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SYSTEMATIC REVIEW OF PHARMACOTHERAPY STRATEGIES IN THE MANAGEMENT OF HIDRADENITIS SUPPURATIVA

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ABSTRACT

Introduction: Hidradenitis suppurativa (HS, acne inversa) is a chronic, recurrent inflammatory dermatosis with an etiopathogenesis that remains not fully understood. Characteristic skin lesions—nodules, abscesses, sinus tracts, and scars—are most commonly located in skin fold areas, leading to a significant deterioration in patients' quality of life, both physically and psychosocially. Despite advances in medical knowledge, the diagnosis of HS is often delayed, and treatment represents a major clinical challenge requiring individualized therapeutic approaches. This article provides a review of current literature on pharmacological treatment strategies for HS, including both topical and systemic therapies. Particular emphasis is placed on antibiotic therapy (e.g., tetracyclines, combination therapy with clindamycin and rifampicin, triple-drug regimens, ertapenem), as well as hormonal and immunomodulatory treatments. Furthermore, the growing role of biologic therapies, including TNF-α and interleukin inhibitors, and the use of emerging targeted agents under investigation are discussed. Attention is also drawn to the importance of androgen receptors and their potential role in the pathogenesis of HS, as reflected in the effectiveness of antiandrogen therapies (e.g., spironolactone or oral contraceptives containing a progestogenic component). The review includes data on the efficacy, safety, and limitations of various therapeutic methods based on clinical trials and systematic reviews. The need for further research on the skin microbiome and immune response mechanisms is highlighted, as it may serve as a basis for the development of new, more targeted therapeutic interventions. It is emphasized that HS treatment should be multidimensional and tailored to disease severity as well as coexisting metabolic and endocrine disorders.
Materials and Methods: The article was written based on scientific papers available on PubMed and Google Scholar
Key findings: Analysis of current evidence indicates that pharmacotherapy constitutes a fundamental component in the management of hidradenitis suppurativa (HS), with treatment outcomes strongly dependent on disease severity. Biological therapies, including adalimumab, secukinumab, and belimumab, have demonstrated significant clinical efficacy in moderate to severe HS, particularly in individuals unresponsive to conventional therapies, and represent a major advancement in disease management. Antibiotics remain widely used, providing symptomatic relief despite HS being a chronic inflammatory rather than an infectious condition. Topical clindamycin (1%) is effective in mild cases with superficial inflammatory lesions but shows limited efficacy in deep nodules and carries a risk of microbial resistance. Systemic antibiotic therapy, especially clindamycin combined with rifampicin, has achieved clinical remission in a substantial proportion of moderate HS cases, whereas severe disease may require intensified regimens, including metronidazole, rifampicin, moxifloxacin, or intravenous ertapenem; however, relapse rates following treatment discontinuation remain high. Anti-androgen therapies, such as spironolactone, finasteride, cyproterone acetate (CPA), and metformin, have demonstrated beneficial effects in women with hormonally driven flares or hyperandrogenic comorbidities. Novel topical and systemic anti-androgen agents (finasteride, flutamide, clascoterone, leuprolide) are currently under investigation, but high-quality randomized controlled trials are
Conclusions: Hidradenitis suppurativa remains a significant therapeutic challenge, with current pharmacological strategies providing only partial and often temporary disease control. Biologic agents offer substantial clinical improvement in refractory moderate to severe HS, whereas antibiotics and anti-androgen therapies remain valuable options in mild to moderate disease, albeit with limitations such as high relapse rates and potential adverse effects, including antimicrobial resistance. The complex and incompletely understood pathophysiology of HS highlights the urgent need for further research into immunologic, microbial, and hormonal pathways to facilitate the development of targeted and personalized treatment approaches.

KEYWORDS

Hidradenitis Suppurativa, Acne Inversa, Biological Therapy, Antibiotics, Multiple Axillary Abscesses, Androgen Receptors, Hormonal Therapy, Chronic Inflammatory Skin Diseases

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Introduction

Hidradenitis suppurativa (HS), also known as acne inversa, is a chronic inflammatory skin disease characterized by the formation of painful lesions—most commonly nodules—in areas subjected to friction, such as the axillae and groin. These lesions may cause significant discomfort, often rupture with the release of purulent or bloody discharge, and subsequently heal with scarring [1].

The diagnosis of HS is often delayed—by an average of approximately seven years—due to the similarity of its symptoms to those of other dermatological conditions. Diagnosis is based on the identification of characteristic clinical features such as deep nodules, sinus tracts, and scarring, as well as the assessment of typical lesion localization in intertriginous areas (e.g., axillary, inguinal) and the chronic, recurrent nature of the disease [2]. In approximately half of the patients, prodromal symptoms such as burning, stinging, pain, itching, or a sensation of heat may occur 12–48 hours before the appearance of skin lesions [3]. Known triggers of HS flare-ups include menstruation, weight gain, stress, hormonal changes, increased heat, and perspiration [4].

Patients with HS typically do not present with systemic symptoms and remain afebrile, unless a secondary infection occurs or the disease reaches an advanced stage. The primary lesions in HS are usually deeply located nodules measuring approximately 0.5 to 2 cm in diameter, which may persist for several days to months. Initially, these nodules exude a bloody-serous fluid that can evolve into a thick, purulent discharge with an unpleasant odor. Due to their deep-seated nature and recurrent course, these lesions are often mistakenly identified as furuncles. Unlike isolated furuncles, HS nodules tend to rupture and may coalesce through interconnected fistulas and sinus tracts, which are susceptible to ulceration or spontaneous drainage. Visualization of deep-seated lesions can be aided by lidocaine injection or ultrasonographic examination [5]. In advanced stages of HS, thick fibrotic scarring and distortion of skin architecture occur. A characteristic finding is the presence of open comedones referred to as “tombstone comedones” [6].

Lesions in HS most commonly localize in the axillary regions; however, they frequently involve the groin, medial thighs, perianal, perineal, inframammary, gluteal, pubic areas (including the scrotum and vulvar region), as well as the trunk. Less commonly, they may be observed on the scalp or in the retroauricular region [7]. It is important to consider the association between HS and comorbid conditions such as metabolic syndrome, dyslipidemia, arterial hypertension, type 2 diabetes mellitus, inflammatory bowel diseases (particularly Crohn’s disease), ankylosing spondylitis, and other spondyloarthropathies [8].

The estimated prevalence of HS in the general population ranges from less than 1% to 4% [9]. These figures are likely underestimated due to underreporting and frequent diagnostic errors. The disease typically begins between puberty and the age of 40, with the highest incidence observed between 21 and 29 years of age. Women are affected approximately three times more often than men [10]. To date, no definitive racial or ethnic predisposition has been confirmed; however, it is important to note that the prevalence of HS among Black and Hispanic individuals may be underestimated due to their underrepresentation in clinical studies [11, 12].

