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ADIS DRUG EVALUATION

Adalimumab: A Review in Hidradenitis Suppurativa

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Abstract Subcutaneous adalimumab (Humira®) is a tumour necrosis factor-α blocker that is the only approved agent for the treatment of moderate to severe hidradenitis suppurativa (HS) in several countries worldwide. This article reviews the clinical efficacy and safety of subcutaneous adalimumab in patients with moderate to severe HS. In clinical trials (PIONEER I and II), a greater proportion of adalimumab than placebo recipients reached HS clinical response (HiSCR) at week 12. The main secondary endpoints, such as the proportion of patients with an abscess and inflammatory nodule count of ≤2 at week 12, were significantly greater with adalimumab than with placebo in PIONEER II, but not in PIONEER I. In addition, adalimumab showed the potential to reduce the high health-related quality of life burden of HS and increase patient satisfaction. HiSCR rates were generally maintained in the longer term, and the safety profile of adalimumab in patients with moderate to severe HS was consistent with the known safety profile of the drug for other indications, with no new emerging safety signals. Adalimumab is an effective and generally well tolerated treatment for patients with moderate to severe HS, and is the first agent approved for this difficult-to-treat disease.

Adalimumab in hidradenitis suppurativa (HS): a summary

Blocks the activity of TNF-α, a proinflammatory cytokine expressed in the basal layer of the epidermis, hair follicles and sweat glands
Induces a significant clinical response in patients with moderate to severe HS
Significantly reduces pain and improves quality of life
Generally well tolerated, with exacerbation of HS, nasopharyngitis and headache occurring most commonly in long-term follow up

1 Introduction

Hidradenitis suppurativa (HS; also known as acne inversa) is a chronic and debilitating inflammatory skin disease that is characterized by painful lesions in apocrine gland-bearing areas (mainly, but not exclusively, the axillary, anogenital and inguinal areas) that often progress to scarring, sinus tract formations and suppuration [1, 2]. Risk factors include family history, obesity and smoking. It is estimated to affect from <1 to 4 % of the general population, with a preponderance among young adults and women [1, 3]. Although most patients have mild or moderate (Hurley stage I or II) disease, severe (Hurley stage III) disease has been reported in up to 22 % of HS patients [4].

HS has a severely negative impact on patients' physical (e.g. pain, restricted movement), psychosocial (e.g.

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depression, embarrassment, isolation) and economic (e.g. work disability, unemployment) aspects of life [3, 4]. Anger, depression, irritation, sadness and worry often result because of the itching, pain, malodourous discharge and scarring associated with HS [5]. In addition, HS may increase patients' risk of cardiovascular comorbidities; evidence suggest that HS patients present with significantly higher rates of cardiovascular risk factors (e.g. dyslipidaemia, diabetes, metabolic syndrome) than those seen in healthy controls [6].

Studies have indicated that HS patients have higher levels of tumour necrosis factor (TNF)-α in the serum [7] and skin (lesional and perilesional) [8] than healthy controls. Interleukin (IL)-1β and IL-10 are also significantly ($p < 0.05$) elevated in lesional HS skin [8]. Levels of certain inflammatory serum markers [e.g. C-reactive protein (CRP) and neutrophil count] can be elevated, and correlate with disease severity in patients with HS [9]. Mild HS is often managed with topical therapy (e.g. topical clindamycin), whereas moderate to severe HS is usually treated with systemic therapy (e.g. oral antibiotics with immunomodulatory properties, systemic immunosuppressive therapy, or TNF-α inhibitors) [10]. HS refractory to medical treatment may necessitate surgery [10].

Adalimumab (Humira®) is a TNF-α inhibitor indicated for the treatment of HS in several countries worldwide, including members of the EU, where it is approved for use in adults with active moderate to severe HS responding inadequately to conventional systemic therapy [11], and the USA, where it is approved for use in patients with moderate to severe HS [12]. This article reviews the pharmacological, efficacy and safety data relevant to the use of adalimumab in these indications. Adalimumab is also approved for several other indications (e.g. Crohn's disease, plaque psoriasis, rheumatoid arthritis, ulcerative colitis) [11, 12]; however, these indications are beyond the scope of this review and are not discussed further.

