Polish guidelines for the diagnosis and treatment of *hidradenitis suppurativa*

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ABSTRACT

Hidradenitis suppurativa is a chronic, recurrent, inflammatory skin disease that affects hair follicles, typically developing after puberty. It is characterized by painful, deep-seated inflammatory lesions that appear in anatomical regions where apocrine glands are located, mainly in the axillar, inguinal, and anogenital areas. The pathogenesis of hidradenitis suppurativa is multifactorial, with follicular occlusion representing the initial stage of the disease and subsequently leading to the formation of neutrophilic abscesses and infiltration by various inflammatory cells. The treatment of hidradenitis suppurativa requires a multidisciplinary approach, involving dermatologists and dermatologic surgeons, as well as physicians of other medical specialties. The primary pharmacological treatments for hidradenitis suppurativa involve antibiotics and biologic disease-modifying drugs, which can be used either in monotherapy or in combination with surgical interventions. The following guidelines provide up-to-date information on the management of patients with hidradenitis suppurativa.

Key words: hidradenitis suppurativa, guidelines, treatment, diagnostics.

DEFINITION

Hidradenitis suppurativa (HS) is a chronic, inflammatory, recurrent, debilitating skin condition that affects hair follicles. It typically manifests after puberty and is characterised by painful, deep-seated inflammatory lesions developing in anatomical regions rich in apocrine glands, usually in the axillary, inguinal, and anogenital areas [1–3].

EPIDEMIOLOGY

Hidradenitis suppurativa impacts around 0.4% of the global population and exhibits variability across geographic regions [4]. In the USA, the prevalence of HS is approximately 0.05% [5], while in Denmark it reaches 4.1% [6]. In Poland, the prevalence of HS has been estimated at 1.6% [7]. Differences in estimation results between Europe and the United States could

be attributed to methodological variations, but they might also reflect actual disparities in HS prevalence or discrepancies in diagnostic criteria.

Symptoms typically emerge between puberty and the age of 40, with the highest incidence observed during the second or third decade of life. Research conducted in North America and Europe indicates a higher predilection for HS among women compared to men [8–10]. In a French study involving 618 consecutive patients with HS, the female-to-male ratio was 3.6 : 1 [9]. As for the prevalence of HS among children and adolescents, there is limited epidemiological data available. A study of nearly 55 million patients in the United States revealed a prevalence of 0.028% among individuals under 18 years of age. Consistent with studies in the adult population, there was a female predominance, with a gender ratio of 3.8 : 1 [11].

Furthermore, population-based studies suggest an elevated prevalence of HS among individuals with lower socioeconomic status, who frequently face restricted availability of healthcare services, suffer from poorer health, and have an impaired quality of life [12, 13]. Furthermore, factors such as smoking, stress, and an inadequate diet (obesity) may increase the risk of developing HS [12].

PATHOGENESIS

Inflammatory process

Hidradenitis suppurativa is classified within the group of neutrophilic dermatoses and is characterised as an autoinflammatory disease [14, 15]. However, the precise pathogenesis of the condition is not entirely understood and seems to involve multiple factors [16]. The prevailing assumption is that the initial stage in the development of HS is hair follicle occlusion. The process results in the formation of a neutrophilic abscess and the influx of macrophages, monocytes, and dendritic cells [15]. In chronic disease, the infiltrate expands, and there is an increase in the number of B cells and plasma cells [17]. One of the characteristic immunological features found in HS-affected skin is a significant increase in the level of interleukin 1β (IL-1β) [18], which is primarily secreted by macrophages, the most abundant inflammatory cells in HS infiltrates [19]. Activation of IL-1β pathways leads to increased production of chemokines including CXCL1 and CXCL6, which contributes to the massive infiltration of immune cells, including neutrophils, thus causing the clinical symptoms of HS [18]. Furthermore, IL-1β promotes the secretion of matrix metalloproteinases, e.g. MMP3 and MMP10, which appear to have a destructive effect on tissues [18]. An increased expression of caspase-1, NLRP3, IL-6, IL-18 and IL-36 has also been observed [18], suggesting an involvement of autoinflammation in the pathophysiology of HS [14, 15].

Another distinctive feature observed in HS lesions is elevated expression of interleukin-17 (IL-17) and tumour necrosis factor α (TNF-α) [16, 18, 20]. The elevation in Th17 cell count and the disruption of the Th17:Treg ratio are probably attributable to the overproduction of IL-1β and IL-6 due to inflammasome activation [21, 22]. The process plays a pivotal role in the autoinflammatory immune response.

Histological picture

An early symptom of HS, which can be observed histologically, is follicular occlusion by keratin, either with or without inflammation [23]. However, early inflammation of the apocrine gland appears to be a rare primary event [24]. Other observed lesions include follicular cysts, reduced volume of sebaceous glands, neutrophilic abscesses, sinus tracts, and massive skin infiltration [24]. In the lesions, there is an increased presence of T cells, plasma cells, neutrophils, and macrophages, whereas the levels of B cells, monocytes, and mast cells are slightly lower but still very high. In long-standing severe cases, granuloma formation in 'pseudo' follicles, abscesses, and follicular openings can be seen. Granulomas are surrounded by a chronic inflammatory infiltrate containing histiocytes, multinucleated giant cells, and granulation tissue [25]. Extensive fibrosis is frequently seen in the late stages when inflammation resolved. However, it needs to be stressed that skin biopsy is not routinely performed for diagnostic purposes in HS [26].

Genetic factors

It has been estimated that 34.3% of first-degree relatives of HS patients also develop the disease, which suggests an inheritance pattern consistent with autosomal dominance [27]. In 2 more recent studies, the heritability of HS in the general population was found to be significantly higher, reaching 80% [28, 29]. Mutations in genes encoding γ-secretase components, including NCSTN, PSENEN, and PSEN1, are recognised as key aetiological factors of HS. Among other effects, these mutations disrupt the Notch signalling pathway, leading to abnormal follicular differentiation, keratinisation, follicular obstruction, and cyst formation [30, 31].

Bacterial factors

Skin areas rich in apocrine glands have a distinct composition of microbiota compared to other skin regions. This promotes the development of a specific cutaneous immune profile which is essential for maintaining healthy skin [32]. In patients with HS, there seems to be a disturbance in the homeostasis between the host and the microbiota. It is worth not-

ing that HS is not an infectious bacterial disease, and recent research findings indicate dysbiosis of the skin microbiota in patients with HS. This observation is attributed to an increased presence of opportunistic anaerobic bacteria belonging to the genera *Bacteroides*, *Corynebacterium*, *Porphyromonas*, *Petoniphilus*, and *Prevotella* on the skin of HS patients. At the same time, a reduced count of commensal bacteria of the genus *Cutibacterium* is observed [33–35].