One of the major risk factors for HS is obesity. Numerous studies indicate that excessive body weight significantly correlates with both the frequency and severity of HS symptoms. This association is attributed to the mechanical irritation of skin folds as well as the pro-inflammatory metabolic activity of adipose tissue [13,14]. Obesity also predisposes individuals to endocrine and metabolic disorders, which may further exacerbate the course of the disease [15]. Another important risk factor is tobacco smoking, which may worsen HS through the effects of nicotine and other harmful substances present in cigarette smoke. These compounds enhance inflammatory responses, impair microcirculation, and negatively affect tissue healing processes [16,17]. HS is frequently associated with autoimmune and endocrine conditions, such as metabolic syndrome, hypothyroidism, and insulin resistance. These disorders can disrupt the hormonal and immunological balance of the body, increasing the predisposition to chronic inflammation [13,14]. Additionally, substance use disorders—including alcohol abuse—have been observed in patients with more severe forms of HS. Such behaviors may impair immune function, intensify oxidative stress, and deteriorate general health status, thereby hindering effective treatment [15,16].

Another important risk factor is chronic skin trauma and mechanical irritation, such as friction, repeated injuries, or excessive sweating. These factors may cause microdamage to the epidermis and secondarily activate local inflammatory mechanisms, thereby initiating or exacerbating disease lesions [16,18]. Understanding the role and modifiability of these risk factors is a crucial component of effective therapeutic management in HS. Treatment depends on the stage of the disease and may include topical and systemic antibiotics, hormonal therapy, immunomodulatory agents, as well as surgical interventions. HS can significantly impact patients’ psychological well-being due to associated pain, involvement of sensitive body

areas, persistent discharge, unpleasant odor, disfigurement, and scarring. Delayed diagnosis further worsens patients' experiences and quality of life [19].

In the following systematic review, the authors evaluated available therapeutic options for the treatment of HS, with particular emphasis on current pharmacological strategies. Both topical and systemic treatments are presented, including antibiotic therapy, hormonal therapy, immunomodulatory agents, and biologic therapy, taking into account their efficacy, safety, and role within current treatment protocols.

Research results

1. Biological Treatment in Hidradenitis Suppurativa

1.1. Introduction to Biological Treatment and pathophysiological basis

Hidradenitis suppurativa (HS) is a chronic, relapsing inflammatory disorder of the hair follicles with an immunologically mediated pathogenesis. Key mediators involved in the development of HS include tumor necrosis factor alpha TNF-α as well as cytokines from the interleukin families IL-1, IL-12, IL-17, IL-23 and IL-36. These pathways represent promising targets for biologic therapies [20,21]. Understanding the molecular and immunologic mechanisms is essential not only for improving disease classification, but also for the effective implementation of targeted treatment strategies [22,23,25].

1.2. Therapeutic criteria and indications

Biological therapy represents one of the available treatment options for hidradenitis suppurativa. However, this therapeutic option is not available to all patients with HS.

The individualized assessment is performed for each patient to determine whether they meet the necessary criteria for initiating this treatment [20].

Biological treatments represent the most effective therapeutic option for patients with moderate to severe hidradenitis suppurativa who have not responded to or cannot tolerate other systemic therapies. The choice of specific biologicals depends on their approved indications, efficacy profiles, and patient-specific comorbidities, such as inflammatory bowel disease [23,24,25,29].

1.3. Diagnostic and Therapeutic Stratification Tools

According to the most recent European treatment guidelines for hidradenitis suppurativa, the International Hidradenitis Suppurativa Severity Score System (IHS4) and the Hurley staging systems are crucial tools for assessing hidradenitis suppurativa severity and have an important role in guiding the selection of further treatment options [29].

A new classification of hidradenitis suppurativa distinguishes between the inflammatory form: mild, moderate and severe based on the IHS4 classification and the primarily non-inflammatory form classified according to Hurley staging. The treatment algorithm includes both medical and surgical approaches. Medical treatment involves the use of oral tetracyclines, clindamycin/rifampicin combination therapy, short-term intravenous clindamycin, and the mentioned biologic agents approved by the EMA - adalimumab, secukinumab and bimekizumab (tab.1) [26,29].

1.3.1. Hurley staging

Hurley staging is a classical system used to classify the severity of HS. It is one of the oldest and most commonly used methods based on clinical assessment of skin lesions and their extent. Stage I represents mild disease with single or multiple abscesses without sinus tracts or scarring. Stage II includes recurrent abscesses and the presence of sinus tracts confined to limited areas, while Stage III involves extensive interconnected sinus tracts and scarring with widespread skin involvement [31].

Although Hurley staging provides a useful initial assessment and helps guide treatment decisions, it is a static system that does not capture disease fluctuations or lesion counts over time. Therefore, it is often supplemented by more dynamic tools such as the IHS4, which quantifies nodules, abscesses and draining tunnels to provide a more precise evaluation of disease activity [30,31].

1.3.2. The International Hidradenitis Suppurativa Severity Score System (IHS4)

The International Hidradenitis Suppurativa Severity Score System (IHS4) is used to assess the severity of HS based on skin lesions, including the number of active nodules, abscesses, and draining tunnels (sinus tracts). The number of nodules is multiplied by one, the number of abscesses by two, and the number of draining tunnels by four, and then the results are summed. A score of 3 or less indicates mild disease, 4 to 10 corresponds to moderate disease, and 11 or more represents severe disease.

This scoring system allows for better clinical assessment and facilitates the implementation of more appropriate treatment strategies for patients with HS [30].

There is also the dynamically evolving IHS4-55, a modified version of the original IHS4 score, which is increasingly being used in clinical trials and practice to assess treatment response more precisely [29].

1.3.3. Further Assessment Measures in the Context of Treatment Optimization

There are also others besides those included in the European guidelines scoring systems that may support better decision-making regarding the treatment pathway for patients. These are important in clinical assessment, such as the Hidradenitis Suppurativa Clinical Response (HiSCR), Hidradenitis Suppurativa Physician Global Assessment (HS-PGA) and Hidradenitis Suppurativa Impact Assessment (HIDRA) scales, as well as tools evaluating the patient's condition and quality of life, including the Dermatology Life Quality Index (DLQI) and Hidradenitis Suppurativa Quality of Life (HiSQOL). DLQI is a widely used, dermatology-specific questionnaire designed to measure the impact of skin diseases on a patient's quality of life. It consists of 10 questions that assess various aspects of daily life affected by skin conditions, including symptoms, their feelings, daily activities, leisure, work or school, personal relationships and treatment [20,26].

Another relevant scale is the Hidradenitis Suppurativa Clinical Response (HiSCR) which is a standardized measure used to evaluate treatment efficacy in patients with hidradenitis suppurativa. The significance of HiSCR has recently been more highlighted, especially when compared to IHS4 by the Food and Drug Administration [29].