2 Pharmacodynamic Properties of Adalimumab

The general pharmacodynamic properties of adalimumab have been reviewed previously [13–15]; this section provides an overview, including discussion of pharmacodynamic effects relevant to HS.

Adalimumab is a recombinant human IgG1 monoclonal antibody that binds specifically to, and blocks the activity of, TNF-α, a proinflammatory cytokine that is expressed in the basal layer of the epidermis, hair follicles and sweat glands [1, 11, 12]. Adalimumab binds to TNF-α with relatively high affinity (antigen dissociation constant of 7.05×10^{-11} to 1.0×10^{-10} M) [16]. It is believed that the binding of adalimumab to TNF-α creates such a large complex that it would be removed rapidly from circulation. By blocking the interaction of TNF-α with cell surface TNF receptors I and II (also known as p55 and p75, respectively), adalimumab prevents the movement of nuclear transcription factor NF-κB into the nucleus where it induces the production of cytokines that contribute to the inflammatory cascade [16]. In addition, adalimumab modulates downstream processes induced or regulated by TNF, such as inhibiting (with a concentration at half-maximal inhibition of 0.1–0.2 nmol/L) endothelial-leukocyte adhesion molecule-1, intracellular adhesion molecule-1 and vascular cell adhesion molecule-1 (adhesion molecules are responsible for the migration of leukocytes) [11, 12]. Adalimumab does not interact with TNF-β [12].

In a phase II trial comparing subcutaneous adalimumab 40 mg with placebo in patients with moderate to severe HS ($n = 154$), the mean change from baseline to week 16 in serum CRP levels was −7.9 mg/L with adalimumab (160 mg at week 0, 80 mg at week 2, and 40 mg/week from week 4) [$p = 0.008$] compared with +4.4 mg/L with placebo [17]. A mechanism-of-action substudy of patients ($n = 9$) who participated in the phase II trial showed a reduction in the production of cytokines in HS skin with adalimumab compared with placebo, particularly IL-1β, IL-11, B-lymphocyte chemoattractant, and CXCL9 (a monokine induced by interferon-γ) [18].

In a study of rheumatoid arthritis patients receiving adalimumab or placebo, similar levels of protection were observed with anti-pneumococcal and influenza vaccines [11, 12]. Patients may receive vaccines, with the exception of live vaccines, concurrently with adalimumab [11, 12].

3 Pharmacokinetic Properties of Adalimumab

Adalimumab is absorbed and distributed slowly following subcutaneous administration, with a peak serum concentration attained in ≈5 days after the administration of a single dose of 40 mg in healthy adults [11, 12]. The average absolute bioavailability of adalimumab was ≈64 % [11, 12].

In a population pharmacokinetic analysis of data from PIONEER I and II and a phase II study, adalimumab pharmacokinetics were described by a one-compartment model with first-order absorption, adalimumab concentrations were dose proportional, the apparent volume of distribution (V/F) was 13.5 L, and the apparent clearance (CL/F) was 27.8 mL/h [19]. V/F and CL/F increased with an increase in bodyweight, CL/F increased with higher baseline CRP levels, and the formation of anti-adalimumab antibodies (AAAs) was associated with a sixfold increase in mean adalimumab CL/F compared with patients without AAAs [19]. The concentration of adalimumab in serum is a

significant ($p = 0.015$) predictor of HS clinical response (HiSCR) [20].

The concomitant use of adalimumab and anakinra, abatacept or other TNF blockers is not recommended, as this may increase the risk of infections and potential pharmacological interactions [11, 12]. It is possible for adalimumab to influence the formation of cytochrome P450 (CYP) enzymes, so monitoring the concentrations and effects of CYP substrates with narrow therapeutic indices (e.g. ciclosporin, warfarin, theophylline) is recommended [12]. Concomitant treatment with antibiotics had no effect on adalimumab trough concentration [19]. Adalimumab has not been studied in patients with impaired renal and/or hepatic function [12].

