



# A Guide to the Management of Hidradenitis Suppurativa in Pregnancy and Lactation

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## Abstract

Hidradenitis suppurativa is a chronic inflammatory condition characterized by recurrent abscesses, nodules, tunnels, and scarring. Fluctuations in disease activity are common during pregnancy, and more than half of women with hidradenitis suppurativa report experiencing post-partum flares. Both treatment efficacy and safety of the woman and fetus or infant must be considered when developing a treatment plan for pregnant and lactating women with hidradenitis suppurativa. Although certain commonly used hidradenitis suppurativa medications, such as tetracyclines and spironolactone, are contraindicated during pregnancy, there are still various medical therapies, including topicals, systemic antibiotics, metabolic modulators, and biologics, as well as procedural therapies that may be utilized during pregnancy. This paper aims to provide an updated evidence-based review of the management of hidradenitis suppurativa in pregnancy with an emphasis on safety data.

## Key Points

Hidradenitis suppurativa disproportionately affects women of childbearing age.

Safety and efficacy of the various available medical and procedural hidradenitis suppurativa treatments must be considered when developing an appropriate treatment plan for pregnant or breastfeeding patients with hidradenitis suppurativa.

## 1 Introduction

Hidradenitis suppurativa (HS) is a chronic inflammatory condition characterized by the formation of recurrent abscesses, nodules, tunnels, and scarring. Although the etiology of HS is multifactorial and not yet fully understood, hormonal dysregulation is thought to play a role in the pathogenesis. This hypothesis is supported by a frequent post-pubertal onset of symptoms, perimenstrual flares, and a strong association with polycystic ovarian syndrome [1]. Furthermore, hormonal modulators such as spironolactone, finasteride, and oral contraceptive pills have shown benefit in patients with HS [2]. Based on current epidemiologic data, HS appears to disproportionately affect women of child-bearing age in the USA [3]. Nearly half of pregnancies are unintended, which highlights the importance of routinely counseling female individuals of reproductive age on medication safety and the potential impacts their treatments may have on pregnancy [4]. The literature suggests that there are currently practice gaps in the care of pregnant individuals with HS. A survey study of 59 women with HS found that the majority had not received information from their physician on how their disease and medications could impact pregnancy outcomes [5]. More than half desired more counseling on HS and pregnancy from their provider [5]. Furthermore, a single-center retrospective cohort study of 127 patients found that dermatologists were involved in HS care for only 14.4% of the pregnancies. Patients managed

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by a dermatologist during pregnancy were more likely to receive an HS therapy or procedure when compared with those who were not [6]. Dermatologists play a crucial role in the management of HS and are especially key when optimizing HS during pregnancy. This paper aims to provide an updated review of the management of HS during pregnancy and breastfeeding with an emphasis on safety data (Table 1).

## 2 Disease Fluctuations and Pregnancy Outcomes

Fluctuations in HS disease activity have been noted during pregnancy. A systemic review and meta-analysis of eight studies found that while HS activity during pregnancy improved in 24% of patients and worsened in 20%, the majority of patients had continued disease activity. Postpartum flares affected 60% (99/164) of women with HS [1]. Given the large proportion of patients who are likely to experience disease activity, a close follow-up with a dermatologist is critical for appropriate HS care during pregnancy [1].

Individuals with HS may be at increased risk for adverse maternal and fetal outcomes. A retrospective cohort study of The United States' Healthcare Cost and Utilization Project-Nationwide Inpatient Sample database found an increased risk of preeclampsia, cesarean sections, and congenital anomalies among pregnant patients with HS [7]. Another retrospective cohort study of 1862 HS pregnancies reported HS as an independent risk factor for spontaneous abortion, gestational diabetes mellitus, and cesarean section [8]. Limitations of these database studies include an inability to evaluate the influence of disease activity or severity during pregnancy or impact of medical treatment of HS on pregnancy outcomes.

## 3 Medical Management of Hidradenitis Suppurativa During Pregnancy and Lactation

### 3.1 Topical Therapies Generally Considered Compatible with Pregnancy

#### 3.1.1 Benzoyl Peroxide Wash

Benzoyl peroxide wash, a commonly used first-line HS topical, is generally considered compatible with pregnancy and lactation [9]. Benzoyl peroxide metabolizes to benzoic acid, a food additive, and has minimal systemic absorption [10]. Benzoyl peroxide is also considered safe during breastfeeding despite a lack of human safety data available [11].

#### 3.1.2 Chlorhexidine Wash

Chlorhexidine wash, an antiseptic, is considered compatible with pregnancy and lactation. A randomized controlled trial of 334 women in labor who underwent vaginal washes (mean 2.6 times) and 335 liveborn neonates who were cleaned with 1% chlorhexidine supported safety and tolerability [12]. A Cochrane review including a total of 1125 infants evaluating vaginal chlorhexidine (any form, including gel or wash) use during labor did not report any infant side effects over four studies [13]. In one randomized study, 0.2% chlorhexidine in alcohol (vs distilled water) was sprayed on the breasts of 200 mothers before and after each feeding with no side effects noted in breastfed infants [14].

#### 3.1.3 Topical Clindamycin

Topical clindamycin is a first-line treatment for mild-to-moderate HS. It is often paired with benzoyl peroxide to reduce development of bacterial resistance [10]. Because of its minimal absorption when applied topically, it is generally considered safe in pregnancy [9] and lactation [11]. Clindamycin 1% solution has limited systemic absorption, varying from 1% [15] to 4–5% of the drug [16]. When breastfeeding, application to breast should be avoided to minimize oral ingestion that could lead to infant diarrhea [17].