1.4. Biologics Approved by the EMA and FDA: Current Standards in HS Treatment

Currently, three biologic agents adalimumab, secukinumab and bimekizumab have received approval from the European Medicines Agency (EMA) and U.S. Food and Drug Administration (FDA) for the treatment of hidradenitis suppurativa (tab.1.) [27,29].

Table 1. Biologic Approved for HS by the EMA and FDA (2025)

Biologic Agent	Mechanism of Action	EMA and FDA Current knowledge until 2025
Adalimumab	TNF-α inhibitor	Approved for moderate-to-severe HS
Secukinumab	IL-17A inhibitor	Approved for moderate-to-severe HS
Bimekizumab	IL-17A and IL-17F inhibitor	Approved for moderate-to-severe HS

1.5. Adalimumab in Hidradenitis Suppurativa

Adalimumab is approved by the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) for patients aged over 12 with moderate to severe hidradenitis suppurativa who have not responded sufficiently to standard systemic treatments. It is used in the inflammatory and destructive phases of HS and it may be used in combination with antibiotics [29]. This drug was approved as the first biologic treatment for hidradenitis suppurativa by the EMA in June 2015 and by the FDA in September 2015 [20,27].

Adalimumab is a human monoclonal IgG1 antibody that specifically binds to tumor necrosis factor-alpha (TNF-α), a cytokine that plays a central role in the pathogenesis of hidradenitis suppurativa. Elevated TNF-α levels in both lesional and perilesional skin contribute to chronic inflammation, immune cell recruitment and tissue damage.

By neutralizing TNF-α, adalimumab inhibits downstream activation of nuclear factor kappa B (NF-κB) and reduces the expression of other pro-inflammatory cytokines, including IL-1β, IL-6, and IL-17. This mechanism results in decreased infiltration of neutrophils and T cells, thereby reducing the formation of nodules, abscesses, and sinus tracts [20,27].

Adalimumab is administered subcutaneously. The induction dose is 160 mg at week 0, followed by 80 mg at week 2. The maintenance dose is 40 mg weekly, starting at week 4. This dose can be increased to 300 mg every 2 weeks based on clinical response. Adalimumab is generally well-tolerated [27].

Contraindications to biologic therapy include New York Heart Association (NYHA) Class III/IV heart failure, demyelinating disorders, active or recent malignancy, active infections, particularly tuberculosis, hepatitis B or other serious opportunistic infections [20,27].

Major adverse events include tuberculosis reactivation and the development or worsening of autoimmune disorders [27].

Clinical trials, specifically PIONEER I and PIONEER II, demonstrated its efficacy. In these trials, adalimumab achieved a Hidradenitis Suppurativa Clinical Response (HiSCR50) in 41.8% (PIONEER I) and 58.9% (PIONEER II) of patients by week 12, compared to placebo [27]. HiSCR50 signifies at least a 50% reduction in inflammatory lesion count with no increase in abscess or draining tunnel counts relative to baseline.

Elevated levels of TNF-α have been found in both lesional and perilesional skin of HS patients, contributing to chronic inflammation, mobilization of immune cells and tissue damage. Clinical trials have demonstrated that adalimumab significantly reduces disease severity, flare frequency, patient-reported pain and quality of life scores [20,27].

1.6. Secukinumab in Hidradenitis Suppurativa

Secukinumab is an approved biologic agent for the treatment of hidradenitis suppurativa. It represents an expanded drug option for moderate to severe forms of the disease who inadequately respond to other systemic therapies or cannot receive them due to side-effects. Secukinumab is indicated for patients in the inflammatory and destructive phases of HS.

Secukinumab was approved by the European Medicines Agency (EMA) in June 2023 and by the US Food and Drug Administration (FDA) in October 2023 [20,27].

Secukinumab works by neutralizing interleukin-17A (IL-17A). Secukinumab is a fully human monoclonal antibody that selectively binds to and neutralizes IL-17A, a pro-inflammatory cytokine involved in the pathogenesis of hidradenitis suppurativa. IL-17A is primarily produced by Th17 cells and plays a central role in the recruitment and activation of neutrophils, moreover the induction of antimicrobial peptides and the maintenance of chronic inflammation observed in HS [20,27].

Secukinumab is administered subcutaneously. The induction dose is 300 mg at weeks 0, 1, 2, and 3. The maintenance dose is 300 mg every 4 weeks, starting at week 4. Based on clinical response, the maintenance dose can be increased to 300 mg every 2 weeks. Secukinumab is well-tolerated and has a good safety profile [20].

Contraindications to biologic treatment encompass conditions such as inflammatory bowel disease (IBD), active or latent tuberculosis, pregnancy, recurrent Candida infections, and other severe infections. Secukinumab should be avoided in patients with IBD [20]. The most frequently observed adverse effects include mucocutaneous candidiasis and headache [20,27].

Clinical trials, specifically SUNSHINE and SUNRISE, demonstrated its effectiveness. In these trials, secukinumab achieved a Hidradenitis Suppurativa Clinical Response (HiSCR50) in 39.5% (SUNSHINE) and 51.0% (SUNRISE) of patients by week 16, compared to placebo. HiSCR50 indicates at least a 50% reduction in inflammatory lesion count with no increase in abscess or draining tunnel counts relative to baseline [20,27].

1.7. Bimekizumab in Hidradenitis Suppurativa

Bimekizumab is a biological drug that has been approved for the treatment of moderate to severe hidradenitis suppurativa similar to Adalimumab and Secukinumab. It represents a significant advancement in the therapeutic options available for this chronic inflammatory skin condition.

Bimekizumab was approved by the European Medicines Agency (EMA) in April 2024 and by the US Food and Drug Administration (FDA) in November 2024 [20, 27].

Bimekizumab is a monoclonal antibody that targets interleukin-17A and interleukin-17F, key cytokines involved in the inflammatory cascade characteristic of hidradenitis suppurativa.

Neutralizing activity is focused specifically on IL-17A and IL-17F. This dual inhibition reduces the expression of neutrophil-attracting chemokines, interleukin-19 (IL-19), and antimicrobial peptides in the epidermis. In affected skin, IL-17 family cytokines induce the expression of pro-inflammatory chemokines such as CCL20, neutrophil-recruiting chemokines such as CXCL1 and CXCL8, as well as cytokines including granulocyte colony-stimulating factor as G-CSF and IL-19. These mediators promote the recruitment of innate and adaptive immune cells, including neutrophils, monocytes and additional Th17 lymphocytes, leading to long-term inflammation [28].

As a result, immune cell infiltration is reduced, contributing to attenuation of the sustained inflammatory response and moreover limiting tissue destruction observed in HS lesions [30, 31]. Bimekizumab is administered subcutaneously. The induction dose is 640mg at week 0 and 320mg every 2 weeks thereafter [20].

Bimekizumab generally shows a good safety profile. However, it is not recommended for patients with concomitant inflammatory bowel disease [27].

Contraindications to biologic therapy include inflammatory bowel disease, tuberculosis, pregnancy, frequent Candida infection or other severe infections.

