The Evolving Treatment Landscape of Moderate to Severe Hidradenitis Suppurativa: Approved Therapies and an Expanding Late-Stage Pipeline

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First to submit AI-SLR to HTA

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1. INTRODUCTION

- **Hidradenitis suppurativa (HS)** is a chronic, recurrent inflammatory skin disease characterized by painful nodules, abscesses, sinus tracts, and scarring, primarily affecting intertriginous areas such as the axillae, groin, and inframammary regions[1]
- HS imposes a substantial disease burden, leading to chronic pain, impaired quality of life, reduced work productivity, psychological distress, and social stigma[1, 2]
- The disease is driven by dysregulated innate and adaptive immune responses, involving key inflammatory pathways such as TNF-α, IL-17, IL-1, and JAK-mediated signaling[3]
- Although approved biologic therapies have improved management of moderate-to-severe HS, many patients experience inadequate responses or fail to achieve sustained disease control[4]
- Advances in HS immunopathology have facilitated the development of novel targeted therapies, including agents targeting IL-17, JAK1, IL-1, BTK, and TL1A, highlighting a rapidly evolving treatment landscape and ongoing efforts to address unmet clinical needs[5]
- Despite therapeutic advances, a significant proportion of patients with moderate-to-severe HS remain inadequately controlled, underscoring the need for novel therapies targeting diverse inflammatory pathways

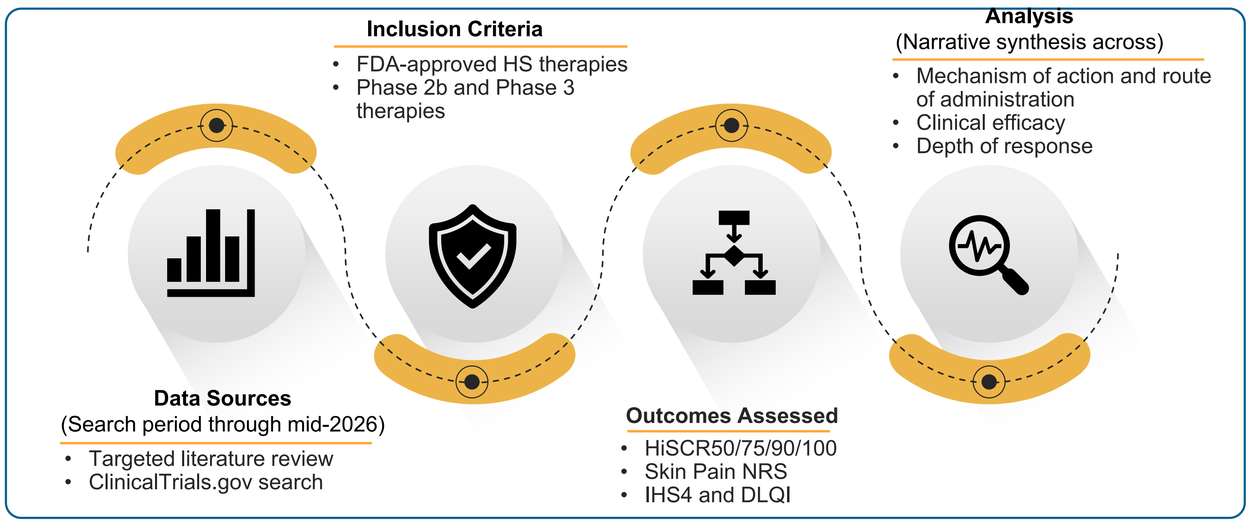
2. OBJECTIVES

- To provide an overview of currently approved therapies for moderate-to-severe HS, including their mechanisms of action and treatment modalities
- To evaluate emerging late-stage pipeline therapies by summarizing their therapeutic targets, mechanisms of action, and key efficacy outcomes in moderate-to-severe HS

3. METHODS

- **Data sources and scope:** A targeted literature review and a ClinicalTrials.gov search, run through mid-2026, identified FDA-approved therapies and pipeline therapies in Phase 2b or Phase 3 development for moderate-to-severe hidradenitis suppurativa
- **Outcomes and synthesis:** Efficacy was summarized across HiSCR50/75/90/100, skin pain NRS, IHS4 and DLQI. The findings were synthesized narratively by mechanism of action, route of administration and depth of response (**Figure 1)**