### 3.2 Topical Therapies to Avoid Using in Pregnancy

#### 3.2.1 Topical Resorcinol

Topical resorcinol, a keratolytic with anti-inflammatory properties, is utilized by experts in the management of HS [2]. However, because of a lack of safety data in humans, resorcinol should generally be avoided in pregnant and lactating individuals [18]. One case report of a 30-week pregnant patient consuming resorcinol orally resulted in seizures, respiratory failure, and death of the fetus [19].

#### 3.2.2 Topical Ruxolitinib

Topical ruxolitinib, a Janus kinase inhibitor approved for use in atopic dermatitis and vitiligo, met its primary endpoint in a randomized phase II trial for HS [20]. Ruxolitinib has not been studied in pregnant or lactating individuals. In animal studies, oral ruxolitinib exposure led to a drop in fetal weight in both rats and rabbits when exposed to 60 mg/kg/day of oral ruxolitinib [21]. Currently, it is recommended to avoid topical ruxolitinib

**Table 1** Hidradenitis suppurativa treatments and their compatibility with pregnancy and lactation

Recommendation <sup>a</sup>	Pregnancy	Lactation
Generally considered compatible	<b>Topical therapies</b> Benzoyl peroxide wash [9] Chlorhexidine wash [13] Clindamycin [9] <b>Systemic antibiotics</b> Clindamycin [26] Amoxicillin-clavulanic acid [29, 30] Metronidazole [32] Cephalexin [36] Cefdinir [36] <b>Metabolic/hormonal/oral retinoids</b> Metformin [56] <b>Biologics</b> Certolizumab [71] <b>Supplements</b> Zinc [113]	<b>Topical therapies</b> Benzoyl peroxide wash [11] Chlorhexidine wash [14] Clindamycin [11] <b>Systemic antibiotics</b> Clindamycin [26] Amoxicillin-clavulanic acid [31] Cephalexin [38] Cefdinir [38] Rifampin [18] <b>Metabolic/hormonal/oral retinoids</b> Metformin [46, 57] Spironolactone [60] <b>Biologics</b> Certolizumab [72] Adalimumab [84] Infliximab [84] <b>Supplements</b> Zinc [115]
Use with caution	<b>Systemic antibiotics</b> Dapsone [42] Rifampin [45] Ertapenem [50] <b>Biologics</b> Adalimumab [76] Infliximab [76] Secukinumab [87] Ustekinumab [89] Bimekizumab <sup>c</sup> [92] <b>Immunosuppressants</b> Corticosteroids [103] Cyclosporine [111]	<b>Topical therapies</b> Clascoterone [18, 23] <b>Systemic antibiotics</b> Metronidazole (stop breastfeeding for 12–24 hours after taking dose) [34, 55] Dapsone [18] Ertapenem [50] TMP-SMX (limit use in infants <2 months) [55] <b>Metabolic/hormonal/oral retinoids</b> OCPs [18] GLP-1 agonists [66] <b>Biologics</b> Secukinumab [84] Ustekinumab [83] Bimekizumab [93] Anakinra [18, 96] <b>Immunosuppressants</b> Corticosteroids (wait 4 hours after dose to breastfeed) [107] Cyclosporine [18]
Avoid use	<b>Topical therapies</b> Resorcinol <sup>b</sup> [19] Ruxolitinib <sup>b</sup> [21] Clascoterone [23] <b>Systemic antibiotics</b> Tetracyclines [51] Fluoroquinolones [127] TMP-SMX [51] <b>Metabolic/hormonal/oral retinoids</b> Spironolactone [58] OCPs [128] GLP-1 agonists [64] Retinoids [67] <b>Biologics</b> Anakinra [94] <b>Small-molecule inhibitors</b> Apremilast [98] Upadacitinib [102]	<b>Topical therapies</b> Resorcinol <sup>b</sup> [18] Ruxolitinib <sup>b</sup> (do not breastfeed for at least 4 weeks after topical use) [21] <b>Systemic antibiotics</b> Tetracyclines <sup>b</sup> (may consider a ≤21-day course if needed) [18] Fluoroquinolones <sup>b</sup> [127] <b>Metabolic/hormonal/oral retinoids</b> Retinoids [60] <b>Small-molecule inhibitors</b> Apremilast <sup>b</sup> [11, 98] Upadacitinib <sup>b</sup> (do not breastfeed for at least 6 days after last dose) [102]

GLP-1 glucagon-like-peptide-1, OCPs oral contraceptive pills, TMP-SMX trimethoprim-sulfamethoxazole

<sup>a</sup>Each patient's treatment plan should be individually tailored to account for their comorbidities, preferences, and personal risk factors

<sup>b</sup>Recommend to avoid use if possible because of inadequate human and animal data

<sup>c</sup>Generally recommend to avoid use in pregnancy if possible due to inadequate human data, however, animal data show no harm; can be considered with extreme caution on a case-by-case basis

during pregnancy and lactation because of minimal safety and efficacy data [11]. Patients should avoid breastfeeding for at least 4 weeks after last use [21].

### 3.2.3 Topical Clascoterone

Topical clascoterone, an androgen receptor inhibitor, has minimal data supporting its efficacy in HS [22] and has not been studied in pregnant women [9]. In animal studies evaluating the effects of subcutaneous clascoterone administration during organogenesis, pregnant rats had offspring with malformations, and pregnant rabbits had increased rates of post-implantation losses [23]. Patients should avoid using clascoterone during pregnancy because of limited safety data in humans. Use of topical clascoterone during lactation may be considered with caution given the limited systemic absorption and likely low concentration in breast milk [18].

