been added to the matrix under 'comparator companies'

13.	Remove Bayer Healthcare from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Bayer Healthcare has therefore been removed from the matrix under 'comparator companies'.
14.	Remove Bristol Myers Squibb from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Bristol Myers Squibb has therefore been removed from the matrix under 'comparator companies'.

15.	Remove Chemidex Pharma from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Chemidex Pharma has therefore been removed from the matrix under 'comparator companies'.
16.	Remove Focus Pharmaceuticals from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Focus Pharmaceuticals has therefore been removed from the matrix under 'comparator companies'.

17.	Remove Forest Laboratories from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Forest Laboratories has therefore been removed from the matrix under 'comparator companies'.
18.	Add Janssen-Cilag to the matrix of consultee and commentators	NICE Secretariat		Added	This organisation has a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Janssen-Cilag has therefore been added to the matrix under 'comparator companies'

19.	Add Merck Sharp & Dohme Ltd to the matrix of consultee and commentators	NICE Secretariat		Added	This organisation has a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Merck Sharp & Dohme has therefore been added to the matrix under 'comparator companies'
20.	Add Napp Pharmaceuticals to the matrix of consultee and commentators	NICE Secretariat		Added	This organisation has a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Napp Pharmaceuticals has therefore been added to the matrix under 'comparator companies'

21.	Remove Hospira from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Hospira has therefore been removed from the matrix under 'comparator companies'.
22.	Remove Intrapharm Laboratories from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Intrapharm Laboratories has therefore been removed from the matrix under 'comparator companies'.

23.	Remove Kent Pharmaceuticals from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Kent Pharmaceuticals has therefore been removed from the matrix under 'comparator companies'.
24.	Remove Martindale Pharma from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Martindale Pharma has therefore been removed from the matrix under 'comparator companies'.

25.	Remove Moorfields Pharmaceuticals from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Moorfields Pharmaceuticals has therefore been removed from the matrix under 'comparator companies'.
26.	Remove Mylan from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Mylan has therefore been removed from the matrix under 'comparator companies'.

27.	Remove Prospect Pharmaceuticals from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Prospect Pharmaceuticals has therefore been removed from the matrix under 'comparator companies'.
28.	Remove Ranbaxy from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Ranbaxy has therefore been removed from the matrix under 'comparator companies'.

29.	Remove RPH from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). RPH has therefore been removed from the matrix under 'comparator companies'.
30.	Remove Somex Pharma from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Somex Pharma has therefore been removed from the matrix under 'comparator companies'.

31.	Remove Spectrum Thea Pharmaceuticals from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Spectrum Thea Pharmaceuticals has therefore been removed from the matrix under 'comparator companies'.
32.	Remove Stragen from the matrix of consultee and commentators	NICE Secretariat		Removed	This organisation does not have a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Stragen has therefore been removed from the matrix under 'comparator companies'.

33.	Add Novartis to the matrix of consultee and commentators	NICE Secretariat		Added	This organisation has a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Novartis has therefore been added to the matrix under 'comparator companies'
34.	Add Takeda to the matrix of consultee and commentators	NICE Secretariat		Added	This organisation has a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Takeda has therefore been added to the matrix under 'comparator companies'

35.	Add Teva to the matrix of consultee and commentators	NICE Secretariat		Added	This organisation has a technology which meets the definition for a comparator technology as outlined in the scope (based on agreement at the scoping workshop). Teva has therefore been added to the matrix under 'comparator companies'