The dysbiosis associated with HS is progressive in nature. In the initial stages of the disease, commensal coagulase-negative staphylococci and *Cutibacterium* bacteria predominate [35]. In advanced stages, *S. aureus* is additionally detected [36]. The occurrence of *S. aureus* on the skin of HS patients seems to be related to cigarette smoking. In 1 of the published studies [37], all patients tested positive for *S. aureus* were smokers. It has been claimed that the relationship between *S. aureus* and nicotine could influence the development of the disease, with nicotine potentially facilitating the proliferation of this pathogen. Other authors have hypothesised that *S. aureus* may only play a role in the initial stages of disease development, triggering anatomical changes in the hair follicle by inducing inflammation and necrosis [38, 39].

Other factors

Overweight and obesity are highly likely to play a role in the aetiology of HS. In their study, Revuz *et al*. [40] found that each one-point increase in BMI was associated with an elevated risk of HS (OR = 1.12; 95% CI: 1.08–1.15). In a multivariate analysis, overweight (OR = 2.08; 95% CI: 1.40–3.08) and obesity (OR = 4.42; 95% CI: 2.82–6.93) were found to be significant risk factors for HS [40]. The same study also demonstrated a significant association between smoking and HS (OR = 12.55; 95% CI: 8.58–18.38) [40]. Research has shown that nicotine, a constituent of tobacco smoke, contributes to acanthosis, keratosis pilaris, and follicular obstruction [41]. Mechanical stress is believed to serve as another potential trigger for the formation of HS lesions. Mechanical stress and friction induce the activation of metalloproteinases, promoting the release of pro-inflammatory cytokines responsible for the development of pathological lesions [42].

CLINICAL PICTURE AND DIAGNOSIS

Clinical picture and definition

Hidradenitis suppurativa is a chronic, inflammatory, recurrent, debilitating skin disease of the hair follicle that usually presents after puberty with painful, deep-seated, inflamed lesions in the apocrine gland-bearing areas of the body, most commonly the axillae, inguinal, and anogenital regions (Dessau definition, 1st International Conference on Hidradenitis suppurativa, March 30–April 1, 2006, Dessau, Germany).

Diagnostic criteria

The diagnosis of HS is established if the patient meets three primary criteria. The first criterion is the presence of HS-specific skin eruptions: nodules (inflamed or non-inflamed), sinus tracts (inflamed or non-inflamed), abscesses, scarring (atrophic, mesh-like, red, hypertrophic or linear). The second criterion is the presence of lesions in at least one area of predilection (the axilla, genitourinary region, perineum, gluteal region, and suprapubic area in women). The final criterion is recurrence, i.e. the presence of painful inflammatory/suppurating lesions characteristic of HS at least twice over a period of 6 months [26, 43].

Secondary diagnostic criteria include positive family history of HS, presence of skin lesions outside the areas of predilection, and a negative result of microbial swab obtained from pathologically affected areas or the presence of normal skin microbiota [26].

Differential diagnosis

- Bacterial infection presenting as folliculitis (diffuse pustular lesions in random locations)
- Skin abscesses/boils (usually isolated lesions)
- Cutaneous Crohn's disease
- Lymphogranuloma venereum
- Granuloma inguinale
- Actinomycosis
- Scrofuloderma type of cutaneous tuberculosis
- Neoplasms – primary or secondary (systemic and histological signs of tumour)

Comorbidities

HS may be associated with a variety of comorbidities. The most common diseases coexisting with HS include [44–49]:

- Axial spondyloarthritis,
- Inflammatory bowel diseases (IBD): Crohn's disease and ulcerative colitis,
- Pyoderma gangrenosum,
- Rheumatoid arthritis,
- Psoriasis and psoriatic arthritis,
- Skin neoplasms (Marjolin's ulcer),
- Cardiovascular diseases,
- Metabolic syndrome,
- Autoinflammatory syndromes:
  - PAPA (pyogenic sterile arthritis, pyoderma gangrenosum, acne vulgaris),
  - PAPASH (pyogenic sterile arthritis, pyoderma gangrenosum, acne vulgaris, hidradenitis suppurativa),
  - PASH (pyoderma gangrenosum, acne vulgaris, hidradenitis suppurativa),

– PsAPASH (psoriatic arthritis, pyoderma gangrenosum, acne vulgaris, hidradenitis suppurativa).

Classification and staging

Hurley staging

The most widely used grading system to characterise the extent of disease in patients with HS is the Hurley staging system [50] shown in table 1 (fig. 1).

IHS4

The IHS4 scale is a validated and user-friendly scoring tool for evaluating disease severity, suitable for use in clinical trials and integration into routine practice [51].

The IHS4 score is the sum of:

- the number of inflamed nodules (multiplied by 1),
- the number of abscesses (multiplied by 2),
- the number of draining tunnels (fistulae/sinuses) multiplied by 4.

A score of 3 or less signifies mild HS, a score of 4–10 signifies moderate HS, and a score of 11 or higher signifies severe HS [51].

To evaluate the effectiveness of HS treatment, IHS4-55 (an index based on the IHS4 scoring system) can be used. IHS4-55 assesses whether a patient has achieved a 55% reduction in their IHS4 score with therapy compared to the baseline score [52].

HS-IGA

The HS-IGA score is the latest instrument for evaluating both the severity of the disease and response to treatment. The HS-IGA score ranges from 0 to 5 based on the sum of the number of abscesses, fistulas (both draining and non-draining), and nodules (both inflamed and non-inflamed) in the upper or lower body region, depending on which part of the body is more affected at the time of assessment. The body area used for scoring may vary from one visit to the next. Response to treatment is defined as at least a 2-point reduction in HS-IGA score from baseline (table 2) [53–55].

HiSCR

HiSCR is defined as a reduction of at least 50% in the total count of abscesses and inflamed nodules when compared to baseline, with no increase in the number of abscesses or draining fistulae. HiSCR is the primary endpoint in many clinical trials, used to measure treatment outcomes. HiSCR modifications, including HiSCR75 and 90, refer to a reduction in the total number of abscesses and inflamed nodules by 75 and 90%, respectively.

Psychosocial effects

Because of pain, unpleasant odour, and pruritus, HS has a detrimental impact on patients' health-related quality of life. Patients with HS often experience depression, anxiety disorders, and a fear of stigmatisation [56–60]. Moreover, HS significantly influences the sexual lives of patients. Kurek *et al*. [61] found that the sexual health in patients with HS was significantly more impaired compared to controls. It is notable that sexual anxiety was more prevalent in women than in men [61].