## 3.3 Systemic Antibiotics Generally Considered Compatible with Pregnancy

Clindamycin is a common first-line antibiotic for HS and is generally considered safe during pregnancy. One study of 647 newborns exposed to clindamycin during the first trimester did not find any association between drug exposure and congenital defects [24]. Clinical trials of pregnant women taking clindamycin during the second and third trimesters did not reveal any increased frequency of congenital defects [25]. Furthermore, clindamycin demonstrated no teratogenic effects in animal studies [25]. Clindamycin is generally considered safe during breastfeeding [26]. There is one report of bloody stools in a 5-day-old infant breastfed by a mother receiving intravenous clindamycin and gentamicin [18]. Infants breastfed by mothers taking clindamycin should be monitored for side effects such as diarrhea, candidiasis, or bloody stools because of its potential effects on infant gastrointestinal flora [18].

Amoxicillin-clavulanic acid, which has data for use during HS flares [27]. (Table 2), is generally considered compatible with pregnancy, especially after the first trimester, and with lactation. Amoxicillin has been associated with an increased risk of cleft lip and/or palate with fetal exposure in the first trimester [28]; however, other studies did not establish a link between amoxicillin-clavulanic acid and birth defects [29]. One prospective controlled study of 191 pregnant women with amoxicillin-clavulanic acid exposure during the first trimester of pregnancy did not show an increased risk of major malformations [30]. A prospective study evaluating maternal drug exposure and adverse reactions of breastfed infants included 25 maternal-infant pairs exposed to amoxicillin while breastfeeding. Three infants had diarrhea, but no major infant side effects warranting medical attention occurred [31].

Metronidazole is considered compatible with pregnancy and should be used with caution in lactation. In a study of 922 pregnant women exposed to metronidazole, no relationship was established between metronidazole use during pregnancy and preterm births, low birth weight, and congenital abnormalities [32]. Although no adverse outcomes have been reported in infants breastfed by mothers taking metronidazole, metronidazole has demonstrated mutagenicity in bacteria and carcinogenic properties in animals [33]. Because the drug is excreted into breast milk in large quantities, it should be used with caution [34]. Discontinuing breastfeeding for 12–24 hours after a dose of metronidazole is encouraged [26].

Cephalexin, a first-generation cephalosporin, has also been used to treat HS [35] and is generally considered safe during pregnancy and lactation. A case-control study failed to establish a link between cephalosporin exposure during pregnancy and teratogenic effects [36]. Cephalexin has been recommended for mastitis treatment [37] in breastfeeding mothers and is minimally excreted into breast milk [38]. There are a few reports of infant diarrhea with maternal usage [18, 39].

**Table 2** Flare management in pregnant patients with hidradenitis suppurativa

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First line: warm baths and compresses, antiseptic washes, and topical clindamycin [122]
Systemic antibiotic(s) such as clindamycin, amoxicillin-clavulanic acid, metronidazole, cephalexin, or cefdinir can be given as short courses (2–3 weeks) for acute flares, or as longer courses (2–3 months) as a bridge to delivery or more sustainable long-term therapies
Oral corticosteroid (prednisolone or prednisone 40 mg tapered by 10 mg every 3 days) taper alone or in combination with amoxicillin-clavulanic acid [27]
Intralesional triamcinolone injections (10–40 mg/mL, maximum 40 mg total) for acutely inflamed inflammatory nodules or tunnels [122]
Incision and drainage for acutely painful and/or expanding abscesses; lesions should be adequately anesthetized prior to incision
Deroofing procedures with local anesthesia may be considered on a case-by-case basis
Avoid larger excisions that require general anesthesia
When an anesthetic is required (i.e., incision and drainage, deroofing procedures), plain lidocaine is preferred over lidocaine with epinephrine [120]
Analgesic use: acetaminophen preferred during pregnancy and ibuprofen during breastfeeding [122]

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Cefdinir, a third-generation cephalosporin, is used for HS flare treatment [40]. No increased risk of teratogenicity was identified in a population-based case-control study of 308 pregnant women treated with cephalosporins (including third-generation agents) [36]. Third-generation cephalosporins are considered compatible with breastfeeding [38].

### 3.4 Systemic Antibiotics Used with Caution in Pregnancy

Dapsone may be used as a third-line agent or as adjunct therapy for HS [41] and should be used with caution during pregnancy and lactation. Although human data are limited, in pregnant rats and rabbits, oral dapsone (at 75 mg/kg/day and 150 mg/kg/day) exposure during organogenesis was shown to be embryotoxic [42]. A 41-day-old infant experienced hemolytic anemia that was suspected as a result of breast milk exposure from maternal use of oral dapsone [43]. Infants should be closely monitored for hemolysis and jaundice when dapsone is used in lactating mothers. Use should be avoided in infants with G6PD deficiency [18].

Rifampin is commonly used as first-line therapy for HS, often in combination with clindamycin [44]. Pregnant women with tuberculosis or leprosy have been treated with rifampin as part of a multidrug regimen; however, rifampin should be used with caution in pregnant patients. Rifampin has resulted in congenital malformations, cleft palate, embryotoxicity, and skeletal abnormalities in animal studies [45]. Maternal and infant hemorrhage have also been reported with rifampin exposure in the weeks preceding delivery; this risk, however, may be mitigated with prophylactic vitamin K [46]. Rifampin should be used with caution during pregnancy and only when the benefits outweigh the risks of maternal and fetal harm. Rifampin is considered generally compatible with breastfeeding and transferred to breast milk minimally [18]. It should be noted that clindamycin concentrations have been found to be low when rifampin and clindamycin are given concomitantly, likely due to a medication interaction [47]. One trial also demonstrated that clindamycin monotherapy was equally as effective as clindamycin/rifampin combination therapy for HS [48]. Given these data and the favorable safety profile of clindamycin, monotherapy oral clindamycin is now generally recommended over dual therapy with rifampin during pregnancy and lactation.