It is important to note that both secukinumab and bimekizumab are not recommended for patients with concomitant inflammatory bowel disease [20, 27, 28]. Major adverse events include Candidiasis and headache [20, 27].

Bimekizumab's efficacy in treating HS was demonstrated in phase 3 clinical trials, specifically BE HEARD I and BE HEARD II. In these trials, approximately 47.8% of patients in BE HEARD I and 52.0% of patients in BE HEARD II achieved a Hidradenitis Suppurativa Clinical Response 50 (HiSCR50) at week 16, compared to 28.7% and 32.2% in the placebo groups, respectively. [30] Bimekizumab's efficacy in treating HS was demonstrated in phase 3 clinical trials, specifically BE HEARD I and BE HEARD II.In these trials, approximately 47.8% of patients in BE HEARD I and 52.0% of patients in BE HEARD II achieved a Hidradenitis Suppurativa Clinical Response 50 (HiSCR50) at week 16, compared to 28.7% and 32.2% in the placebo groups. HiSCR50 is defined as at least a 50% reduction in inflammatory lesion count (sum of abscesses and inflammatory nodules), with no increase in abscess or draining tunnel counts relative to baseline. The responses observed with bimekizumab are maintained or even increased until week 48 [20, 27].

1.8. Investigational Small Molecules for Hidradenitis Suppurativa

All of the medications listed below are currently under investigation and have not been approved as primary treatments.

1.8.1. TNF-α inhibitors

The use of anti-TNF therapy is not advised in individuals with malignancy, advanced heart failure (Class III or above), systemic lupus erythematosus or active systemic infections [20,27].

Certolizumab pegol is a PEGylated, humanized antibody Fab’ fragment designed to selectively inhibit TNF-α activity. What distinguishes it from other TNF-α blockers is the lack of an Fc (fragment crystallizable) region, which significantly limits its ability to cross the placenta [20].

Infliximab is a chimeric monoclonal antibody of the IgG class that specifically targets and inhibits tumor necrosis factor-alpha TNF-α. Unlike other TNF-α inhibitors commonly administered subcutaneously, infliximab requires intravenous infusion. It is effective in managing moderate to severe hidradenitis suppurativa [20].

Etanercept functions as a circulating TNF receptor, binding both TNF-α and TNF-β to neutralize their activity. Unlike adalimumab and infliximab, its therapeutic potential in moderate to severe hidradenitis suppurativa has been less extensively studied and current findings suggest limited effectiveness [20].

1.8.2. IL-1 inhibitors

Lutikizumab is an experimental dual-variable-domain antibody designed to inhibit both interleukin-1 alpha (IL-1α) and interleukin-1 beta (IL-1β) [20,32].

Bermekimab is a human monoclonal antibody that specifically targets and neutralizes interleukin-1 alpha (IL-1α) by binding directly to the cytokine [20,32].

Anakinra is a recombinant human interleukin-1 receptor antagonist (IL-1Ra) that competitively inhibits the binding of IL-1α and IL-1β to the IL-1 type I receptor. Given the established role of the IL-1 signaling axis

in the inflammatory cascade of hidradenitis suppurativa, anakinra represents a potential therapeutic option targeting this pathway [20,32].

Canakinumab is a fully human monoclonal antibody that selectively binds to interleukin-1 beta (IL-1β), neutralizing its activity by preventing its interaction with the IL-1 receptor on target cells [20,32].

Lutikizumab is a dual variable domain immunoglobulin that acts as a dual antagonist of interleukin 1 alpha and beta (IL-1α/1β). It is designed to effectively neutralize both cytokines, which play a key role in the pathogenesis of HS [27].

1.8.3. IL-12/23 inhibitors

Ustekinumab is a human monoclonal antibody that specifically targets the p40 subunit shared by interleukins 12 and 23, blocking their binding to the IL-12Rβ1 receptor and thus inhibiting downstream signaling [20].

Guselkumab and Risankizumab are human monoclonal antibodies that selectively target the p19 subunit of interleukin-23 (IL-23), a key cytokine involved in the inflammatory pathway of several immune-mediated diseases. By inhibiting IL-23, these agents disrupt the IL-23/IL-17 axis, reducing the activation and proliferation of Th17 cells, which play a crucial role in the pathogenesis of chronic inflammatory conditions such as hidradenitis suppurativa. Both drugs have demonstrated efficacy in clinical trials for psoriasis and are currently being investigated for their therapeutic potential in HS. Their targeted mechanism offers a promising approach for patients who do not respond adequately to other biologic treatments [20,33].

1.8.4. IL-17 Inhibitors

Ixekizumab is an antibody, which is a humanized IgG monoclonal antibody that specifically targets and neutralizes IL-17A, thereby blocking its engagement with the IL-17 receptor complex and reducing the activation of associated inflammatory pathways [20].

Sonelokimab is a single-domain antibody designed to selectively target and inhibit IL-17A and IL-17F. In addition, its albumin-binding domain promotes preferential localization and retention at inflamed tissues, enhancing its therapeutic concentration at disease sites [20].

Brodalumab is a human IgG2 monoclonal antibody that binds to the interleukin-17 receptor A (IL-17RA), thereby inhibiting the signaling of multiple IL-17 isoforms, in contrast to other IL-17 inhibitors that selectively target the IL-17A ligand [20].

Izokibep is a IL-17A inhibitor engineered as a small protein therapeutic with a high affinity for IL-17A and enhanced tissue penetration due to its small molecular size. Izokibep showed promising results in a Phase III clinical trial for hidradenitis suppurativa completed in early 2025, demonstrating significant efficacy and safety. Despite these positive findings, the sponsor discontinued its development, and further progress depends on Affibody's involvement [27].

Solenokimab is a nanobody designed to selectively bind IL-17A and IL-17F, inhibiting their dimeric forms (IL-17A/A, IL-17A/F, IL-17F/F) and includes a central domain that binds to human albumin, enhancing its accumulation at sites of inflammation [27].

1.8.5. IL-36 inhibitors

Spesolimab is a humanized monoclonal IgG1 antibody that targets the interleukin-36 receptor (IL-36R), a key component of the IL-1 cytokine family involved in skin inflammation. It is a monoclonal antibody that blocks the activation of this receptor by IL-36 cytokines (IL-36α, IL-36β, and IL-36γ), which are involved in the pathogenesis of inflammatory conditions, including chronic skin diseases.

Spesolimab has successfully completed a Phase II/III clinical trial, demonstrating promising efficacy and safety in patients with moderate to severe hidradenitis suppurativa, positioning it as a potential future therapeutic option for this condition [25,37].

1.8.6. PDE4 inhibitors

Apremilast is an oral small-molecule inhibitor that selectively targets phosphodiesterase 4 (PDE4) [20].