Table 1. Hurley staging system for evaluating the severity of hidradenitis suppurativa

Stage I	Abscess formation, single or multiple, without sinus tracts and cicatrisation
Stage II	Recurrent abscesses with tract formation and cicatrisation, single or multiple, widely separated lesions
Stage III	Diffuse or near-diffuse involvement, or multiple interconnected tracts and abscesses across the entire area

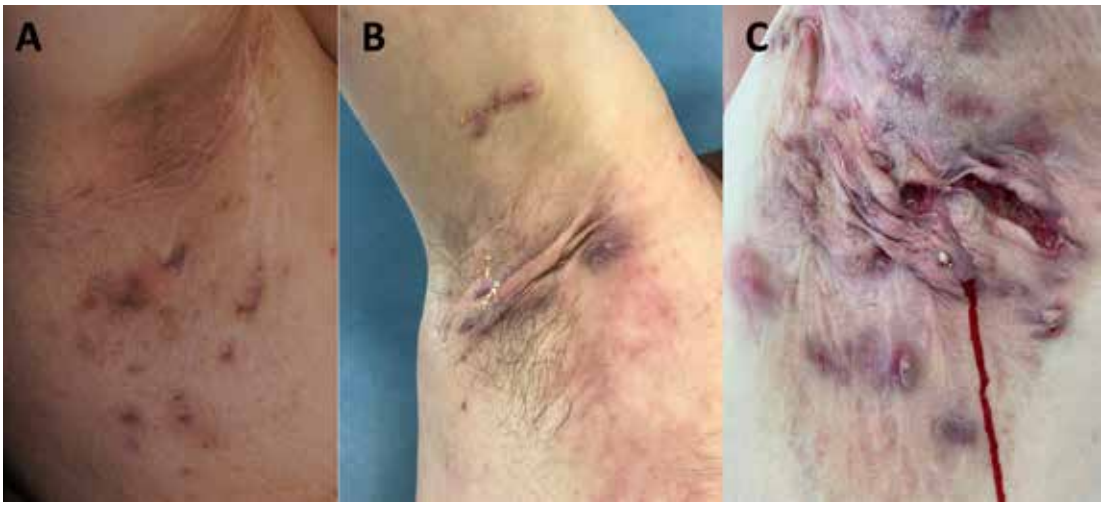


Figure 1. Severity of hidradenitis suppurativa in the Hurley staging system: **A** – stage I, **B** – stage II, **C** – stage III

Numerous tools have been developed for determining the effect of dermatological diseases on patients' quality of life. The most commonly used questionnaire is the Dermatology Life Quality Index (DLQI) [62]. Although it is a general scale used for evaluating the impact of dermatological diseases, its universality allows for easy comparison of HS to other dermatoses. Thorlacius *et al*. [63] proposed a new scale, Hidradenitis Suppurativa Quality of Life (HiSQOL), which is a disease-specific instrument used for the assessment of HS. The HiSQOL questionnaire is used to evaluate the impact of HS on 17 aspects of the patient's quality of life over the preceding 7 days (table 3) [63, 64].

Table 2. HS-IGA score for the assessment of hidradenitis suppurativa severity

HS-IGA score	Number of lesions
0	0–1
1	2–5
2	6–10
3	11–15
4	16–20
5	> 20

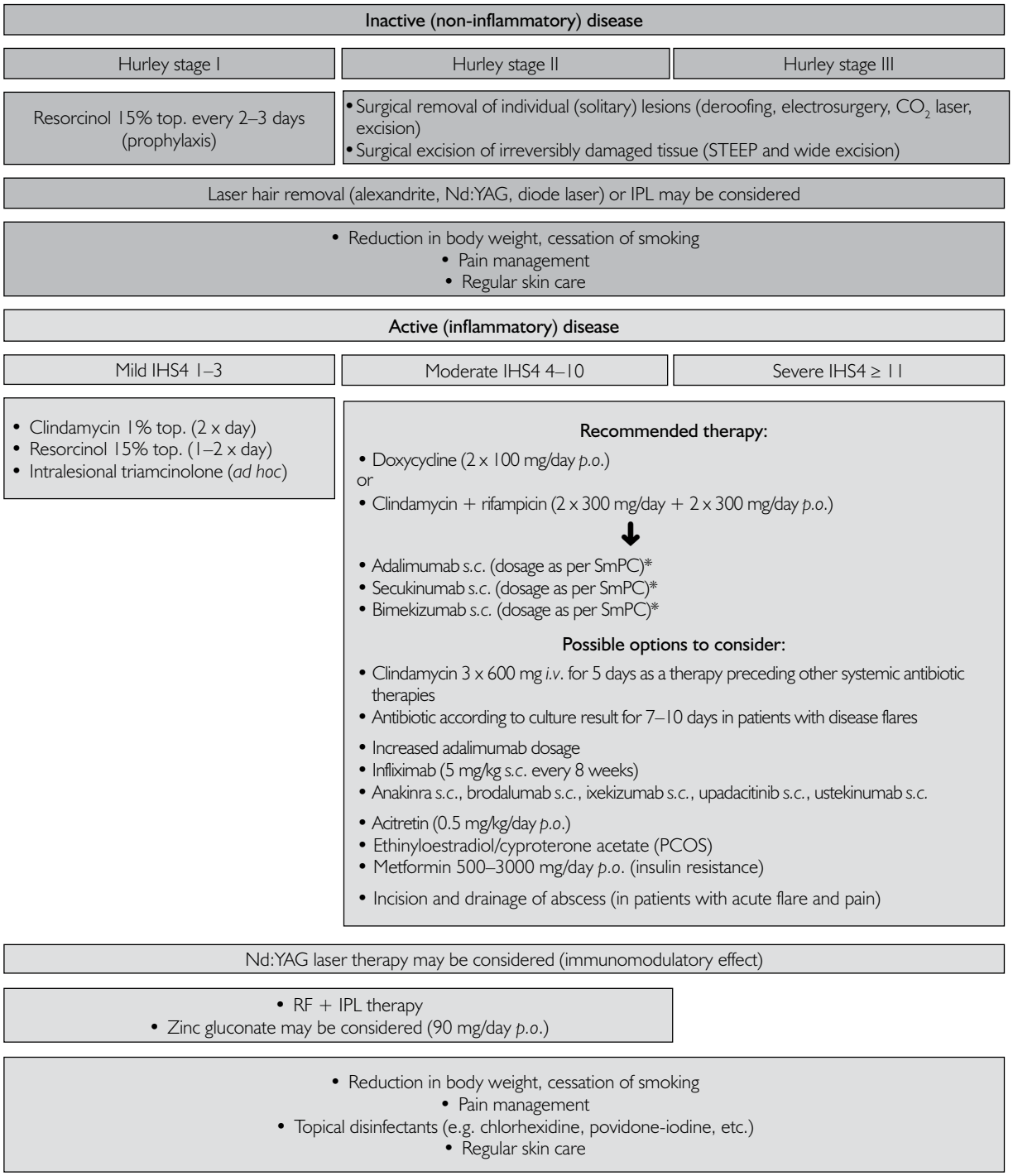
THERAPY

The choice of treatment modality for patients with HS is based on the disease activity and the severity of the manifestations (fig. 2).