4 Therapeutic Efficacy of Adalimumab

This section focuses on results of two randomized, double-blind, placebo-controlled, multinational, phase III trials [PIONEER I ($n = 307$) and PIONEER II ($n = 326$) [21], including pooled data from both [22–27]] that investigated the efficacy of subcutaneous adalimumab in patients with moderate to severe HS. As data are available from these phase III trials, an earlier, phase II trial [17] is not discussed. Some data are from abstracts and/or posters [22–28]. Where the adalimumab dosage is not specified, data are from patients receiving the approved treatment regimen (adalimumab 160 mg on week 0, 80 mg on week 2 and 40 mg weekly from week 4).

4.1 PIONEER I and II

The PIONEER trials enrolled patients aged ≥18 years, with a ≥1 year history of diagnosed HS involving ≥2 anatomical areas, who had an inadequate response to, or were intolerant of, oral antibiotics [21]. Patients had to have at least one region at Hurley stage II or III and a total abscess and inflammatory nodule (AN) count of ≥3. Exclusion criteria included patients previously treated with adalimumab or other anti-TNF agents, and patients who received any oral antibiotic within 28 days of the baseline visit (PIONEER I) or patients on permitted antibiotics who were not on stable doses for at least 28 days before the baseline visit (PIONEER II) [21].

The trials were of similar design and consisted of two periods, one of 12 weeks (period 1) and the other of 24 weeks (period 2) [21]. In period 1, patients were randomized 1:1, to receive adalimumab (160 mg at week 0, 80 mg at week 2, and 40 mg weekly from week 4) or placebo. All patients were to participate in period 2. In period 2, patients previously randomized to adalimumab were re-randomized 1:1:1 to receive adalimumab 40 mg weekly, adalimumab 40 mg every other week (eow) or matching placebo from week 12. Patients previously randomized to placebo in period 1 were assigned in PIONEER I to receive adalimumab (160 mg at week 12, 80 mg at week 14, and 40 mg weekly from week 16) and in PIONEER II to continue receiving matching placebo from week 12 [21]. All patients were required to use antiseptic washes [20, 21].

The primary efficacy endpoint in both trials was the proportion of patients in the ITT population achieving an endpoint termed the HS clinical response (HiSCR) by the end of the first treatment period (week 12); HiSCR was defined as a ≥50 % reduction from baseline in total AN count, without increases in abscess or draining fistula counts relative to baseline [21]. At baseline, across all treatment arms in both trials, the mean patient age was 34.9–37.8 years, 59.5–69.3 % were female, the median disease duration was 8.8–9.9 years, and 8.4–16.6 % had prior HS surgery. Baseline characteristics were generally similar across treatment arms, except for bodyweight [significantly ($p = 0.04$) higher in placebo than adalimumab recipients in PIONEER II] [21].

Patients who achieved HiSCR by the end of the first treatment period (HiSCR responders), but had a loss of response (defined as a ≥50 % loss of improvement in AN count achieved from baseline to week 12) during period 2, were discontinued from the trial and given the opportunity to receive adalimumab 40 mg weekly in an open-label extension (OLE) (Sect. 4.2) [21]. HiSCR non-responders who had no improvement or a worsening of disease (AN count greater than or equal to that at baseline on two consecutive visits at least 14 days apart) at or after week 16 were also discontinued from the trial and given the opportunity to enter the OLE. At week 36, all patients were given the opportunity to enter the OLE [21].

4.1.1 Short-Term Efficacy

In both trials, a significantly greater percentage of patients achieved HiSCR at week 12 with adalimumab than with placebo (Table 1). This occurred irrespective of whether patients had Hurley stage II or III disease (PIONEER I and II), or concomitant antibiotic therapy (PIONEER II) [prespecified subanalyses] [21]. Of note, approved oral antibiotics were allowed as rescue therapy in PIONEER I only (patients did not receive any other oral antibiotics) and as concomitant therapy in PIONEER II only (continuation of antibiotics used at baseline; no additional antibiotics started) [21].