Roflumilast is also a selective PDE4 inhibitor. By inhibiting PDE4, it increases intracellular cyclic AMP levels, leading to a reduction in the production of pro-inflammatory cytokines. Although not yet approved for HS, its mechanism of action and established efficacy in other inflammatory skin conditions suggest potential therapeutic benefit, and it is under investigation for use in HS [20].

1.8.7. JAK inhibitors

Upadacitinib is a selective inhibitor of JAK1, demonstrating greater specificity for JAK1 compared to JAK2, JAK3, and TYK2 isoforms [20,27].

Povorcitinib, formerly known as INCB054707, is a small-molecule inhibitor that selectively targets Janus kinase 1 (JAK1) with about 52 times higher specificity compared to JAK2. This selective inhibition effectively reduces cytokine signaling pathways implicated in the pathogenesis of hidradenitis suppurativa (HS) while minimizing adverse effects associated with JAK2 inhibition [20,27].

Tofacitinib functions as a selective inhibitor of JAK1 and JAK3. It is an oral small-molecule inhibitor that targets Janus kinase 1 (JAK1) and Janus kinase 3 (JAK3), enzymes involved in the signaling pathways of various pro-inflammatory cytokines.

By inhibiting these kinases, tofacitinib modulates the immune response and reduces inflammation [20].

1.8.8. Complement receptor inhibitors

Avacopan is an orally administered antagonist of the complement C5a receptor (C5aR). Given the elevated levels of C5a observed in individuals with hidradenitis suppurativa, targeting this pathway has been proposed as a potential therapeutic strategy for managing the disease [20].

Vilobelimab (known as IFX-1) is an intravenously administered monoclonal IgG antibody designed to selectively target and inhibit complement component C5a. By neutralizing C5a, it aims to reduce complement-mediated inflammation, offering a potential therapeutic approach for conditions like hidradenitis suppurativa [20].

2. Antibiotic Therapy in Hidradenitis Suppurativa

2.1 Introduction to Antibiotic Therapy

Antibiotic therapy has long been the first-line treatment for HS. However, it is important to emphasize that despite the documented efficacy of antibiotics in alleviating HS symptoms, the condition should not be classified as a classical infection of bacterial origin. The chronic inflammatory process associated with HS-related skin lesions may contribute to cutaneous microbiota dysbiosis, which in turn exacerbates inflammation and promotes its persistence [34].

2.2 Topical Antibiotics

In selected patients with mild HS presenting primarily with superficial inflammatory lesions, topical antibiotics may serve as a component of maintenance therapy. Clindamycin, in particular, has long been regarded as the first-line topical treatment for HS. Its use is supported by studies demonstrating a reduction in the number of pustular lesions compared to placebo, although it shows limited efficacy against deeper lesions such as nodules or abscesses [34]. According to more recent studies, the application of 1% clindamycin gel twice daily for 12 weeks can lead to significant clinical improvement in individuals with mild to moderate HS [35]. However, prolonged exposure to clindamycin may result in the development of microbial resistance [35], including increased colonization by Staphylococcus aureus. In this context, a 2023 study demonstrated that combining clindamycin with benzoyl peroxide produced therapeutic effects comparable to clindamycin alone—as measured by the IHS4 —while potentially limiting the emergence of antibiotic resistance [36]. Other topical antibiotics, such as fusidic acid or gentamicin [37], have also been used in HS treatment, although data on their efficacy remain limited. While topical antibiotics may play a role in managing mild forms of HS, further studies are needed to determine their actual effectiveness and role within treatment strategies for more advanced stages of the disease.

2.3 Tetracyclines

Tetracyclines represent one of the most frequently used classes of first-line antibiotics in the treatment of mild to moderate forms of HS. Within this group, oral tetracycline has been evaluated in a randomized controlled trial comparing its efficacy to that of topical clindamycin [38]. The study demonstrated that tetracycline administered at a dose of 500 mg twice daily was comparably effective in reducing abscesses, although it did not yield significant improvements in patient-reported outcomes [38]. According to current knowledge, the risk of developing antibiotic resistance is higher with topical therapy than with systemic treatment [39], which supports the use of tetracyclines as an initial systemic option. Nevertheless, Matusiak et al. [40] argue that tetracyclines should not be considered the primary treatment due to their limited antimicrobial activity, instead recommending their use

as maintenance therapy based on their anti-inflammatory properties. Within this class, doxycycline is of particular interest. Studies have shown that doxycycline (100 mg twice daily) is effective, as assessed by the Hidradenitis Suppurativa Score [41] and the clinical response index [42]. However, findings from the PIONEER study suggest limited efficacy [43], and patient preferences reported in surveys favored other treatments such as laser therapy (69%), surgical fistula excision (58%), conventional surgery (54%), or combination therapy with clindamycin and rifampicin (44%). Only 37% of participants indicated doxycycline as their preferred option [44]. This low preference may be related to the side effect profile of tetracyclines, which includes gastrointestinal complaints and photosensitivity [34]. The use of tetracyclines is contraindicated during pregnancy and in children under 8 years of age due to the risk of hepatotoxicity and potential impairment of fetal and pediatric skeletal development.

2.4 Combination Therapy with Clindamycin and Rifampicin

In the treatment of patients with mild to moderate HS, a well-documented therapeutic regimen involves the combined oral administration of clindamycin and rifampicin [45]. A retrospective study comparing this combination with tetracycline therapy (limecycline) demonstrated superior efficacy in reducing abscesses and skin fistulas [46], supporting its use in patients with more advanced stages of the disease. The effectiveness of this regimen has been confirmed in multiple retrospective and prospective studies. A treatment protocol consisting of 300 mg of clindamycin and 300 mg of rifampicin administered twice daily for 10 weeks led to remission in 57% of patients in a small 2006 study [47]. Subsequent studies reported clinical improvement in 73% of patients, with 41% maintaining the therapeutic effect [48]. Other publications support similar results: one study documented improvement in 82% of patients and remission in 47% [49]. In a larger cohort of 70 patients, a significant reduction in the Sartorius score was observed, with the median decreasing from 29 points before treatment to 14.5 after therapy completion [50]. The clindamycin-rifampicin combination is widely used in the management of HS. While it was previously believed that the optimal treatment duration should not exceed 10 weeks, detailed analyses have shown that extending therapy beyond this period does not increase the incidence of adverse effects [51]. Interestingly, clindamycin monotherapy has been shown to be more effective than combination therapy in the management of fistulas. This phenomenon may be attributed to the fact that rifampicin is a potent inducer of cytochrome P450 3A4, an enzyme involved in the metabolism of clindamycin. Such induction may reduce serum clindamycin concentrations, which is particularly relevant during long-term treatment required for draining sinus tracts [34]. Notably, data suggest that the use of a tumor necrosis factor-alpha (TNF-α) inhibitor, such as adalimumab, in conjunction with this antibiotic regimen, may enhance its efficacy [52]. These findings highlight that, despite the growing importance of targeted therapies, antibiotic treatment continues to play a significant role in the management of HS.