With a growing number of reports highlighting the effectiveness of immunomodulatory therapies in treating HS, it is important to consider the concept of the "window of opportunity". The latest scientific evidence indicates that patients in whom biological therapy has been delayed or who have previously undergone several different therapies exhibit lower

Table 3. HiSQOL questionnaire for the assessment of quality of life in patients with hidradenitis suppurativa

Question		Possible answer
In the past 7 days, how much has your HS impacted:	Walking (not for exercise) Exercising (for example: swimming, jogging, biking, yoga, aerobics) Sleeping Washing yourself Getting dressed Concentrating	Unable to do due to my HS Extremely Very much Moderately Slightly Not at all
In the past 7 days, how has your HS influenced:	What you wear to avoid discomfort	Extremely Very much Moderately Slightly Not at all
In the past 7 days, due to HS, how impacted have you been by:	Pain Itch Drainage Odour	Extremely Very much Moderately Slightly Not at all
In the past 7 days, how much has HS caused you to feel:	Down or depressed Embarrassed Anxious or nervous	Extremely Very much Moderately Slightly Not at all
In the past 7 days, how much has HS:	Made sexual activities difficult Affected your desire for sexual activities	I am not sexually active Unable to do due to my HS Extremely Very much Moderately Slightly Not at all
In the past 7 days, how much has HS influenced:	Your ability to work or study	I do not work or study Unable to do due to my HS Extremely Very much Moderately Slightly Not at all



*In patients with inadequate response to treatment, an antibiotic may be added

Figure 2. Therapeutic options in HS

SmPC – Summary of Product Characteristics, IPL – intense pulsed light, top – topical use, PCOS – polycystic ovary syndrome, i.v. – intravenous administration, p.o. – oral administration, RF – radiofrequency, s.c. – subcutaneous administration, STEEP – Skin-Tissue-sparing Excision with Electrosurgical Peeling.

efficacy of secukinumab and adalimumab treatment [65, 66].

Topical non-antibiotic treatment

Resorcinol

Topical resorcinol is the only exfoliant used in the treatment of patients with HS. Resorcinol 15% exhibits keratolytic, antiseptic, and antipruritic effects. It is recommended for treating patients with mild to moderate HS. Resorcinol cream applied once a day has demonstrated positive effects on persistent painful HS skin lesions (inflamed nodules and abscesses). In patients with flares, the recommendation is to promptly initiate treatment with resorcinol cream twice daily. Subsequently, the frequency of application can be gradually decreased to once daily or every 2 days, depending on individual tolerance and observed effectiveness [26, 67].

Resorcinol can give rise to specific contact dermatitis and skin irritation, while its sensitising power seems to be only moderate [68, 69]. Systemic toxicity following topical use of resorcinol is extremely rare, but physicians need to be aware of the potential risk [26].

No studies or guidelines are available on the use of resorcinol in pregnancy [26].

Topical antibiotic treatment

Clindamycin

Clindamycin is the only antibiotic that has been studied as a topical agent. The efficacy of topical treatment with clindamycin was confirmed in a double-blinded randomised trial involving a total of 27 patients with stage I or mild stage II HS. The subjects were treated with topical clindamycin 0.1% or with placebo. Both the patients and physicians performed monthly evaluations of the overall therapeutic effect, and determined the abscess and nodule count. All patient assessments were in favour of clindamycin, with beneficial effects reported at 2 and 3 months of topical treatment, particularly with respect to superficial skin lesions i.e. folliculitis, papules and pustules. The effect on deep lesions, such as nodules or abscesses, was minimal [70].

Topical clindamycin is recommended for treating patients with mild to moderate HS. Skin irritation and selection of resistant microbes may occur with therapy. Clindamycin preparations should be applied twice daily for a duration of 3 months. Treatment may be prolonged, if clinically indicated [26].

Systemic antibiotic therapy

Tetracyclines

Systemic antibiotic therapy is recommended for severe or widely disseminated lesions associated with HS. Tetracyclines should be considered as first-line therapy in patients with moderate and severe Hurley stage I or mild stage II HS [26]. In a randomised trial, a total of 49 patients with HS were allocated to receive either modified-release doxycycline (40 mg once daily) or regular-release doxycycline (100 mg twice daily) for 12 weeks. Clinical response to therapy occurred in 64% of patients treated with modified-release doxycycline and 60% of patients treated with regular-release doxycycline [71].

Tetracyclines are not recommended in pregnant women due to their potential teratogenic effects, nor in children under 8 years of age due to the risk of tooth discolouration [72]. Patients should be informed that direct exposure to sunlight may lead to hypersensitivity reactions. Renal dysfunction can result in the accumulation of tetracyclines, potentially leading to liver toxicity. Major adverse effects associated with tetracycline treatment include the risk of microbial resistance and the need to use oral contraceptives during therapy because of potential teratogenic effects [26].

Clindamycin – rifampicin

Results from clinical trials indicate potential benefits of combination therapy with clindamycin and rifampicin in patients with HS. Gener *et al*. [73] evaluated the efficacy of a combination therapy with systemically administered clindamycin (300 mg twice daily) and rifampicin (600 mg daily) in treating patients with severe HS over a 10-week period. The combination demonstrated efficacy in reducing disease severity, as evaluated by the Sartorius score. The median was 14.5 points after 10 weeks of treatment with clindamycin/rifampicin compared to 29 points before therapy ($p < 0.001$). In the study by van der Zee *et al*. [74], at least partial remission was achieved by 28 of 34 patients (82%) treated with clindamycin/rifampicin, while complete remission of HS was observed in 16 (47%) patients. The maximum treatment effect was reached after 10 weeks. Van Straalen *et al*. conducted a prospective cohort study [75] evaluating the efficacy of oral tetracyclines (tetracycline 500 mg twice daily, doxycycline 100 mg once daily, or minocycline 100 mg once daily) and a combination of clindamycin (300 mg twice daily) with rifampicin (600 mg once daily) over a 12-week period. Patients in both groups exhibited a significant decrease in the severity of disease symptoms. Clinical response to treatment was noted in 40.1% and 48.2% of patients treated with tetracyclines and with clindamycin with rifampicin, respectively ($p > 0.05$) [75]. According to the guidelines, biological treatment is recommended to be initiated following failure of conventional therapy, often after attempting combination treatment with clindamycin and rifampicin [26]. However, the

results of the study by van Straalen *et al*. suggest that the effects of treatment with clindamycin and rifampicin are similar to those achieved with tetracyclines. Consequently, treatment failure with these drugs may constitute sufficient justification for implementing biological treatment [75].