Pooled data from the PIONEER trials also showed a greater proportion of adalimumab than placebo recipients (50.6 vs. 26.8 %; $p < 0.001$) achieving HiSCR at week 12 [25]. The median time to HiSCR was significantly shorter

Table 1 Efficacy of subcutaneous adalimumab in patients with hidradenitis suppurativa, in the phase III PIONEER trials at week 12 (period 1) [20, 21]

Trial	Treatment	No. of pts All [stage II HS]	HiSCR[a] rate All (% pts)	Change from BL in mean MSS score [BL]	AN count ≤2 in pts with BL stage II HS (% pts)	NRS30[b] (% pts)
PIONEER I [21]	ADA	153 [83]	41.8**	−24.4 [151.0]	28.9	27.9
	PL	154 [84]	26.0	−15.7 [147.3]	28.6	24.8
PIONEER II [21]	ADA	163 [85]	58.9***	−28.9*** [107.5]	51.8**	45.7***
	PL	163 [87]	27.6	−9.5 [122.6]	32.2	20.7

The mean AN counts at BL were 14 and 11 in PIONEER I and II, respectively, and the mean NRS scores (daily pain at worst) at BL were 5.0 and 4.5. Patients received adalimumab (160 mg on week 0, 80 mg on week 2 and 40 mg weekly from week 4) or matching placebo

ADA adalimumab, *AN* abscess and inflammatory nodule, *BL* baseline, *HiSCR* hidradenitis suppurativa clinical response, *HS* hidradenitis suppurativa, *MSS* modified Sartorius Scale, *NRS* numerical rating scale, *PL* placebo, *pts* patients

* $p < 0.05$, ** $p \leq 0.01$, *** $p < 0.001$ vs. PL

[a] Primary endpoint; defined as ≥50 % reduction from BL in total AN count, without an increase in abscess or draining fistula counts

[b] Reduction of ≥30 % and ≥1 unit from BL in Patient's Global Assessment of Skin Pain NRS, based on 24-h recall of worst pain at week 12, in patients who had BL skin pain NRS ≥3

with adalimumab 40 mg weekly than with placebo treatment (31 vs. 92 days; $p < 0.001$) [26, 27]. A significant between-group difference in time to HiSCR was observed after just 2 weeks [26].

Results were mixed for the three ranked secondary endpoints [achievement of AN count ≤2 at week 12 among patients with Hurley stage II at baseline; achievement at week 12 of a ≥30 % reduction and a ≥1-unit reduction in patients' global assessment of skin pain numerical rating scale (NRS) score in patients with a baseline NRS score ≥3; and mean change in MSS score from baseline to week 12]: all were significantly ($p < 0.02$) greater with adalimumab than placebo in PIONEER II, but no significant treatment differences were observed in PIONEER I [21] (Table 1).

The mean improvement from baseline in MSS score was significantly ($p < 0.02$) greater with adalimumab than with placebo at weeks 2, 4 and 8 in PIONEER I and at weeks 2, 4, 8 and 12 in PIONEER II [21]. The proportion of patients with baseline NRS scores of ≥3 achieving a ≥30 % reduction and a ≥1-unit reduction in pain scores was significantly ($p \leq 0.02$) higher with adalimumab than with placebo at weeks 2, 4 and 8 in PIONEER I and at weeks 2, 4, 8 and 12 in PIONEER II [21]. Patients were significantly more likely to experience a ≥30 % improvement in pain with adalimumab than with placebo in both PIONEER I [odds ratio (OR) 2.03; 95 % CI 1.25–3.29] and II (OR 4.78; 95 % CI 3.00–7.63) [28]. In addition, the proportion of time patients spent with a ≥30 % improvement in pain in the first 12 weeks was significantly higher with adalimumab than with placebo in both PIONEER I (41.66 vs. 27.11 %) and II (50.62 vs. 25.34 %) [both $p < 0.001$] [28].