Intravenous ertapenem is used as a rescue therapy for severe recalcitrant HS [49]. Although no human pregnancy data exist, the offspring of mice treated with ertapenem did have increased ossification defects and decreased fetal weight with a dose of 700 mg/kg/day but no side effects below this dose [50]. As for breastfeeding, ertapenem is expected to be found in low concentrations in breast milk

[18]. Because of limited data in pregnancy and lactation, it should be used with caution.

### 3.5 Systemic Antibiotics to Avoid Using in Pregnancy

Tetracyclines should be avoided during pregnancy because of concern for an increased risk of spontaneous abortion, fetal tooth discoloration, enamel hypoplasia, and fetal bone abnormalities. In a systematic review evaluating 27,751 prenatal exposures to various antibiotics, doxycycline ( $n = 2351$ ) was associated with cardiovascular abnormalities in one study and spontaneous abortion in another [51]. Third-trimester exposure has been linked to acute maternal fatty liver of pregnancy in case reports [52]. Tetracyclines should generally be avoided and only considered during lactation if administered for a short course (less than 3 weeks). Shorter courses result in minimal accumulation of tetracyclines in breast milk and calcium in the milk also limits infant absorption of the drug. There are some reports available for tetracycline use during breastfeeding that did not show adverse events; however, data are limited [18].

Moxifloxacin and other fluoroquinolones should generally be avoided during pregnancy because of concern for fetal arthropathy; however, data are unclear. One prospective observational cohort study of 411 women exposed to fluoroquinolones during the first trimester found no increased risk of congenital anomalies [53]. There are no human data available regarding fluoroquinolones during breastfeeding and thus use during lactation should be avoided.

Trimethoprim-sulfamethoxazole is considered contraindicated in pregnancy. A systematic review of 23,602 first-trimester exposures found an elevated risk of neural tube defects (pooled odds ratio [OR] 2.5), spontaneous abortion (OR 3.5), preterm birth (OR 1.5), and small for gestational age (OR 1.6) [51]. Trimethoprim-sulfamethoxazole should be used with caution in breastfeeding mothers, especially with stressed, premature, jaundiced, or sick infants because of the possibility of inducing a rise in bilirubin levels and kernicterus, and avoided in newborns younger than 2 months of age [54, 55].

### 3.6 Metabolic/Hormonal/Oral Retinoid Treatments Generally Considered Compatible with Pregnancy

#### 3.6.1 Metformin

Metformin, a biguanide typically used to treat diabetes mellitus, is commonly used as adjunct therapy for HS. Metformin is generally considered safe during pregnancy. One prospective randomized placebo-controlled trial compared pregnant women with type 2 diabetes taking metformin 1000



mg twice daily with insulin versus placebo with insulin. The study found no significant difference in neonatal outcomes, such as stillbirth, neonatal hypoglycemia, preterm birth, or spontaneous abortion or miscarriage [56]. Metformin is also generally compatible with breastfeeding [57], there is negligible risk of hypoglycemia in exposed infants [46].

### 3.7 Metabolic/Hormonal/Oral Retinoid Treatments to Avoid Using in Pregnancy

#### 3.7.1 Spironolactone

Spironolactone, an aldosterone antagonist, is frequently used in female patients with HS to counteract hormonal influences on disease activity. Spironolactone is not compatible with pregnancy because of its antiandrogen properties and ability to cross the placenta, which can interfere with the sexual development of a male fetus [58]. A 2019 systematic review evaluating exposure to spironolactone in utero did not find significant evidence of feminization of male individuals; however, human data were limited to case reports [59]. Of note, spironolactone is generally considered compatible with breastfeeding despite a potential risk of lactation suppression from diuresis [60].

#### 3.7.2 Oral Contraceptive Pills

Combined oral contraceptive pills are used as monotherapy or in combination with spironolactone for female patients with HS [2], but are contraindicated during pregnancy. In terms of compatibility with breastfeeding, oral contraceptive pills may suppress lactation and there are some reports of infants experiencing breast enlargement while being breastfed by exposed mothers [18]. Thus, it is generally recommended to wait until at least 6 weeks after delivery to start oral contraceptive pills.

#### 3.7.3 Glucagon-Like Peptide-1 Agonists

Glucagon-like-peptide-1 (GLP-1) agonists, used to treat diabetes, are emerging as a potential therapeutic class for patients with HS, though more data are needed [61, 62]. Given the current limited literature, GLP-1 agonists should generally be avoided during pregnancy if possible. Per the US Food and Drug Administration (FDA) label, subcutaneous semaglutide administered to rats (0.06, 0.2, and 0.6 times the maximum recommended human dose) led to offspring with cardiovascular and skeletal defects. Early pregnancy losses and fetal organ/skeletal abnormalities were also identified in pregnant rabbits (0.02-fold, 0.2-fold, and 1.2-fold the maximum recommended human dose) [63]. A 2023 systematic review of animal and human studies of GLP-1 agonists in pregnancy and lactation found that in animal

studies, GLP-1 agonists were associated with reduced fetal weight/growth and skeletal abnormalities [64]. A 2024 observational population-based cohort study investigating live births of pregnant women with type 2 diabetes found no statistically significant increased risk for major congenital malformations between exposure to GLP-1 agonist versus insulin (relative risk of 0.95, 95% confidence interval 0.72–1.26) [65]. In terms of lactation, while human data are not available, GLP-1 agonists were found in breast milk in animal studies [64]. In one study evaluating breast milk samples (0, 12, and 24 hours after dose) from eight mothers taking semaglutide, the drug was undetectable in all samples [66]. In addition, all infants in the study were reported to have normal development, with one report of infant diarrhea [66]. There is currently a lack of safety data for other GLP-1 agonists such as liraglutide and tirzepatide during breastfeeding. Glucagon-like-peptide-1 agonists may currently be considered with caution during lactation.