It is important to consider that clindamycin therapy carries a risk of developing *Clostridioides difficile* pseudomembranous colitis.

Furthermore, rifampicin is a potent cytochrome P450 inducer, potentially influencing the metabolism and toxicity of other drugs metabolised through the same pathway, such as oral contraceptives [26].

Before starting combination therapy with clindamycin and rifampicin, it might be worth considering a five-day monotherapy course of intravenous clindamycin [76].

During disease flares, cultures can be obtained from the affected skin areas, and antibiotic therapy can be initiated based on test results, typically for 7 to 10 days. However, the procedure is not considered standard practice and might not be universally recognised by experts.

Anti-inflammatory treatment

Intralesional corticosteroids

Intralesional injections of triamcinolone acetonide at doses of 10–40 mg/ml are recommended for the rapid reduction in inflammation associated with acute flares and for the management of recalcitrant nodules and sinus tracts [77]. Triamcinolone acetonide can be used alone or in combination with systemic therapy. Clinical response to treatment is achieved in 44–70% of cases [77], a decrease in pain severity is often seen as early as the first day of treatment, while a reduction in the severity of skin lesions is observed within 7 days [78]. Local complications may include atrophy, pigmentary changes, and telangiectasias [26].

Retinoids

Isotretinoin

Isotretinoin achieves its efficacy by influencing cell cycle progression, cell differentiation, cell survival, and apoptosis [79]. In addition, isotretinoin has been shown to have anti-inflammatory properties. It might act directly by modifying monocyte chemotaxis and exert a secondary effect through its antikeratinising properties and protection against hair follicle rupture [79].

In 7 published studies, comprising a total of 174 patients, the range of daily dosages was 0.5 to 1.2 mg/kg, with treatment lasting 4–12 months. However, based on the available data, the therapeutic effect of isotretinoin is questionable, with 64.4% (112/174) of patients classified as non-responders [80–86].

While isotretinoin therapy for HS is typically not advised, when it is prescribed, lipid levels and liver enzyme activity should be evaluated before initiating treatment. Moreover, pregnancy testing should be performed directly before the start of isotretinoin therapy, and an effective method of contraception must be recommended to patients.

Acitretin/etretinate

The therapeutic efficacy of acitretin stems primarily from its impact on the growth cycle of skin cells. Acitretin helps to normalise cell differentiation and thin the epidermal layer by directly reducing the rate of keratinocyte proliferation. At the same time, acitretin reduces inflammation in the dermis and epidermis by inhibiting neutrophil chemotaxis [26, 87].

Acitretin is primarily recommended in the treatment of follicular HS and in the early HS stages (Hurley I and mild Hurley II). However, it may also be considered in the chronic stages of HS characterised by recurrent abscesses, sinus tracts, and/or scarring [88, 89]. A total of 7 studies on acitretin/etretinate therapy, comprising 32 patients, have been reported to date. Patients treated with acitretin received daily doses of 0.25–0.88 mg/kg, while the doses for etretinate ranged from 0.35 to 1.1 mg/kg. These retinoids were administered for a period of 3 to 12 months (mean: 9.3 ±3.3 months). The response rate was high, with 21 of 32 patients (65.6%) achieving a significant improvement and 8 patients (25%) achieving a moderate improvement. Only 3 patients (9.4%) were non-responders [88–94].

Before initiating treatment with acitretin, it is recommended to measure liver enzyme activity and lipid levels. Given the potential teratogenic risk associated with acitretin, physicians should conscientiously inform patients about the need to use contraception. It should be initiated 4 weeks before the commencement of treatment, maintained throughout the therapy duration, and continued for an additional 3 years following the conclusion of treatment. Additionally, the physician should obtain written consent from the patient before initiating acitretin therapy [26].

Hormonal therapy

For women experiencing menstrual disorders and symptoms of hyperandrogenism or polycystic ovary syndrome, hormone therapy may be a viable option. Antiandrogenic treatment with cyproterone acetate and ethinyl oestradiol may alleviate the progression of HS. Before starting hormone therapy, it is necessary to confirm that the patient is not pregnant, assess cardiovascular risk, and evaluate liver and kidney function [26, 95, 96].

Zinc gluconate

Zinc gluconate may be used for maintenance treatment in patients with Hurley stage I and II HS. Treatment usually begins with high doses, i.e. 90 mg/day, and dosage adjustments may be made depending on treatment response and potential occurrence of gastrointestinal adverse effects. Treatment should be conducted on a long-term basis [26, 97].

Immunomodulatory therapy

Adalimumab

Adalimumab is a fully human monoclonal antibody that was the first to be approved for the treatment of HS in 2015. It corresponds to the human immunoglobulin IgG1 and has heavy and light chain variable regions exhibiting specificity for human TNF-α. Adalimumab binds with high affinity and specificity to soluble and membrane-bound TNF-α. Thus, it prevents the binding of TNF-α to its receptors (p55 and p75) and suppresses the biological effects of TNF-α [26].

Before initiating treatment with adalimumab, it is necessary to rule out acute infection, tuberculosis, HIV infection, or viral hepatitis. Women of childbearing potential should confirm the absence of pregnancy and use effective contraception while taking the medication. However, the drug has been classified in pregnancy category B, which indicates that it is likely safe for pregnant women. Patients should be advised that the course of infection during treatment with adalimumab may be more severe or atypical, and they should promptly consult a physician if they have any concerns [26].

According to the summary of product characteristics, dosing in adults typically begins with 160 mg on day zero, followed by 80 mg on day 15. In the subsequent stage, adalimumab may be administered at a dose of 40 mg every week or 80 mg every 2 weeks [98]. However, there have been reports suggesting that the 40 mg dose may not be adequate for obese patients. Williams *et al*. [99] found that escalating the dose of adalimumab to 80 mg per week was linked to improved treatment outcomes in overweight and obese patients diagnosed with moderate or severe HS. In their study, Zouboulis *et al*. [100] reported a benefit from treatment with an increased dose of adalimumab (80 mg weekly) in patients who failed to respond to the standard-dose regimen. The clinical efficacy of adalimumab was confirmed in the PIONEER I and II trials, i.e. similarly designed multicentre, double-blind, placebo-controlled studies enrolling 307 and 326 HS patients, respectively. In the PIONEER II study, participants could use antibiotics in addition to the study treatment. The clinical response rates at week 12 after starting treatment were significantly higher in the adalimumab (40 mg weekly) groups compared to the placebo groups: 41.8% vs. 26.0% in the PIONEER I trial ($p = 0.003$) and 58.9% vs. 27.6% in the PIONEER II trial ($p < 0.001$) [101].