Figure 1: Illustrating the methodology overview

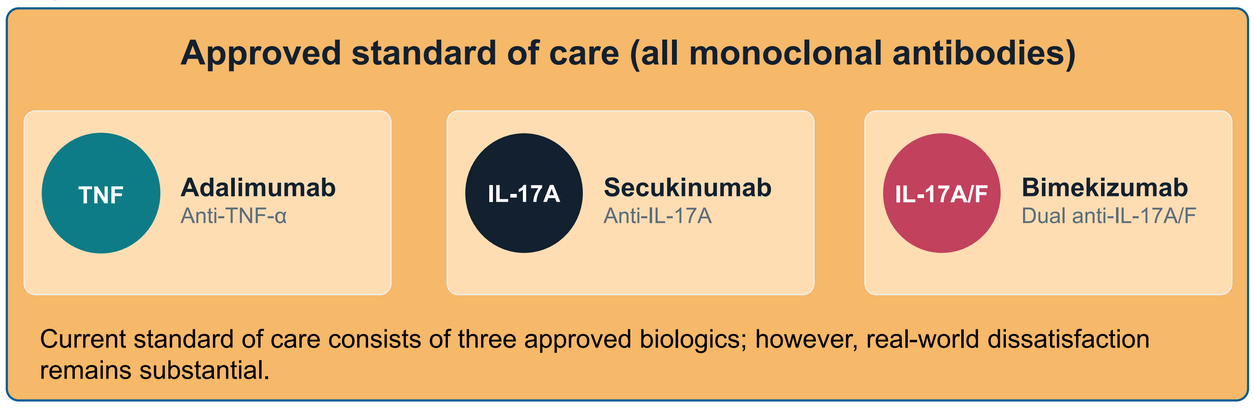


4. RESULTS

Approved therapies

- Three monoclonal antibodies are currently approved for the treatment of moderate-to-severe HS: adalimumab (TNF-α), secukinumab (IL-17A) and bimekizumab (IL-17A/F) **(Figure 2).**
- Real-world dissatisfaction persists despite these options

Figure 2: Approved standard of care



Late-stage pipeline

- **Eight** late-stage pipeline therapies were identified, including povorcitinib, upadacitinib, sonelokimab, izokibep, lutikizumab, remibrutinib, spesolimab, and tulisokibart, reflecting a rapidly expanding therapeutic landscape
- Novel mechanisms of action extend beyond TNF-α and IL-17 inhibition, with emerging therapies targeting JAK1, IL-1α/β, BTK, TL1A, and IL-36 pathways
- **JAK1 inhibitors** demonstrated promising efficacy, with povorcitinib achieving approximately 60% HiSCR50 response at Week 24 and upadacitinib showing activity in patients with previous anti-TNF treatment failure **(Figure 3)**
- **Advanced IL-17-targeting therapies** showed encouraging clinical outcomes, including HiSCR75 responses of up to 62% and HiSCR100 responses of up to 32% with sonelokimab, while izokibep achieved superior HiSCR50 responses compared with placebo **(Figure 3)**
- The pipeline includes both biologic and oral therapies, potentially expanding treatment options and allowing more individualized management strategies for patients with moderate-to-severe HS
- Recent clinical development programs increasingly emphasize deeper treatment responses, including HiSCR75, HiSCR90, and HiSCR100, alongside improvements in pain and quality-of-life outcomes