#### 3.7.4 Oral Retinoids

Both isotretinoin and acitretin are contraindicated during pregnancy. Isotretinoin has been linked to fetal abnormalities, including craniofacial, cardiac, thymic, and central nervous system abnormalities, [67]. spontaneous abortions, and preterm births [60]. It is recommended to discontinue isotretinoin at least 1 month prior to conceiving and to discontinue acitretin at least 3 years prior to conceiving [46]. Both acitretin and isotretinoin are excreted in breast milk, thus breastfeeding should be avoided [60].

### 3.8 Biologics Generally Considered Compatible with Pregnancy

#### 3.8.1 Certolizumab

Certolizumab, a tumor necrosis factor-alpha (TNF $\alpha$ ) inhibitor, has very limited data regarding efficacy in HS [68]. It is thought to be the safest TNF $\alpha$  inhibitor to use in pregnancy given minimal placental transfer because of its lack of an Fc region. A systematic review of nine studies encompassing a total of 22 patients, two of whom were pregnant, found certolizumab to be safe and efficacious for treatment-resistant HS [68]. A 34-year-old woman with Hurley stage 3 HS who stopped adalimumab after becoming pregnant had a significant improvement in HS symptoms after starting certolizumab. She tolerated the medication well and delivered at 40 weeks with no complications [69]. Another 33-year-old pregnant woman with Hurley stage 2 HS and comorbid Crohn's disease experienced an improvement in her HS when taking certolizumab [70]. Data from the UCB Pharma safety database found no increased risk of teratogenic effects or fetal demise amongst 528 pregnancies that

were exposed to certolizumab [71]. Live births resulted from 85.6% (452/528) of pregnancies and of the pregnancies with live births, 44.5% (201/452) were exposed to certolizumab throughout all trimesters [71]. Certolizumab is also considered safe during breastfeeding, as it has minimal excretion into breast milk and is largely undetectable [72]. Certolizumab may be especially useful in patients with comorbid inflammatory disorders such as psoriasis and Crohn's disease, for which certolizumab has established efficacy [73]. Because of its robust safety data, certolizumab can be considered for the treatment of HS during pregnancy and lactation.

### 3.9 Biologics to Be Used With Caution in Pregnancy

#### 3.9.1 Adalimumab

Adalimumab, a TNF $\alpha$  inhibitor, was the first FDA-approved treatment for patients (ages 12+ years) with moderate-to-severe HS [74]. Overall, TNF $\alpha$  inhibitors are the biologic class with the most evidence supporting their use during pregnancy. In general for biologics, placental transfer is minimal during the first and second trimester with increased transfer during the third trimester after organogenesis and critical fetal development have already occurred [75]. The European League Against Rheumatism's 2016 systematic review on the safety of antirheumatic drugs before and during pregnancy and lactation found no significant difference in miscarriages amongst 524 adalimumab-exposed pregnancies (266 prospective, 258 retrospective) when compared to controls [76]. Data from the Organization of Teratology Information Specialists adalimumab pregnancy registry do not support a relationship between adalimumab and birth defects [74]. A prospective controlled observational cohort study of the Organization of Teratology Information Specialists registry found no significant difference in spontaneous abortions, preterm delivery, or major birth defects between pregnant individuals with rheumatoid arthritis or Crohn's disease who were exposed to adalimumab versus the disease-matched control group [74, 77]. There were no differences in the rate of severe infections in infants between the exposed versus non-exposed disease-matched cohorts [77]. Similarly, the Pregnancy in Inflammatory Bowel Disease and Neonatal Outcomes (PIANO) registry found no significant increased rates of spontaneous abortions, prematurity, congenital defects, low birth weight, or infections in the first year of life in neonates born to 869 biologic-exposed women, 279 of whom had exposure to adalimumab [78]. Additionally, one study comparing the birth outcomes of pregnant women with inflammatory bowel disease (IBD) who had received their last adalimumab dose more than ( $n = 73$ ) versus less than ( $n = 447$ ) 90 days before delivery found

no significant differences in the rates of stillbirths and birth defects or differences in infant growth and development [79].

A survey study evaluating HS expert perspectives on management during pregnancy found that 59% (29/49) of respondents have prescribed or continued a biologic in a pregnant patient with HS. Of those that prescribed or continued, 90% (26/29) had used adalimumab [80]. The 2023 Australian IBD consensus statements for preconception, pregnancy, and breastfeeding recommend continuing TNF $\alpha$  inhibitors throughout pregnancy, including the third trimester [81]. Mothers who continue a biologic throughout their pregnancy should be counseled to avoid giving live vaccinations to their infant during the first 6 months of life [82].

It is considered safe for women to continue adalimumab while lactating. One prospective study evaluating the concentrations of various biologics in breast milk found that only 9.5% (2/21) of women taking adalimumab had detectable concentrations in their breast milk [83]. Infants breastfed by biologic-exposed mothers in the study did not have statistically significant differences in developmental milestones or infections within the first year [83]. Furthermore, adalimumab is minimally absorbed by the infant gut [18]. The 2020 American College of Rheumatology guidelines on the treatment of psoriasis during pregnancy strongly recommends continuing adalimumab during breastfeeding [84].