Flares, defined as an increase in the total AN count of ≥25 % with an increase of ≥2 from baseline, occurred in a significantly ($p < 0.001$) lower proportion of adalimumab than placebo recipients in the first 12 weeks [21]. For example, in PIONEER I, 13.7 % of adalimumab recipients compared with 35.7 % of placebo recipients ($p < 0.001$) experienced flares by week 12. In patients who experienced flares, adalimumab treatment was associated with a significantly shorter mean flare duration than placebo ($p < 0.05$) in both PIONEER I and II [21].

Health-related quality of life (HR-QOL) improved significantly with adalimumab compared with placebo in the PIONEER trials. In PIONEER I, adalimumab recipients reported significantly greater mean changes (improvements) than placebo recipients in several physical aspects (physical component summary score, role physical, bodily pain, general health; $p < 0.01$) of the Short Form 36-item health survey, the activity impairment aspect ($p < 0.05$) of the work productivity and activity impairment (WPAI) questionnaire, and in dermatology life quality index (DLQI) scores ($p < 0.001$) from baseline to week 12 [21]. In PIONEER II, significantly ($p < 0.01$) greater improvements in the EQ-5D scores, DLQI scores, and the activity impairment aspect of WPAI questionnaire scores were seen with adalimumab than with placebo from baseline to week 12 [21].

In a pooled analysis, DLQI scores decreased from baseline to a significantly greater extent in adalimumab than in placebo recipients ($p < 0.001$) [22]. Moreover, significantly greater proportions of adalimumab than placebo recipients achieved the predefined minimal clinically important difference of a ≥5-point decrease from baseline in DLQI scores (49.8 vs. 33.9 % of patients; $p < 0.001$) [among patients with baseline DLQI scores of ≥5] and DLQI scores of 0 or 1 (meaning no effect on skin-related QOL) [7.3 vs. 1.9 %; $p < 0.001$] at week 12 [22]. A significant difference between adalimumab and placebo

recipients was also seen in treatment satisfaction; patients rated adalimumab higher ($p < 0.01$) than placebo for effectiveness and global satisfaction in both PIONEER I and II [21] and in a pooled analysis [23].

4.1.2 Effects of Dosage Reduction or Interruption

Among patients who had received adalimumab in period 1 who were re-randomized in period 2 to continuous-administration (adalimumab 40 mg weekly; $n = 99$), reduced-dosage (adalimumab 40 mg eow; $n = 101$) or interrupted-therapy (placebo; $n = 100$) treatment groups, the HiSCR rates were 43.4, 30.7 and 28.0 %, respectively, at week 36 (pooled analysis of the PIONEER trials) [24]. Among week 12 responders and partial responders (partial responders defined as HiSCR non-responders who had a reduction in AN counts of ≥25 % relative to baseline) who had received adalimumab in period 1, HiSCR rates at week 36 were 55.7 % with continuous administration, 40.0 % with a dosage reduction and 30.1 % with interrupted therapy [20, 24]. Of note, among patients who had received placebo in period 1 who were re-randomized in period 2 to switch to adalimumab (PIONEER I) or continue receiving placebo (PIONEER II), HiSCR rates were 41.4 and 15.9 % at week 36 [21].

4.2 Extension Study

Patients from PIONEER I and II who had completed both study periods, had achieved HiSCR by the start of period 2 then experienced a loss of response, or had not achieved HiSCR by the start of period 2 and experienced no improvement or a worsening of disease on or after week 16, were eligible to receive adalimumab 40 mg weekly in an OLE study, regardless of previous treatment assignment [21]. From week 24 of the PIONEER OLE study, patients achieving HiSCR (relative to their baselines in the prior PIONEER trials) and AN counts of 0 or 1 on at least two consecutive visits were permitted to reduce their dosage of adalimumab to 40 mg eow [20]. Patients had to use topical antiseptics daily on areas of the body affected by HS lesions [20].

An interim analysis, covering up to 48 weeks' treatment in the OLE, demonstrated sustained HiSCR with continuous treatment [20]. In the adalimumab 40 mg weekly/weekly/weekly (period 1/period 2/extension) group ($n = 84$), the proportion of patients achieving HiSCR remained above 50 % (range 51–60 %) at all visits. Retreatment with adalimumab 40 mg weekly after dosage reduction or interrupted therapy resulted in a rebound of HiSCR achievers; HiSCR rates increased from 37 % at OLE baseline to 61 % at OLE week 48 in the weekly/eow/weekly ($n = 90$) group and from 31 to 52 % in the weekly/placebo/weekly ($n = 91$) group [20].