2.5 Metronidazole, Moxifloxacin, and Rifampicin

A treatment protocol consisting of moxifloxacin 400 mg once daily, metronidazole 500 mg three times daily, and rifampicin 300 mg twice daily has demonstrated high efficacy in inducing complete remission of disease lesions in HS across various stages of clinical severity [34]. The effectiveness of this regimen has also been confirmed in a study focusing specifically on severe cases of HS at Hurley stage I, in which 75% of patients achieved remission [53]. Caution is advised with long-term use of metronidazole due to the risk of adverse effects, particularly peripheral neuropathy. Recent studies on the skin microbiome in patients with HS highlight the significant presence of anaerobic flora, which may support the use of metronidazole as a targeted therapeutic intervention [54].

2.6 Ertapenem

A 2015 study demonstrated that a six-week course of intravenous ertapenem (1 g daily) in patients with severe HS resulted in significant clinical improvement, as measured by a reduction in the Sartorius score [55]. A retrospective study also confirmed that ertapenem therapy had a substantial positive impact on patients' quality of life [56]. Therefore, ertapenem appears to be a potentially valuable adjunctive treatment option for severe cases of HS. However, despite its high clinical efficacy, symptom recurrence is frequently observed upon discontinuation of the drug [57]. One of the most recent reports documented clinical improvement in 15 patients who received intramuscular ertapenem, suggesting that this route of administration may be a viable alternative to intravenous delivery [58].

2.7 Other Antibiotic Combinations

The literature also describes several other antibiotic combinations with varying degrees of efficacy. In one study, a combination of trimethoprim-sulfamethoxazole and cephalexin was administered to 16 patients, with clinical improvement observed in 68.8% of cases [59]. Promising results were also reported for dalbavancin—a modern antibiotic used in the treatment of skin infections—which has shown preliminary beneficial effects in HS management [60]. Due to its wound-healing properties, dalbavancin may represent an interesting subject for further clinical research [34]. Although HS is primarily an inflammatory disease, skin microbiome analyses suggest that antibiotic therapy continues to play an important role in the complex etiopathogenesis of the condition. Nevertheless, further studies are needed to precisely define the role of specific antibiotics and to establish their optimal treatment regimens.

3. Anti-Androgen Therapy in HS

As previously noted, hormones—particularly androgens—are believed to play a significant role in the pathogenesis of HS. Although the association between HS and sex hormones appears evident, the precise mechanisms underlying this relationship remain unclear. Available data indicate that HS occurs nearly three times more frequently in women than in men [61], and symptom exacerbations during the premenstrual phase are reported by 44% to 63% of female patients. The onset of HS after menopause appears to be rare. Moreover, improvement in symptoms during pregnancy and frequent postpartum flare-ups suggest that hormonal fluctuations may contribute to the pathophysiology of HS [62].

3.1. Tissue Hypersensitivity to Physiologic Androgen Levels

Multiple studies have failed to demonstrate the presence of hyperandrogenemia in patients with HS—baseline levels of sex hormones such as estrogens, progesterone, testosterone, and dehydroepiandrosterone sulfate (DHEA-S) do not differ significantly from those observed in healthy controls [63,64]. Therefore, it is increasingly hypothesized that HS pathogenesis may involve hypersensitivity of target tissues to physiologic androgen levels and/or local conversion of these hormones into more active metabolites [65].

3.2. HS and Metabolic Disturbances

The link between metabolic syndrome and androgen activity appears to be indirect—both elevated insulin levels and insulin-like growth factor 1 (IGF-1) enhance the binding affinity of endogenous and exogenous androgens to androgen receptors. Furthermore, increased body mass correlates with higher serum levels of free androgens, primarily due to reduced concentrations of sex hormone-binding globulin (SHBG) [66].

Anti-androgen therapy is particularly indicated in women with HS (acne inversa) who present with at least one of the following factors [62,66,67]:

- disease flare-ups associated with the menstrual cycle;
- acneiform manifestations;
- comorbidities such as diabetes mellitus, polycystic ovary syndrome (PCOS), or hyperandrogenism.

Anti-androgenic agents with proven clinical efficacy include spironolactone, finasteride, cyproterone acetate (CPA), and metformin. In addition, other agents such as topical finasteride, flutamide, clascoterone, and leuprolide are currently under investigation for their therapeutic potential in HS.

4. Spironolactone

Spironolactone, a mineralocorticoid receptor antagonist, is primarily known as a potassium-sparing diuretic and is widely used as adjunct therapy in systolic heart failure management [68]. Beyond its primary indication, it possesses potential anti-androgenic effects—by blocking dihydrotestosterone (DHT) from binding to androgen receptors in the skin, spironolactone reduces keratinocyte proliferation and sebaceous gland activity. Retrospective clinical analyses indicate that spironolactone treatment (typically 75–100 mg/day for approximately 7 months) leads to significant reductions in inflammatory lesion count, pain, and improvement in HS-PGA scores, with minimal changes in Hurley stage. In a study involving women of reproductive age, 31 of 157 patients achieved a meaningful clinical response, while Hurley stage 3 was associated with a significantly reduced likelihood of treatment success, suggesting that women with advanced disease had an 85% lower chance of responding to spironolactone therapy [69]. Another analysis involving 53 women (mean dose: 104 mg/day) showed clinical improvement in 84.1% after 3 months and 81.8% after 6

months of therapy. Notably, the presence of menstrual-related HS flares or polycystic ovary syndrome (PCOS) did not significantly impact treatment response [69]. Nicole M. Golbari et al. also confirmed that lower doses of spironolactone can be effective and may serve as a viable therapeutic option in patients with reduced drug tolerance. Their retrospective review of medical records from a single center (2000–2017) reported a mean daily dose of 75 mg and an average follow-up duration of 7.1 months. Significant improvements were observed in pain, inflammatory lesion count , and HS-PGA score, while no changes were noted in Hurley stage or fistula count. There was no difference in treatment efficacy between patients receiving <75 mg/day and those receiving >100 mg/day[70]. Kraft and Searles evaluated spironolactone as monotherapy and in combination with CPA, comparing these regimens to antibiotic therapy in a retrospective case series. Hormonal therapy using CPA/EE, CPA alone, or spironolactone monotherapy demonstrated higher clinical response rates than antibiotic therapy. However, no specific hormonal regimen—whether monotherapy or combination therapy—was shown to be clearly superior [71]. In another single-center retrospective study by Golbari et al., spironolactone was administered to 67 women with HS. A significant reduction in inflammatory lesions and improvement in HS-PGA scores was observed after 3 months, while pain reduction became apparent after 6 months of treatment. No significant difference in efficacy was found between low-dose and high-dose groups. Concomitant use of other medications, such as antibiotics, did not significantly affect outcomes compared to spironolactone monotherapy. Anatomic remodeling parameters such as Hurley stage and fistula count showed no statistically significant improvement [70]. In another single-center case series, Lee and Fischer analyzed 20 women with HS treated with spironolactone at a dose of 100 mg daily for 3 months. The drug was not always used as monotherapy and was often combined with minocycline (100 mg/day), CPA, or oral contraceptives containing levonorgestrel. The authors reported no differences in treatment response between patients receiving spironolactone alone and those treated with combination therapy. A clinical response was observed in 85% of patients after 3 months of treatment. In one clinical analysis, 17 of 20 women with HS maintained compliance during 3–6 months of therapy, and complete remission was achieved in 11 of 20 cases [72]. Spironolactone has also been described as a safe and effective long-term treatment option, outperforming therapies such as tetracyclines or oral contraceptives (OCPs) in certain cases [73]. Therefore, spironolactone may represent an effective therapeutic option for women of reproductive age with HS. However, patients with severe disease (Hurley stage 3) exhibit significantly lower response rates. Further prospective studies are necessary to confirm these findings and to identify the optimal patient profile most likely to benefit from spironolactone treatment.