#### 3.9.2 Infliximab

Infliximab, a TNF $\alpha$  inhibitor, is recommended as a second-line therapy for moderate-to-severe HS [2]. No significant differences in congenital malformations or miscarriages were seen across multiple studies including 1161 pregnancies exposed to infliximab in the European League Against Rheumatism systematic review [76]. The PIANO study included 421 pregnant women on infliximab who were found to have no significant differences in maternal and fetal outcomes, including spontaneous abortions, prematurity, low birth weight, congenital anomalies, and infant infections [78]. A 2019 controlled multicenter observational study looking at the outcomes of infants exposed to TNF $\alpha$  inhibitors ( $n = 54$  for infliximab;  $n = 72$  total) in utero found no significant difference in the median rate of infection requiring treatment and/or hospitalization in the year after birth when comparing the exposed and control infants (23.6% [17/72], vs 17.4% [12/69],  $p = 0.36$ ) [85]. There were also no significant differences in growth or psychomotor development between exposed and unexposed children [85]. A Canadian clinical trial evaluating the pharmacokinetics of infliximab over the course of 15 pregnancies of women with IBD found that infliximab trough concentrations increased by 4.2  $\mu\text{g/mL}$  each trimester and spontaneously reverted to pre-pregnancy concentrations during the post-partum period. This was a small study, but authors suggested monitoring

therapeutic drug concentrations in the second trimester and adjusting dosing in the third trimester accordingly [86]. Infliximab can be used with caution during pregnancy.

Infliximab use during lactation is generally considered safe. In a multicenter prospective study of biologic concentrations in the breast milk of breastfeeding women with IBD, infliximab was found in small amounts in breast milk (maximum, 0.74 µg/mL) of 66% (19/29) of mothers and was undetectable in the rest. Infants breastfed by exposed mothers were not found to have significant differences in infections or developmental milestones [83]. The 2020 American College of Rheumatology guidelines on the treatment of psoriasis during pregnancy has strongly recommended continuing infliximab during breastfeeding [84].

### 3.9.3 Secukinumab

Secukinumab is an interleukin (IL)-17A inhibitor that is FDA approved for adults with moderate-to-severe HS. There are limited safety data on its use in pregnancy but among available data, there are currently no indications of increased risk of miscarriage or congenital malformations. In one study of the Novartis global safety database, there were 292 pregnancies with maternal ( $n = 238$ ) or paternal ( $n = 54$ ) exposure to secukinumab during pregnancy, with 153 known pregnancy outcomes. There was no increased rate of spontaneous abortions, stillbirths, or congenital malformations compared with the general population rates [87]. Of note, the majority of patients in this study discontinued treatment within the first trimester. Another retrospective study utilizing the EudraVigilance database looked at ORs for congenital malformations and found no safety signal after exposure to secukinumab during pregnancy ( $n = 128$ ) compared to a biologic with established safety (certolizumab) [88].

In general, TNFα inhibitors are currently preferred over IL-17 inhibitors during pregnancy because of more robust data regarding their safety. However, secukinumab can be exercised cautiously after a thorough risk/benefit discussion in those who have not responded to or have a contraindication to TNFα inhibition.

There is a paucity of data available regarding safety of secukinumab during breastfeeding; however, minimal transfer of secukinumab to breast milk is expected because of its large molecular size [84]. While there are no clear guidelines for use of secukinumab during lactation, it may be considered with caution.

### 3.9.4 Ustekinumab

Ustekinumab, an IL-12/23 inhibitor, is a second-line therapy for HS and should be used with caution in pregnancy and lactation. Similar to adalimumab and infliximab, ustekinumab did not result in significant differences

in spontaneous abortions, preterm birth, low birth weight, congenital malformations, and neonatal infections, amongst 18 exposures according to the PIANO study [78]. One 2022 prospective multicenter observational study found no significant differences in pregnancy or newborn outcomes in 49 pregnant women (54 total pregnancies) exposed to ustekinumab versus controls taking TNF inhibitors [89]. One infant was diagnosed with congenital toxoplasmosis and treated successfully [89]. Ustekinumab concentrations were found to be higher in cord blood than maternal blood in 88.5% (23/26) of cases, reflecting placental transfer of the drug [89]. Children exposed to ustekinumab in utero were not at an increased risk of atopy, growth and psychomotor impairments, infections needing antibiotics, or hospitalization in the first year of life [89]. Ustekinumab use during pregnancy should be exercised with caution but can be considered in patients with uncontrolled HS who have not responded to or who have an absolute contraindication to TNFα inhibition.

Data on breastfeeding while taking ustekinumab are limited. Ustekinumab was found in low concentrations in the breast milk of 66% (4/6) of patients; however, infants breastfed by biologic-exposed mothers in this study were not found to have significant differences in the risk of neonatal infections or developmental milestones [83].

### 3.9.5 Bimekizumab

Bimekizumab, an IL-17A and IL-17F dual inhibitor, was recently approved in November 2024 for the treatment of moderate-to-severe HS in adult patients. Given the minimal pregnancy safety data in humans [90, 91], bimekizumab should generally be avoided in pregnant women at this time in favor of TNFα inhibitors and IL-17A inhibitors with more pregnancy data. However, bimekizumab may still be considered with extreme caution when it is a reasonable clinical scenario to do so (e.g. for a patient with severe HS who has failed or is intolerant to multiple other biologics). A 2024 paper included 11 cases of reported exposure to bimekizumab in pregnant psoriasis patients using the World Health Organization Pharmacovigilance Database [92]. There was no increased risk in adverse pregnancy-related outcomes compared to TNF-α inhibitors. Regarding animal data, one study of pregnant monkeys on doses of bimekizumab up to 38 times the maximum human dosing did not find any adverse developmental abnormalities in exposed infants [91]. In terms of breastfeeding, there is a lack of data on its presence in human breast milk or the effects on infants who are breastfed by exposed mothers [93]. Overall, bimekizumab may be considered with caution during lactation given it is a large protein molecule that is most likely present in low concentrations in breast milk and at



least partial break down by the infant gastrointestinal tract would be expected [18].