Figure 3: Reported Phase 3 response rates

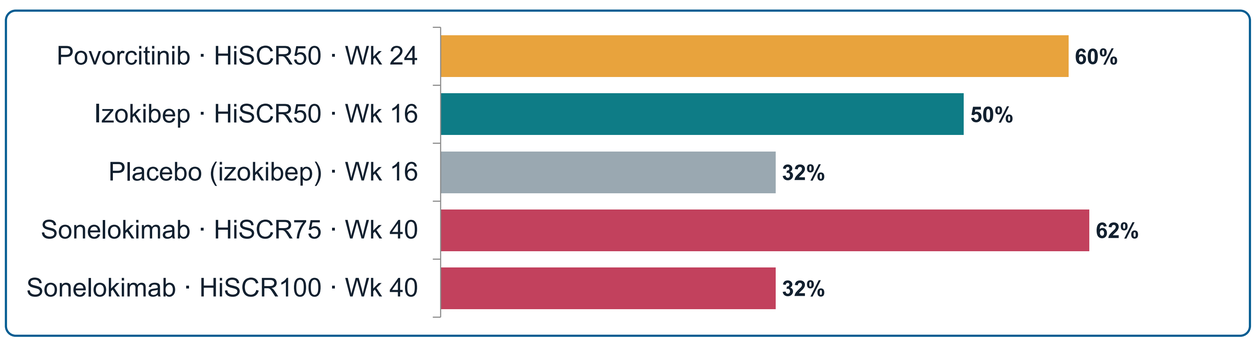


Table 1: Late-stage pipeline: evidence snapshot

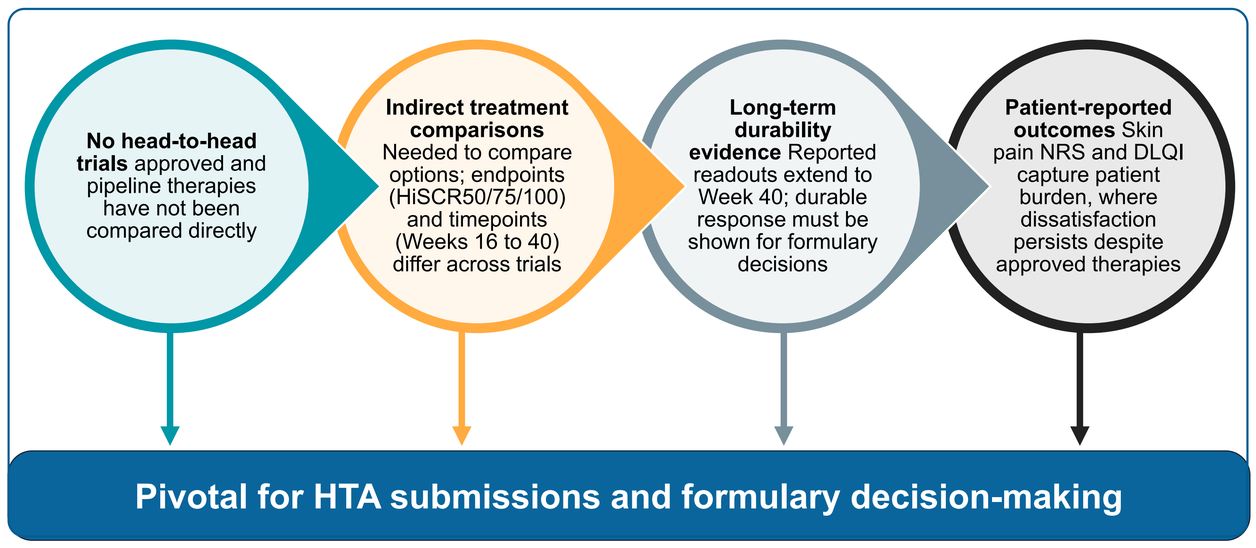
Therapy (sponsor)	Mechanism	Modality	Stage	Key findings/status
Povorcitinib[6] (Incyte)	JAK1 inhibitor	Oral	Phase 3 (STOP-HS)	Met primary endpoints in both trials; nearly 60% achieved HiSCR50 at wk 24
Upadacitinib[7] (AbbVie)	JAK1 inhibitor	Oral	Phase 3	Studied in patients who have failed anti-TNF therapy
Sonelokimab[8] (MoonLake)	IL-17A/F (trivalent nanobody)	Biologic	Phase 3 (VELA)	HiSCR75 62%, HiSCR100 32% at wk 40
Izokibep (ACELYRIN)*[9]	IL-17A inhibitor	Biologic	Phase 3	HiSCR50 50% vs 32% placebo at wk 16
Lutikizumab[10] (AbbVie)	IL-1α/β (dual antagonist)	Biologic	Phase 3	Advanced after positive Phase 2 in anti-TNF inadequate responders
Remibrutinib[11] (Novartis)	BTK inhibitor	Oral	Phase 3	Primary completion est. 2027
Spesolimab[12] (Boehringer Ingelheim)	IL-36R	Biologic	Phase 3 completed (Mar 2025)	Results awaited
Tulisokibart[13] (MSD)	Anti-TL1A antibody	Biologic	Phase 2b	Primary completion est. Nov 2026

**ACELYRIN was acquired by Alumis in 2025, and the izokibep HS development status is under review*

Evidence gaps for HTA

- Although three monoclonal antibodies are approved and eight late-stage molecules are in development, no head-to-head data exist. Endpoints (HiSCR50/75/100) and timepoints (Weeks 16 to 40) also differ across trials, so indirect comparisons will be needed. Long-term durability and patient-reported outcomes (skin pain NRS, DLQI) will be equally important, and together these are pivotal for HTA submissions and formulary decisions **(Figure 4)**

Figure 4: Evidence gaps for HTA and formulary decisions



CONCLUSION

- The HS treatment landscape is rapidly evolving from a limited biologic-based paradigm to a diverse portfolio of biologic and oral therapies targeting multiple inflammatory pathways
- Emerging agents have demonstrated promising efficacy, with several offering deeper clinical responses and potential alternatives for patients inadequately controlled on existing treatments
- Further comparative, long-term, and patient-centered evidence will help define the future treatment algorithm for moderate-to-severe HS

Abbreviations: HS: Hidradenitis Suppurativa; HiSCR: Hidradenitis Suppurativa Clinical Response; IHS4: International HS Severity Score System; DLQI: Dermatology Life Quality Index; NRS: numeric rating scale; HTA: Health Technology Assessment

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