Secukinumab

Secukinumab is a monoclonal antibody that targets IL-17A. It works by binding to IL-17A and blocks the interaction of the cytokine with IL-17 receptors, thereby inhibiting inflammatory responses [102, 103]. The drug was approved for the treatment of HS in 2023.

The clinical efficacy of secukinumab was confirmed in the recently published results of the SUNSHINE and SUNRISE trials [103]. Both studies were designed similarly as multicentre, double-blind, placebo-controlled trials, involving 541 and 543 patients with moderate and severe HS, respectively. Results obtained in the trials showed that after 16 weeks of therapy patients treated with secukinumab at a dose of 300 mg every 2 weeks were more likely to achieve a positive clinical response (at least a 50% reduction in the number of inflamed nodules and abscesses) compared to those who received placebo, with the rates of 45.0% vs. 33.7% ($p = 0.007$) (SUNSHINE) and 42.3% vs. 31.2% ($p = 0.0149$) (SUNRISE) [103].

As per the summary of product characteristics, the recommended dose of secukinumab administered via subcutaneous injection is 300 mg at weeks 0, 1, 2, 3, and 4. In the subsequent stage, the drug is given at a maintenance dose of 300 mg every 4 weeks or, if there is an inadequate response to treatment, every 2 weeks. Each 300 mg dose can be administered as a single 300 mg injection or as two separate 150 mg injections [104].

Bimekizumab

Bimekizumab is a monoclonal antibody that targets IL-17A and IL-17F. The drug was approved by the European Commission for the treatment of HS in April 2024. The clinical efficacy of bimekizumab was confirmed in two double-blind, placebo-controlled studies, BE HEARD I and BE HEARD II [105] which enrolled a total of 505 and 509 HS patients, respectively. The studies evaluated the therapeutic efficacy of 16 weeks of active treatment and 32 weeks of maintenance treatment with bimekizumab at two different dosage regimens: 320 mg every 2 weeks and 320 mg every 4 weeks. In both the BE HEARD I and BE HEARD II trials, after 16 weeks of therapy, a significantly greater proportion of patients receiving bimekizumab every 2 weeks experienced a reduction in the total number of abscesses and inflamed nodules by at least 50% compared to those in the placebo group. The proportions were 47.8% versus 28.7%

(p = 0.006) and 52.0% versus 32.2% (p = 0.003) in the BE HEARD I and BE HEARD II trials, respectively. Similar results were achieved in patients receiving bimekizumab every 4 weeks, but statistical significance was confirmed only in the BE HEARD II trial [105]. Based on the findings from these two phase III studies and in accordance with the summary of product characteristics, the recommended dosage for adult patients with HS is 320 mg every 2 weeks up to week 16, followed by every 4 weeks thereafter [106].

Infliximab

Infliximab is a monoclonal antibody that targets TNF-α. Before initiating infliximab treatment, the patient should undergo assessment, similar to the protocol used in adalimumab treatment [26].

The clinical efficacy of infliximab was evaluated in a double-blind, placebo-controlled study in a group of 38 patients with HS. The subjects received infliximab (5 mg/kg) or placebo at the start of the study, then again at weeks 2 and 6, followed by every 8 weeks thereafter. With respect to infliximab, a significantly higher proportion of patients achieved an improvement in the HSSI (HS Severity Index) score within the range of 25–50% (60% compared to 5.6% in the placebo group; $p < 0.001$) [107]. Clinical observations show that more frequent dosing, such as 5 mg/kg at weeks 0, 2, and 6, followed by every 4 weeks thereafter, may offer greater benefits for patients with HS [108]. Some experts recommend a dosing regimen of 10 mg/kg of infliximab every 4 to 8 weeks [109].

Other immunomodulatory therapies

Literature reports suggest that brodalumab, a monoclonal antibody targeting IL-17R, exhibits therapeutic efficacy in the treatment of HS. The drug was administered subcutaneously every 2 weeks at a dose of 210 mg [110, 111].

Based on the analysis of 5 cases, Esme *et al*. described the effectiveness of ixekizumab, a monoclonal antibody against IL-17A, in the treatment of severe HS. Out of the 5 patients, four achieved HiSCR after 12 weeks of therapy [112].

Anakinra is a recombinant interleukin-1 receptor antagonist. Clinical trial results demonstrated that 78% of patients receiving anakinra achieved HiSCR after 12 weeks, compared to 30% in the placebo group. Furthermore, reduced production of interferon-γ by peripheral blood monocytes was observed in patients receiving treatment with anakinra [113].

There have also been reported cases of favourable therapeutic outcomes after ustekinumab treatment (anti-IL-12/23 antibody) in patients presenting with moderate to severe HS [114, 115].

In a randomised phase II clinical trial, encouraging results were obtained in the treatment of HS with povorcitinib, a selective Janus kinase-1 inhibitor. The rate of HiSCR achievement after 16 weeks of treatment ranged from 44.2% to 48.1% [116]. Additional phase III clinical trials are currently under way to further assess the efficacy of povorcitinib. In the study conducted by Kozera *et al*., patients with moderate and severe HS were treated with upadacitinib, another JAK-1 inhibitor. The study outcomes were promising. A total of 15 patients (75%) achieved HiSCR at week 4, with the proportion increasing to 100% by week 12, and the therapeutic effects were sustained until week 24 [117]. A phase III study of upadacitinib is currently in progress.

Ongoing clinical trials are also investigating the potential application of deucravacitinib (TYK-2 inhibitor), spesolimab (anti-IL-36R antibody), and nanoparticles of izokibep (anti-IL-17A antibody) and sonelokimab (anti-IL-17A/IL-17F antibody) in managing HS [118, 119].

Surgical treatment

Since non-surgical therapies often fail to provide satisfactory therapeutic outcomes, surgery emerges as a widely accepted option. Several surgical methods are available for HS treatment [120–128]:

A. Surgical methods for removal of HS lesions

- Incision and curettage;
- Surgical removal of individual lesions (deroofing, electrosurgery, CO_2 laser, excision) – "laying open" techniques;
- Skin-Tissue-sparing Excision with Electrosurgical Peeling (STEEP);
- Wide excision:
  - excision of the skin area affected by HS lesions,
  - excision of the entire affected skin region (for example, the entire axilla) where HS lesions occur.

