ABSTRACT

In 2014, the US FDA removed the Pregnancy Category Drug lettering system and enacted the “Pregnancy and Lactation Label Ruling.” This ruling required drug products to contain contact information for drug-specific exposure pregnancy registries, narrative-style sections summarizing the known effect of pregnancy, lactation counseling data, and data describing risks for females and males of reproductive potential. This new ruling has added more dialogue and discussion to the patient-provider decision-making process and requires clinicians to provide more individualized counseling based on the current medical literature. This article summarizes the recent evidence for the safety of the most common dermatological therapies for pregnant and lactating women.

KEYWORDS

pregnancy, lactation, dermatologic therapy

INTRODUCTION

During pregnancy, there is an early critical period during the first trimester for the proper structural development of major organs. On average, patients realize they are pregnant at 5.5 weeks in the United States, which can result in unintended exposure to the medication. In addition, about half of all pregnancies in North America are not planned with a medical professional, leading to possible unintended exposure to teratogenic pharmacotherapy. Therefore, in all women of reproductive potential, family planning goals should be regularly addressed in medical office visits involving the management of long-term medications to ensure maternal and fetal well-being.

STRATEGIES TO MITIGATE RISK IN PRACTICE

Medical references discussing medication safety in pregnancy and lactation contain phrases to protect from liability. Risk communication in the form of shared decision-making is a part of the counseling process that educates the patient about choices and alternatives, allowing the patient to make informed decisions. In practice, two significant scenarios require communication regarding medication risk with the patient. In the first scenario, there is risk communication before a therapeutic choice has been made or before pregnancy is initiated. The second scenario occurs when discussing potential side effects after the drug exposure has already happened.

In the first scenario, there are multiple facets to consider, including determining if the patient is currently pregnant or planning a pregnancy and how a
change in her medication regimen or pregnancy status will change the management of her chronic condition. In the case where she was previously controlled on a medication regimen for many years, and this medication has been available for study over many years, an older and more established medication may be the preferred choice. Newer medications have a relatively unappraised risk given they have been studied for a much shorter period than an older one. Counseling should be directed to maximize the control of the maternal dermatologic therapy while preventing fetal harm by using the lowest dose, monotherapy, and non-drug alternatives. In the second scenario, after drug exposure has occurred, risk management relies on an accurate assessment of the specific exposure. Primary resources for counseling include state teratology information services, pregnancy risk information centers, and referrals to prenatal specialists. When counseling the patient, it is best to avoid referring to literature with lower levels of evidence, as well as experimental data and case reports.

Regarding drug risk classification during pregnancy, there are three widely accepted international organizational classification systems: the FASS (Swedish Catalogue of Approved Drugs), US FDA (United States Food and Drug Administration), and ADEC (Australia Drug Evaluation Committee). However, a study of these three systems found that only 26% (61 of 236) of common medications were in the same risk category. A comparison of the US FDA drug classification to the FASS (Table 1) revealed that the former gave considerable weight to animal data. Most medications were placed as class C where the risk could not be ruled out. Overall, the US FDA system had an “innocent until proven guilty” bias toward newer medications, and a study of approximately one thousand physicians and pharmacists in one study found that they favored the European system over that of the US FDA.

In December 2014, to work around the deficiencies in the original system, the US FDA removed the lettering system and enacted the “Pregnancy and Lactation Label Ruling (PLLR),” also known as the “Physician Label Ruling (PLR).” This ruling introduced new labeling requirements, including contact information for drug-specific exposure pregnancy registries, narrative-style sections summarizing the known effect of pregnancy, lactation counseling data, and data describing risks for women and men of reproductive potential. PLLR offered a solution to what many considered an arbitrary system that placed too much weight on newer medications, allowing for more individualized risk-benefit analysis. However, this new system also brought forth new challenges in the complexities of the patient-provider decision-making process, given that it is written in a narrative form and requires a clinician to counsel the patient on the details of this narrative.

### SAFETY OF SELECTED MEDICATIONS IN PREGNANCY

#### ANTI-INFLAMMATORY DRUGS WITH TOPICAL AND SYSTEMIC FORMULATIONS

**Corticosteroids**

Systemic steroids do not interfere with male or female fertility; however, it is optimal that conception should be planned at a period of low disease activity. Maternal systemic steroid use has been associated with lower fetal

<table>
<thead>
<tr>
<th>TABLE 1. Comparison of Drug Classification Systems</th>
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<tr>
<td><strong>US FOOD AND DRUG ADMINISTRATION</strong></td>
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<tr>
<td>Lettering Categories <em>(Discontinued in 2015)</em></td>
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<tr>
<td>A: No risk in 1st, 2nd, or 3rd trimester</td>
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<tr>
<td>B: No risk in 2nd, 3rd trimesters; 1st trimester studies not available</td>
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<tr>
<td>C: Human data not available, animal studies adverse fetal effects</td>
</tr>
<tr>
<td>D: Evidence of human fetal risk</td>
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<td>X: Contraindicated</td>
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gestational age (38 vs. 39.5 weeks), increased rates of premature delivery (17% vs. 5%), and lower birth weight (3112 g vs. 3429 g). Consistent with animal studies, two meta-analyses of systemic steroid use in the first trimester of pregnancy showed a slight increase in major malformations with a significantly associated three-fold risk of oral cleft palate. Oral prednisone is the steroid of choice in pregnancy due to limited placental transfer and rapid placental metabolism compared to betamethasone and dexamethasone, which cross the placenta to a smaller extent. An extensive study of 2658 patients with maternal topical steroid use showed no association between orofacial cleft, preterm delivery, fetal death, or Apgar score. However, there was a risk of low birth weight when the amount dispensed throughout the pregnancy exceeded 300 g.