5 Tolerability of Adalimumab

The adverse event profile of adalimumab in patients with HS was consistent with the known safety profile of the drug [11, 12].

In PIONEER I and II, in period 1 (the first 12 weeks), at least one treatment-emergent adverse event (TEAE) was reported in 50.3 and 57.1 % of adalimumab recipients and 58.6 and 63.2 % of placebo recipients [21]. TEAEs occurring in ≥10 % of adalimumab or placebo recipients were headache (9.2 vs. 9.9 % in PIONEER I and 12.9 vs. 12.9 % in PIONEER II) and nasopharyngitis (5.9 vs. 10.5 % and 5.5 vs. 6.1 %). Of note, worsening of disease was not included in the reported rates of TEAEs [21]. Recipients of adalimumab, a TNF blocker, have an increased risk of developing serious infections and may have an increased risk of developing malignancies [11, 12]. Overall, infections occurred in ≈25 % of adalimumab and ≈30 % of placebo recipients, and malignancies occurred in 0 and <1 % of patients [21]. In period 1 of PIONEER I and II, serious TEAEs occurred in 1.3 and 1.8 % of adalimumab recipients and 1.3 and 3.7 % of placebo recipients, serious infections occurred in 0.7 and 0.6 % of adalimumab recipients and 0 and 1.2 % of placebo recipients, and TEAEs led to discontinuation of treatment in 0 and 2.5 % of adalimumab recipients and 1.3 and 3.7 % of placebo recipients. No deaths were reported in period 1 [21].

No new safety signals were identified in period 2 (weeks 12–36) [21, 24]. In PIONEER I and II, in period 2, at least one TEAE was reported in 58.3 and 56.9 % of patients in the adalimumab continuous administration group, 45.8 and 56.6 % of patients in the dosage reduction group and 57.1 and 64.7 % of patients in the treatment discontinuation group [21]. Serious TEAEs were reported in 2.1 and 3.9 %, 2.1 and 3.8 %, and 0 and 0 % of patients respectively. One death was reported in a patient in the dosage reduction group in PIONEER II; the patient died of a cardiorespiratory arrest 42 days after the last dose of adalimumab [21].

Long-term tolerability data were reported from an interim integrated population analysis of all subjects who received at least one dose of adalimumab weekly or eow in phase II and III HS trials ($n = 727$; cumulative exposure of 635.7 patient-years) [20]. Almost half (46 %) of patients in this population had received >1 year of adalimumab treatment. At least one TEAE was reported in 78.7 % of

patients; 44.3 % had adverse events possibly related to adalimumab. Serious TEAEs occurred in 10.7 % of patients; 2.8 % had serious adverse events possibly related to the study drug. TEAEs occurring in >10 % of the integrated population included hidradenitis (21.0 %), nasopharyngitis (14.3 %), headache (13.3 %) and upper respiratory tract infection (10.6 %). Infections (any) were seen in 51.9 % of patients (most commonly nasopharyngitis, upper respiratory tract infection and urinary tract infection), and serious infections were seen in 2.9 % of patients. Malignancies (any) were seen in 0.7 % of patients. Discontinuation because of TEAEs was seen in 9.6 % of patients, and TEAEs leading to death were seen in 0.3 % of patients (septic shock and cardio-respiratory arrest; these were not considered related to adalimumab) [20].

AAAs (only detectable in patients with serum adalimumab concentrations <2 μg/mL as a result of assay limitations) were found in 6.5 % of adalimumab recipients with moderate to severe HS [12]. In ≈22 % of patients who had discontinued treatment for up to 24 weeks (and thus had adalimumab concentrations <2 μg/mL), the proportion of patients positive for antibodies to adalimumab was 28 % [12].