B. Methods of defect reconstruction

- Simple:
  - Primary intention healing,
  - Secondary intention healing,
  - Reconstruction with immediate or delayed skin grafting,
  - Reconstruction with flap-plasty;
- Complex (combinations of any of the above).

Incision and drainage is a procedure employed in the acute phase of the disease, primarily to alleviate symptoms and prevent the potential spread of bacterial superinfection. Following the administration of local anaesthesia, an incision is performed to drain the abscess cavity. Although the method proves to be extremely helpful for the immediate relief of pain and discomfort, incision and drainage in HS is associated with a very high recurrence rate, up to even 100% [129–131].

For patients with Hurley stage II and III HS, most surgeons advise complete excision of the apocrine gland–bearing skin area in the affected location. The goal of surgical treatment is extensive excision of pathological skin and underlying tissue. The recurrence rates following radical surgery depend on the method used for wound reconstruction. For primary intention healing, the recurrence rate is 34% [132], for delayed primary intention healing – 39% [133], for secondary intention healing – 12 to 19% [134], and for skin grafting – 21 to 33% [134, 135]. In this context, the findings of a meta-analysis by Riddle *et al*. are particularly noteworthy, indicating a 0% recurrence rate after flap reconstruction [134].

The deroofing technique is an effective and quick surgical method recommended primarily for patients with Hurley II stage HS. This minimally invasive procedure can be conducted outside of the operating theatre (in a treatment room) for the removal of HS lesions while ensuring cosmetically acceptable scars with minimal disturbance to the surrounding healthy tissue [121]. Across 3 prospective studies comprising a total of 183 lesions in 104 patients, the overall recurrence rate was 14.7% [136–138]. In a retrospective study by Blok *et al*. [139], including a total of 363 procedures, Skin-Tissue-sparing Excision with Electrosurgical Peeling (STEEP) was associated with a 29% recurrence rate [139].

Scanner-assisted CO_2 laser treatment aims at focal radical vaporisation of all nodules, abscesses and fistulas, leaving healthy tissues between the pathological lesions. The lesions are vaporised from 'inside and out' until surrounding healthy tissue is reached, both superficially and deep. In this way, the technique can be tissue-sparing while still being radical [26, 140, 141]. The recurrence rate associated with CO_2 laser treatment is estimated to range from 1.1% to 11.8% [141–143].

Combination therapies

The effectiveness and safety of combining surgical treatment with adalimumab administered at a weekly dose of 40 mg were evaluated in the multicentre, randomised, controlled SHARPS trial [144]. Adalimumab subcutaneous injections were administered for a total of 12 weeks preoperatively and for 2 weeks perioperatively, and continued for 10 weeks postoperatively. After 12 weeks, a significantly higher proportion of patients receiving adalimumab (49 out of 103, 48%) achieved a clinical response in all body areas compared to the placebo group (35 out of 103, 34%; p = 0.049). Treatment-related adverse events were reported in 72% and 67% of patients receiving adalimumab and placebo, respectively. There was no observed increased risk of surgical wound infection, complications, or haemorrhage with concomitant adalimumab compared to the placebo group [144]. The above study was the first to demonstrate the feasibility and safety of concurrent biological and surgical treatments without the need to discontinue the former due to concerns about potential complications.

Other therapies

Nd:YAG laser therapy

Based on the assumption that HS starts in the hair follicle, treatment with Nd:YAG laser, designed for hair removal, was attempted [26]. In a prospective randomised controlled trial [145], a series of 3 monthly laser sessions were performed in 22 patients with stage II to III HS. Response to treatment was evaluated before each laser session and again 1 month after the completion of therapy. At 3 months of treatment, the percentage change in HS severity measured on the HS-LASI scale was as follows: –65.3% across all anatomical sites, –73.4% in the inguinal area, –62.0% in the axillary area, and –53.1% in the axillary-thoracic region. The results were statistically significant [145].

Intense pulsed light (IPL)

It is claimed that reducing the number of hairs in anatomical regions prone to HS may decrease the rate of HS recurrence. Intense pulsed light is one of the methods used for hair removal [26, 146]. Significant improvement was observed after IPL treatment in a prospective study involving 18 patients with HS [147]. However, further research is needed to precisely determine the role of IPL therapy in the management of HS.

LAight® therapy

LAight® therapy uses a combination of radiofrequency and IPL. The findings from the RELIEVE study revealed that combination therapy with LAight® and 1% topical clindamycin led to a significant decrease in disease severity, with a reduction in the IHS4 score of 7.2 points after 16 weeks of treatment, in contrast to clindamycin alone, which showed a decrease in IHS4 of only 1.8 points [148]. LAight® therapy is indicated for patients with Hurley stage I and II HS.

Metformin

Research findings point to the efficacy of metformin in treating HS [149, 150]. Jennings *et al*. evaluated the therapeutic effectiveness of metformin in 53 patients with HS. Subjective clinical improvement was noted in 68% of study subjects, with 19% experiencing symptom resolution with metformin monotherapy. The mean duration of metformin treatment was 11.3 months, and the mean dose was 1.5 g/day

[149]. The therapy is worth considering for patients with concomitant insulin resistance.

Botulinum toxin

The potential therapeutic mechanism of botulinum toxin in the treatment of HS involves a reduction in hyperhidrosis, a factor contributing to the development of skin lesions associated with HS. A decrease in hyperhidrosis involves a reduction in the number of microbiota colonies and changes in their composition, which indirectly implies a decrease in their pro-inflammatory effects. Nonetheless, the precise mechanism of action of botulinum toxin in HS still remains uncertain [151]. Ravi and Trinidad [152] conducted a systematic review which included a total of 7 studies. Clinical improvement or an improved quality of life was observed in 96.8% of patients (30/31) treated with botulinum toxin. The level of evidence in the study was rated as moderate.

Adjuvant therapy

Non-steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory drugs (NSAIDs) encompass a group of medications with analgesic and antipyretic properties. At higher doses, they also exhibit anti-inflammatory effects. NSAIDs act by blocking cycloxygenase enzymes, which leads to a reduction in prostaglandin levels and thus relieves pain and inflammation [26].

Pretreatment assessment should include an evaluation of the drugs the patient is currently taking. Special attention should be given to antidepressants, warfarin and antihypertensives, as there are well-documented interactions between NSAIDs and drugs of these classes which can potentially lead to serious adverse effects [26]. Contraindications to NSAID treatment include liver and renal impairment, severe heart failure, recent or active gastrointestinal bleeding, symptomatic peptic ulcer, and inflammatory bowel disease [26].