### 3.10 Biologics to Avoid Using in Pregnancy

#### 3.10.1 Anakinra

Anakinra is an IL-1 antagonist that can be considered for patients with moderate-to-severe HS who have not responded to anti-TNF $\alpha$  and anti-IL-17 therapies. Anakinra, however, should generally be avoided during pregnancy. A World Health Organization pharmacovigilance database study found a 7.18 OR for fetal musculoskeletal malformations with anakinra exposure during pregnancy [94]. One prospective study of five women taking anakinra during pregnancy resulted in five full-term live births. However, two women developed pregnancy-induced oligohydramnios, and one developed concurrent hypertension. Two of these women breastfed with no issues post-delivery and simultaneously continued taking anakinra [95]. Fetal renal abnormalities have been reported in cases of in utero anakinra exposure; however, it remains unclear whether there is a true association [95]. One retrospective study of 23 pregnant women exposed to anakinra included 39% (9/23) who started anakinra before conception and continued through birth and 35% (10/23) who continued breastfeeding while taking anakinra for up to 10 months. One infant from the anakinra-exposed group developed unilateral renal agenesis and ectopic neurohypophysis [96]. No serious infant infections or developmental concerns were reported in the breastfed infants [96]. A EudraVigilance database study looking at ORs for congenital malformations found no concerning safety signal after exposure to anakinra ( $n = 20$ ) compared with the control (certolizumab) [88]. There are reports of patients continuing anakinra while breastfeeding with no adverse effects on the infants [18]; overall, anakinra may be used with caution during lactation.

### 3.11 Small-Molecule Inhibitors to Avoid Using in Pregnancy

#### 3.11.1 Apremilast

Apremilast, a phosphodiesterase 4 inhibitor, has not been studied in pregnant patients and should generally be avoided [18]. In animals, apremilast crossed the placenta in both mice and monkeys and was associated with fetal demise, insufficient ossification, and a dose-dependent decline in infant birth weight [97]. Although apremilast has not been studied in human breastfeeding mothers, it is recommended to avoid while breastfeeding because of potential systemic absorption of the drug and demonstrated excretion into breast milk of mice [11, 98].

#### 3.11.2 Upadacitinib

Upadacitinib, a Janus kinase inhibitor, is currently undergoing phase III trials for HS [99]. There are limited human data exploring the effects of upadacitinib during pregnancy, but in general, it is not recommended for pregnant patients with HS. An analysis of 128 clinical trial and post-marketing cases of in utero exposure to upadacitinib (mean drug exposure time of 5 weeks and 3 days) did not find any increased rates of spontaneous abortions or congenital anomalies [100]. There is a report of a 36-year-old pregnant woman with rheumatoid arthritis who took upadacitinib during the first 4 weeks of gestation and had a miscarriage at 11 weeks [101]. The FDA label for upadacitinib supports contraception use while taking it and for at least 1 month after upadacitinib is stopped [102]. Animal studies of pregnant rats and rabbits exposed to upadacitinib resulted in skeletal and cardiovascular abnormalities and decreased fetal weight [102]. Upadacitinib has been found in breast milk in animal studies and because of a lack of human studies, should be avoided during lactation [102]. It is recommended to avoid breastfeeding for at least 6 days after the last dose [102].

### 3.12 Traditional Immunosuppressants Used with Caution in Pregnancy

#### 3.12.1 Systemic Corticosteroids

Systemic corticosteroids are used in HS as a pulse therapy for acute flares or for longer courses as a bridge to long-term treatments [2]. Some studies have reported that maternal use of corticosteroids during the first trimester is associated with increased risk of infant cleft lip and/or palate and a drop in birth weight [103]; however, there are conflicting data [104]. The PIANO registry data from 1490 mothers with IBD demonstrated an association between pregnancy corticosteroid use and adverse outcomes, including preterm birth (OR 1.79), low birth weight (OR 1.76), and admission to the neonatal intensive care unit (OR 1.54). Corticosteroid use in the second/third trimesters was linked to a significant increase in the rate of severe neonatal infections requiring hospitalization at 9 and 12 months (4% vs 2%,  $p = 0.03$  and 5% vs 2%,  $p = 0.001$  respectively). Additionally, five corticosteroid-exposed newborns had cleft defects compared with one case in the control group [105]. Prednisolone and prednisone are preferred over dexamethasone because of their more rapid metabolism and lower risk of fetal exposure [106]. It is estimated that for a pregnant women taking an 80-mg daily dose of prednisolone, a negligible 0.1% of this dose would be absorbed by the infant [107]. Corticosteroid excretion into breast milk is minimal. The National Transplantation Pregnancy Registry reported no harm to 169 infants breastfed by mothers taking prednisone while

breastfeeding [108]. Lactation may be temporarily suppressed by high doses of corticosteroids, but no long-term complications have been cited [18]. It is generally recommended to wait 4 hours after a dose to continue breastfeeding to limit infant exposure [107, 109].

### 3.12.2 Cyclosporine

Cyclosporine, a calcineurin inhibitor, can be used for severe, recalcitrant HS [110]. It should be used with caution in pregnancy or breastfeeding individuals. A meta-analysis of cyclosporine use during pregnancy did not find statistically significant increases in preterm deliveries or major malformations [111]. If used during pregnancy, maternal blood pressure and kidney function should be monitored closely [112]. Cyclosporine is found in negligible concentrations in breast milk. The National Transplantation Pregnancy Registry, including data from 1991 to 2013, found that 43 post-transplant mothers taking cyclosporine while breastfeeding 55 infants did not report any significant side effects or complications in the infants. One infant had a transient rise in platelet count and abnormal albumin/globulin ratio that resolved by 16 months [18].