6 Dosage and Administration of Adalimumab

Adalimumab is approved in several countries for the treatment of moderate to severe HS, including the USA (where it is indicated in patients with moderate to severe HS) [12] and the EU (where it is indicated in adults with active moderate to severe HS responding inadequately to conventional systemic therapy) [11]. Adalimumab is administered subcutaneously by injection to the abdomen or thigh [11, 12].

The recommended dosage regimen for adults consists of an initial dose of adalimumab 160 mg (four 40 mg injections on day 1 or two 40 mg injections per day on days' 1 and 2), followed by adalimumab 80 mg on day 15 (two 40 mg injections in one day), and 40 mg weekly from day 29 [11, 12]. If a patient shows no improvement by week 12, continued treatment with adalimumab should be reconsidered [11]. During treatment with adalimumab, daily use of a topical antiseptic wash on HS lesions is recommended. If necessary, antibiotics may be continued during adalimumab treatment [11].

The US prescribing information contains a boxed warning about the risk of serious infections (e.g. bacterial sepsis, invasive fungal infections, tuberculosis, infections due to other opportunistic pathogens) and malignancy (e.g. lymphomas in children and adolescents) [12]. Contraindications listed in the EU SPC include moderate to severe (NYHA class III/IV) heart failure and active tuberculosis or other severe infections (e.g. opportunistic infections, sepsis) [11]. Adalimumab should not be used in patients with active infections [11, 12].

Local prescribing information should be consulted for further, detailed information, including contraindications, warnings, precautions, drug interactions, and use in special patient populations.

7 Current Status of Adalimumab in Hidradenitis Suppurativa

Current European guidelines for the treatment of HS generally recommend topical clindamycin as first line therapy for mild disease, oral clindamycin and rifampicin combination therapy (first line), oral tetracycline (first line) or oral acitretin (second line) for mild to moderate disease, and biological drugs as second-line treatment for moderate to severe disease (of which adalimumab is first line and infliximab is second line) [3, 29]. The National Institute for Health and Care Excellence in the UK recommends using adalimumab as a treatment option for adults with active moderate to severe HS that has not responded to conventional systemic treatment options [30]. Surgery may be needed for locally recurring or widely spread lesions, and adjuvant therapy (e.g. aseptic washes, bandages) is recommended at all stages [3]. Of the available treatment options, adalimumab is the only approved drug for HS in either the EU and the USA [31, 32]. With the exception of adalimumab, interventions used to treat HS generally lack high-quality evidence [i.e. randomized, multicentre clinical trials using validated outcome measures (e.g. HiSCR) and adequate sample sizes] [33, 34].

In phase III trials, adalimumab was effective in patients with moderate to severe HS, with a significant proportion of adalimumab recipients achieving a clinical response (Sect. 4.1). In addition, adalimumab showed the potential to reduce the high HR-QOL burden of HS and increase patient satisfaction compared with placebo. HiSCR rates were generally maintained in the longer term (Sect. 4.2), with sustained HiSCR rates with continuous treatment compared with temporary decreases in HiSCR rates with dosage reduction or treatment interruption strategies, and the safety profile of adalimumab in patients with moderate to severe HS was consistent with the known safety profile of the drug (Sect. 5). Reports based on clinical experience with adalimumab in patients with moderate to severe or severe HS support these findings [35–37].

In conclusion, subcutaneous adalimumab is an effective and generally well tolerated treatment for patients with

moderate to severe HS and is the first agent approved for this difficult to treat disease.

Data selection sources: Relevant medical literature (including published and unpublished data) on adalimumab was identified by searching databases including MEDLINE (from 1946), PubMed (from 1946) and EMBASE (from 1996) [searches last updated 22 August 2016], bibliographies from published literature, clinical trial registries/databases and websites. Additional information was also requested from the company developing the drug.
Search terms: Hidradenitis suppurativa, adalimumab, Humira.
Study selection: Studies in patients with hidradenitis suppurativa who received adalimumab. When available, large, well designed, comparative trials with appropriate statistical methodology were preferred. Relevant pharmacodynamic and pharmacokinetic data are also included.

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Compliance with Ethical Standards

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