For the relief of acute pain associated with HS, NSAIDs are recommended in standard dosage regimens. It was also suggested that topical preparations of ketoprofen, particularly patches, could be beneficial for treating inflammatory pain because of their anti-inflammatory and analgesic properties [26, 153].

Opioids

Opioids exert their effects by binding to opioid receptors located in both the central and peripheral nervous systems. Through this mechanism, they reduce the intensity of pain signals transmitted to the brain. Their action leads to decreased perception of pain, increased pain tolerance, and reduced reaction to pain.

As part of pretreatment assessment, it needs to be determined what other medications the patient is taking, with a special focus on medications that suppress the central nervous system, such as antihistamines, barbiturates, and benzodiazepines. These interactions can lead to life-threatening respiratory depression. In addition, it is essential to assess haematological parameters, and kidney and liver function in patients. Special attention must be given to the respiratory capability. Contraindications to opioid therapy include liver and kidney impairment as well as severe pulmonary and respiratory failure.

For the treatment of acute pain in HS, codeine and hydrocodone should be used in their standard dosage regimens. Opioid treatment should be reserved exclusively for cases with the highest resistance to other therapeutic modalities, and the duration of therapy should be closely monitored.

Furthermore, it is important to consider the risk of opioid dependence with prolonged use. Furthermore, a 2022 study revealed that patients with HS who were prescribed opioids faced a 48% higher risk of readmission to the emergency department due to the recurrence of symptoms [154].

Maintenance therapy

In dermatology, maintenance therapy refers to the period after the active phase of treatment, once satisfactory clinical outcomes have been achieved. The primary objective of maintenance therapy is to sustain the benefits obtained from treatment and to prevent the recurrence of the disease. Jemec *et al*. [155], based on the results of the PIONEER trial, established that if patients achieved HS remission after treatment with adalimumab, maintenance therapy with the drug should be continued at a dose of 40 mg every week for another 36 weeks [155].

SPECIAL PATIENT GROUPS

Special groups of patients with HS include pregnant women and individuals under 18 years of age.

HS in pregnant and breastfeeding women

Data on the effects of HS on pregnancy and childbirth are limited [156]. Fitzpatrick *et al*. [157] reported the findings of a study showing that pregnant women with HS had an elevated risk of spontaneous miscarriage (by 37%), premature birth (by 25%), gestational diabetes (by 59%), gestational hypertension (by 38%), preeclampsia (by 57%), and caesarean section (by 19%), compared to pregnant women without HS. HS comorbidities are also associated with an unfavourable course of pregnancy. Research data show that while prevention and treatment of typical HS comorbidities

may have a positive impact on the progression of pregnancy and childbirth, they do not entirely eliminate the elevated risk of spontaneous miscarriage, gestational diabetes, and caesarean section [158, 159].

Pharmacotherapy

Active HS lesions can be treated with topical antibiotics such as clindamycin 1%, metronidazole 0.75%, and erythromycin 2%, applied twice daily until resolution [70, 160].

Combination oral therapy with clindamycin and rifampicin is considered first-line treatment for moderate to severe HS [70, 160, 161].

Adalimumab and infliximab are considered potentially safe in pregnancy and are used in first- and second-line therapies, respectively, in patients with moderate to severe HS not responding to antibiotics. Despite a growing body of scientific data [107, 160, 162], employing these therapies in pregnant women is a somewhat contentious issue. Data from populations with rheumatologic diseases indicate that exposure to TNF-α antagonist drugs does not significantly elevate the risk of pregnancy-related complications or foetal malformations. However, IgG class antibodies may cross the placenta during pregnancy, particularly in the last trimester; hence it is advisable to consider discontinuing monoclonal antibody therapy during this period [163–165]. Adalimumab passes into breast milk in very low concentrations; thus, it can be used by breastfeeding women [166, 167].

Surgical procedures

During pregnancy, it is advisable to avoid surgery whenever possible, particularly during the first trimester [160, 168]. Past the first trimester, limited surgical excision under local anaesthesia may be considered; however, the interventions should not impede the ability to breastfeed [160, 169]. Intralesional injections of triamcinolone acetonide are acceptable to quickly reduce inflammation of active nodules/abscesses and sinus tracts [160]. CO_2 and Nd:YAG laser therapy can provide an alternative to surgery [160].

Analgesic treatment

Acetaminophen (paracetamol) is the preferred analgesic agent during pregnancy, while ibuprofen is considered safe for use during breastfeeding [170, 171].

HS in the paediatric population

The management of HS in paediatric patients poses a challenge due to the limited data available on the efficacy and safety of different therapeutic modalities in this age group [172].

Topical preparations containing clindamycin 1%, resorcinol 15%, and antiseptics are used in treating mild forms of HS; however, they frequently prove ineffective in moderate to severe HS [173, 174].

Systemic antibiotics are recommended for the treatment of moderate and severe cases of HS. The combination of clindamycin and rifampicin is a safe therapeutic option for children [172, 175]. Antibiotics belonging to the tetracycline group, including tetracycline and doxycycline, are also effective in HS therapy. However, this class of drugs is not recommended for treating HS in children under 8 years of age due to the risk of discolouration of permanent teeth and dental enamel hypoplasia [176, 177].

The efficacy of systemic retinoids is attributed to their anti-inflammatory properties and their impact on reducing follicular hyperkeratinisation [178]. It is advisable to avoid acitretin in patients who are nearing reproductive age because of its long-term teratogenic effects, which can persist for up to 3 years after drug discontinuation. There are scarce reports showing that children may experience bone changes, such as premature epiphyseal closure, hyperostosis, and extraosseous calcifications, following prolonged treatment with acitretin. Hence, it is essential to closely monitor the parameters of growth and bone development in paediatric patients [179].

As mentioned above, adalimumab is the first biologic drug approved by the FDA for the treatment of HS. In 2018, the approved drug indications were expanded to include paediatric patients over 12 years old, with a body weight of at least 30 kg, diagnosed with moderate to severe HS, who fail to respond adequately to conventional systemic therapy [167]. The recommended dose of adalimumab in this patient group is 80 mg on day zero, followed by 40 mg every other week starting from week 1, administered via subcutaneous injection. For adolescents who fail to respond adequately to the 40 mg dose every other week, increasing the dosage to 40 mg once weekly or 80 mg every other week may be considered. If needed, antibiotics may be continued during treatment with adalimumab, similarly to the approach used in the adult population.

The principles governing the use of surgical treatment in the paediatric population are essentially the same as those applied in adults [180].

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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