## 3.13 Supplements Generally Considered Compatible with Pregnancy

### 3.13.1 Zinc

Oral zinc may be used as an adjunct therapy [2] and is considered compatible with pregnancy. An umbrella review of meta-analyses evaluating the effect of zinc supplementation on pregnancy and perinatal outcomes noted no adverse fetal and maternal outcomes with exposure of up to 62 mg of zinc daily [113]. If zinc is recommended, patients should be advised to supplement with low-dose copper because of the risk of copper deficiency with excessive zinc supplementation [114]. Zinc is a normal part of breast milk, and levels in breast milk have not been found to fluctuate greatly when doses of 15–25 mg are taken daily [18]. Higher doses can lead to an increase in zinc levels in breast milk, as seen in six mothers with Wilson's disease who took 50–150 mg of zinc daily; all infants who were breastfed had normal development [115].

## 3.14 Procedural Treatments Generally Considered Compatible with Pregnancy

The North American clinical guidelines recommend the utilization of procedures in addition to topical treatments and compatible systemic therapies for the treatment of HS in pregnant patients [2].

### 3.14.1 Intralesional Corticosteroids

Intralesional steroids are considered compatible with pregnancy and can be used as a flare management tool [116] (Table 2). They are also considered safe in breastfeeding because of minimal systemic absorption expected with small doses [18]. However, transient lactation suppression has been reported with larger doses. For example, a patient with 40 mg of triamcinolone with 2mL of 1% lidocaine injected into the wrist for de Quervain tenosynovitis experienced a 90% reduction in lactation, with gradual recovery of 50% at 1 week and a return to sufficient levels at 1-month post-injection [117]. Another patient with 40 mg of triamcinolone injected into the left breast for mastitis experienced lactation suppression for 2 weeks on that side [118]. As a result, the lowest doses needed to provide relief with longer intervals between injections should be used to minimize the risk of lactation suppression.

### 3.14.2 Incision and Drainage/Deroofing

Incision and drainage and local deroofings can be pursued during pregnancy and lactation with minimal maternal or fetal risk. Lidocaine is considered safe when used at standard dosages, with one study demonstrating no fetal abnormalities in 293 infants after exposure to lidocaine during the first trimester of pregnancy [119]. Plain lidocaine is preferred over lidocaine with epinephrine, especially in patients with comorbidities such as hypertension, eclampsia, and gestational diabetes [120]. Povidone iodine should be avoided as the skin preparation agent because of its potential to cause fetal hypothyroidism [120]. Chlorhexidine gluconate can be safely used as an antiseptic in this scenario. Whenever possible, patients should be reclined in the left lateral decubitus position, especially for prolonged procedures, to avoid compression of the inferior vena cava.

## 3.15 Procedural Treatments to Use with Caution in Pregnancy

### 3.15.1 Cryoinsufflation

Cryoinsufflation, a technique involving injection of liquid nitrogen into HS sinus tracts, may be considered during pregnancy. One patient, a female individual with HS who was trying to conceive, opted for cryoinsufflation with 3-monthly treatments, with no recurrence at 6 months and no scarring or hyperpigmentation noted [121].

### 3.15.2 Local Excision

Local excisions can be considered for pregnant patients with HS if clinically warranted and if delaying until after delivery

would be difficult [122]. Any HS surgical procedures requiring general anesthesia should be avoided because of surgical positioning risks as well as fetal exposure to anesthetic agents [122]. There is a report of a 36 year-old pregnant woman with HS who underwent excision of a secondarily infected HS region in her right breast. The patient experienced improvement in her quality of life without any fetal harm and was able to breastfeed after surgery [123]. Data are scarce on patients undergoing excision for HS while breastfeeding. Consider optimizing medical management and delaying the excision of breast HS lesions until the patient is no longer lactating.

### 3.16 Procedural Treatments to Avoid Using in Pregnancy

#### 3.16.1 Botulinum Toxin Injection

In general, it is recommended to avoid botulinum toxin injections during pregnancy [124]. In case reports, botulinum toxin has not led to adverse fetal outcomes in most patients receiving treatment for achalasia, migraine prevention, or cervical dystonia, but there are limited data [125]. As for breastfeeding, toxin was detected in approximately 50% of breast milk samples collected over 5 days from four lactating women who received facial injections of botulinum toxin type A [126]. There are reports of women with botulism breastfeeding their infants with no complications; however, botulinum toxin injections for HS should generally be avoided during breastfeeding because of the lack of safety data [18].

#### 3.16.2 Laser Therapy

It is recommended to avoid laser therapy during pregnancy and breastfeeding [120]. Preliminary data suggest potential safety during pregnancy, but larger studies are still needed. Case reports have reported safely treating urolithiasis during pregnancy with yttrium aluminum garnet and pulse-dye lasers and genital condyloma with carbon dioxide and neodymium-doped yttrium aluminum garnet lasers [125]. Of note, there is a greater risk of hyperpigmentation during pregnancy from lasers, which may be undesirable [120]. Overall, the use of lasers during pregnancy remains controversial and their use should generally be delayed until after delivery unless necessary. There is a paucity of data regarding the use of lasers in breastfeeding patients with HS; however, the risk is likely low [125].

## 4 Conclusions

Safety and efficacy of the various available HS treatments must be considered when developing an appropriate treatment plan tailored to a pregnant or breastfeeding patient with

HS. Both medical and procedural therapies may be considered after a thorough risk-benefit discussion with the patient. Pregnancy and breastfeeding risk factors, comorbidities, and patient preference should also be accounted for when selecting individualized therapies. Patient education and collaboration between dermatology and obstetrics is necessary to optimize management of our pregnant patients with HS.

### Declarations

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