5. Finasteride

Finasteride is a selective type II 5α-reductase inhibitor—an enzyme responsible for converting testosterone into the more potent DHT. This enzyme is abundantly present in the pilosebaceous unit and apocrine glands. Finasteride is commonly used in the treatment of androgenetic alopecia and benign prostatic hyperplasia in men, as well as hirsutism in women. Its therapeutic effects may persist for up to a year following discontinuation, suggesting a potential modulatory effect on disease progression. Compared to other anti-androgenic agents, finasteride is generally well tolerated; however, due to its teratogenicity, effective contraception is recommended for women of reproductive age [66]. As early as 2005, Joseph et al. reported seven cases of patients with hidradenitis suppurativa (HS) refractory to antibiotic therapy who were treated with oral finasteride monotherapy. The observation period ranged from 8 months to 2 years. Six patients experienced significant clinical improvement, with three achieving complete lesion resolution. In two patients followed for more than one year, remission lasted between 8 and 18 months. The drug was generally well tolerated; two women developed breast enlargement [74].

In 2017, Mota et al. investigated oral finasteride (1–5 mg/day) in pediatric HS patients, all of whom began treatment after entering puberty. All five patients experienced clinical improvement, including reduced frequency and severity of disease flares [75]. A retrospective chart review involving 20 women aged ≥18 years with a diagnosis of HS also assessed finasteride's use. It was most often prescribed in cases of spironolactone intolerance or inefficacy. Notably, 90% of respondents expressed willingness to continue treatment or to resume it if needed. Half of the patients reported overall satisfaction, 35% were neutral, and 15% were dissatisfied. No patient reported worsening of HS activity during therapy, and only one noted a decrease in quality of life. Adverse effects were reported by 4 women, including headache, nausea, irregular menstruation, breast tenderness, and decreased libido. These findings suggest that finasteride may represent a safe and effective alternative for women with HS, particularly in those who are unable to tolerate spironolactone or have contraindications to its use [76].

5.1 Topical Finasteride

In recent years, the topical use of finasteride has also been investigated as a strategy to inhibit locally produced excess androgens. A case series described four patients who applied over-the-counter topical finasteride to 2–3 affected areas, using 50 µl of a 2275 mg/ml solution per lesion. These patients demonstrated clinical improvement of HS lesions and enhanced quality of life after three months of localized therapy. The mean reductions in IHS4 and DLQI scores were 3.75 and 8.5, respectively. However, no change was observed in disease severity according to the Hurley staging system [77].

6. Antidiabetic Drugs with Indirect Antiandrogenic Effects

As previously mentioned, hidradenitis suppurativa is significantly associated with metabolic disturbances. In a hospital-based case-control study involving 80 patients with HS and 100 age- and sex-matched controls, metabolic syndrome was present in 40% of individuals with HS compared to only 13% of the control population. This association has been confirmed in two cross-sectional studies: one conducted in primary care among 3,207 HS patients, and another involving 326 patients diagnosed in a hospital setting [78,79]. A 2022 meta-analysis further demonstrated that the risk of developing metabolic syndrome is 2.66 times higher in individuals with HS compared to those without the disease [80]. Moreover, HS is associated with an increased risk of developing type 2 diabetes, with the risk estimated to be 69% higher than in the general population [81]. Patients with HS also exhibit an abnormal adipokine profile, including decreased levels of adiponectin and elevated levels of leptin and resistin, which correlate with BMI and inflammatory activity. Additionally, increased levels of visfatin and retinol-binding protein 4 (RBP4) have been identified as independent risk factors for HS, with RBP4 also correlating with insulin resistance and disease severity. Elevated omentin-1 levels further support the presence of metabolic-hormonal dysregulation in this population [65].

6.1 Metformin

Given the above associations, the use of metformin — a drug with insulin-sensitizing and anti-inflammatory properties — may represent a promising therapeutic strategy. In a prospective study, clinical improvement was observed in 72% of HS patients receiving metformin, and 64% reported improved quality of life. In a retrospective study involving pediatric HS patients, the therapeutic response rate was 50% [83]. In the largest study to date involving patients treated with metformin, Jennings et al. reported a therapeutic response in 68% of patients, with complete remission achieved in 19% of cases [83]. The efficacy of metformin in HS has also been evaluated in the first randomized, double-blind clinical trial (NCT04649502). The primary endpoint of the trial was clinical response measured by the IHS4. One group received metformin and doxycycline, while the control group received placebo and doxycycline. Despite completion of the trial in 2023, the results have not yet been published [84].

6.2 Liraglutide

Obesity has been shown to reduce SHBG levels, thereby increasing circulating androgen availability. Weight loss, on the other hand, improves insulin sensitivity and may alleviate chronic inflammatory lesions in HS [85]. Liraglutide, a GLP-1 receptor agonist with weight-reducing properties, has been investigated as a potential treatment option for patients with HS. In 2024, a study was published evaluating the effects of liraglutide (3 mg/day) on metabolic and dermatological parameters in 14 patients with HS and obesity over a 3-month period. Statistically significant improvements were observed in BMI (39.3 ± 6.2 vs. 35.6 ± 5.8; $p = 0.002$), waist circumference (121.3 ± 19.2 vs. 110.6 ± 18.1 cm; $p = 0.01$), CRP levels (4.5 ± 2.2 vs. 3 ± 2.1 mg/L; $p = 0.04$), homocysteine (16.2 ± 2.9 vs. 13.3 ± 3 µmol/L; $p = 0.005$), and plasma cortisol (15.9 ± 4.8 vs. 12.6 ± 4.5 µg/dL; $p = 0.007$). Significant improvement was also noted in the Hurley staging system (2.6 ± 0.5 vs. 1.1 ± 0.3; $p = 0.002$) and Dermatology Life Quality Index (DLQI) (12.3 ± 2.8 vs. 9.7 ± 6.9; $p = 0.04$). These findings suggest that liraglutide at a dose of 3 mg may be a safe and effective treatment option for patients with HS and obesity. However, long-term studies are necessary to assess whether clinical improvement is independent of weight loss [86].

7. Cyproterone Acetate

CPA is a potent progestogen that acts by blocking androgen receptors. It is used in the treatment of androgen-dependent conditions such as acne, hirsutism, precocious puberty, and prostate cancer. However, high doses of CPA may lead to infertility, sexual dysfunction, depression, menorrhagia, weight gain, and cardiovascular complications. Low-dose CPA (2 mg), in combination with ethinylestradiol (EE), was previously widely used as a standard form of contraception. Due to a fourfold increased risk of deep vein thrombosis compared to levonorgestrel, it is now primarily recommended for women with diagnosed hyperandrogenic disorders. CPA has demonstrated efficacy in women with HS across multiple studies [66].

Sawers et al. were the first to describe clinical improvement in HS patients treated with CPA in combination with ethinylestradiol. All four patients achieved clinical symptom control with a daily dose of 100 mg of CPA administered in a reverse sequential regimen. Reducing the dose to 50 mg/day led to a relapse of HS lesions. Before starting therapy, serum testosterone levels were within the normal reference range, whereas androstenedione levels were elevated, and SHBG levels were decreased. During treatment, a decrease in androstenedione and an increase in SHBG were observed. Since these parameters did not change significantly after reducing the CPA dose, it is assumed that the main mechanism of therapeutic action involves androgen receptor blockade in target tissues, rather than merely altering circulating hormone levels [87].

In a randomized, double-blind, crossover trial, Mortimer et al. enrolled 24 women. CPA was used as the investigational treatment, while the contraceptive agent norgestrel served as the control. Unexpectedly, norgestrel demonstrated antiandrogenic properties, reducing plasma testosterone levels more significantly than CPA. Moreover, no significant differences were found between the two therapies in terms of HS activity scores and visual analog scale (VAS) assessments [88].

8. Antiandrogenic Drugs with Potential Therapeutic Role in HS

8.1 Clascoterone

Clascoterone (cortexolone 17α-propionate) is a topical androgen receptor antagonist approved for the treatment of acne vulgaris. Its mechanism of action involves blocking the interaction of DHT with androgen receptors in the skin, which may reduce hyperkeratinization, seborrhea, and local inflammatory responses. Given the role of androgens in the pathogenesis of HS, clascoterone has become the subject of preliminary clinical investigations for this condition. In 2024, the results of a single-center, open-label, prospective study involving 23 female patients with Hurley stage I–II HS were published. The application of 1% clascoterone cream twice daily for 12 weeks led to clinical improvement in 83% of participants. A reduction in inflammatory lesions and an improvement in DLQI scores were observed. The treatment was well tolerated and no significant adverse events were reported [89]. Additionally, a case report documented successful use of clascoterone in a female HS patient, with a reduction in recurrence of skin lesions during the course of treatment [90]. Currently, a randomized clinical trial (NCT05914805) is underway to assess the efficacy of clascoterone in patients with mild HS [91]. Due to the limited data available, further controlled clinical trials in larger patient populations are needed to clearly define the role of clascoterone in HS therapy.

8.2 Flutamide

Flutamide is an oral non-steroidal androgen receptor antagonist that has attracted interest as a potential therapy for HS. The medical literature includes a case report in which HS was treated with flutamide at a low dose of 250 mg/day, resulting in a significant reduction in frequency and severity of lesions in one female patient [92]. Furthermore, a systematic review by Masson et al. (2023) described individual cases of successful flutamide use in HS [93]. Despite these promising findings, the available evidence is largely limited to single case reports, which precludes drawing definitive conclusions. Moreover, the use of flutamide requires caution due to the risk of hepatotoxicity, underscoring the need for further prospective, controlled clinical trials to evaluate the safety and efficacy of this treatment in HS.

8.3 Leuprolide

Leuprolide (leuprolide acetate), a gonadotropin-releasing hormone (GnRH) agonist, shows potential for the treatment of hidradenitis suppurativa through suppression of the hypothalamic-pituitary-gonadal/adrenal axis, resulting in decreased levels of testosterone, androstenedione, and DHEA-S. In a case report involving a 33-year-old female patient with advanced, hereditary HS affecting the anogenital region, combination therapy with dexamethasone and leuprolide led to marked clinical improvement correlated with hormonal suppression

[94]. Systematic literature reviews also support the beneficial effects of GnRH agonists, such as leuprolide, in achieving remission of inflammatory lesions in HS [93]. Additionally, practical guidelines suggest that short-term courses of GnRH agonists combined with glucocorticoids may be effective as salvage therapy in severe, refractory HS cases [95]. Despite encouraging outcomes, randomized controlled trials are lacking, making further clinical research essential to confirm the efficacy, optimize dosing, and assess the safety profile of leuprolide in this patient population.

9. Conclusions

Hidradenitis suppurativa remains a significant clinical challenge, often diagnosed at an advanced stage and associated with substantial physical and psychosocial burden. Biological therapies represent a significant advancement in the management of HS, especially for moderate to severe cases unresponsive to conventional treatments. While several biologics have already gained approval and demonstrated clinical efficacy, ongoing research continues to explore novel agents and targets, offering hope for more effective and personalized treatment options in the future. The currently approved treatments include three agents: adalimumab, secukinumab, and belimumab. Antibiotics remain a key component in the treatment of HS, offering symptom relief despite the disease being a chronic inflammatory condition rather than a classic bacterial infection. In mild cases, topical agents such as 1% clindamycin may reduce superficial inflammatory lesions, although they are less effective for deep nodules and carry a risk of microbial resistance. For moderate HS, systemic antibiotic therapy—particularly combination regimens such as clindamycin with rifampicin—has shown superior clinical outcomes, including remission in a substantial proportion of patients. In severe cases, intensified protocols involving agents like metronidazole, rifampicin, moxifloxacin, or intravenous ertapenem can provide significant improvement, though relapses are common after treatment discontinuation, highlighting the need for cautious, targeted antibiotic use within comprehensive management strategies. A growing body of evidence supports the use of anti-androgen therapies in HS, particularly in women who experience menstruation-related flares, have co-existing hyperandrogenic disorders (e.g., polycystic ovary syndrome), or demonstrate an inadequate response to—or intolerance of—antibiotics. The best-documented agents are spironolactone, finasteride, CPA, and metformin, while topical finasteride, flutamide, clascoterone, and leuprolide are currently under investigation. Available data suggest that anti-androgen drugs may serve as valuable adjuncts in mild to moderate HS; however, well-designed randomised trials are needed before they can be incorporated into standard treatment algorithms. Despite recent advances, the underlying pathophysiology of HS is still not fully elucidated, and current treatments are frequently insufficient or only partially effective. This underscores the urgent need for further research, particularly into the immunologic mechanisms, skin microbiota, and hormonal pathways involved in HS, to enable the development of more targeted, effective, and individualized therapeutic strategies.

Author's contribution:

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