Phosphodiesterase-4 Inhibitors

Crisaborole is a topical phosphodiesterase-4 inhibitor for the treatment of atopic dermatitis approved in 2016 for adults and in 2020 for infants as young as three months old. The manufacturer makes no specific recommendations on its use in pregnancy or lactation. Transdermal absorption of crisaborole is minimal, with no studies published on its use in pregnant women. Initially approved in 2011 as an oral treatment for chronic obstructive pulmonary disease, in 2022, roflumilast 0.3% cream was approved for plaque psoriasis in patients 12 years and older. Currently, there is no available data on oral or topical roflumilast pregnancy exposure. In animal studies, oral roflumilast administered up to nine times the maximum recommended human dose produced no congenital fetal abnormalities. However, stillbirth, decreased pup viability, and pup post-natal development was observed in mice at doses 5, 15, and 15 times the maximum human recommended dose respectively. The manufacturer does not make a recommendation during pregnancy but states that it should not be used in labor and delivery due to animal studies demonstrating disruption in the labor and delivery process in mice.

Tapinarof

Tapinarof is an aryl hydrocarbon receptor agonist approved in 2022 for use as a topical cream in psoriasis; the exact mechanism leading to its therapeutic action is not fully understood. In rat studies, there was no evidence of mutagenicity or impairment of fertility at subcutaneous doses 268 times the maximum recommended human dose. In the prenatal and postnatal development study, these rats were noted to experience maternal toxicity causing a decrease in body weight gain and food consumption, reduced fetal survival, and litter sizes at 45 times the maximum recommended human dose. There are no published pregnancy exposure data, and there are no specific recommendations from the manufacturer regarding the use of this product during pregnancy or lactation.

Calcineurin Inhibitors

Oral calcineurin inhibitors used for immunosuppression in organ transplant patients are associated with low birth weight or pre-term birth but are not associated with an increased risk of major congenital malformations. Manufacturers recommend topical calcineurin inhibitors be avoided during pregnancy despite low systemic absorption (<5%). The focal use of calcineurin inhibitors may be permissible if first-line topical therapy for atopic dermatitis is insufficient.

Coal Tar

Crisaborole is approved by the US FDA as an over-the-counter topical product. It has been shown to produce mutagenicity in vitro but did not cause a difference in spontaneous abortions or congenital malformations.

Calcipotriene

There are no studies evaluating topical calcipotriene in pregnant or lactating women. The manufacturer states that it should only be used when the benefits outweigh the risks due to its effects on calcium metabolism and supporting systemic studies in animals showing fetal toxicity, incomplete ossification, and skeletal abnormalities.

SYSTEMIC THERAPY FOR PSORIASIS AND ATOPIC DERMATITIS

Previously, Janus kinase (JAK) inhibitors were used in systemic autoimmune disease. Recently, JAK inhibitors have become widely used for multiple conditions, including atopic dermatitis, vitiligo, psoriasis, and alopecia areata. Data for tofacitinib use in non-interventional studies on rheumatoid arthritis and psoriasis have not been associated with the increased risk of fetal death, spontaneous abortion, or congenital abnormalities, however, animal studies of tofacitinib (100 mg/kg/day) have noted the potential for placental transfer and the effects of reduced fetal body weight and the number of viable fetuses. Other JAK inhibitors, such as ruxolitinib (60 mg/kg/day) when given orally in animal models, showed no reduction in viable fetuses, however reduced fetal body weights were observed. The tyrosine kinase 2 inhibitor deucravacitinib was not associated with increased rates of fetal loss or fetal malformations based on information from pre-clinical trials.
**BIOLOGIC AGENTS TARGETING INTERLEUKINS**

The Immunoglobulin G (IgG) monoclonal antibodies class of biologics characteristically have large hydrophilic protein Fc receptor exhibit placental transfer in the late second and third trimester. There have not been adverse outcomes reports for dupilumab, a biologic agent targeting interleukin 4 (IL-4) and IL-13, but this is limited to case reports and case series. In a limited case series of four female patients who took dupilumab, two of whom discontinued the drug before conception, there were no reports of adverse effects on female fertility. Fetal exposure to dupilumab is highest during the third trimester, but the significance of this is not yet known; thus, the decision to use the drug is weighed against the benefits of treating the mother and breastfeeding the infant to the unknown risk associated with fetal exposure.

Exposure to ustekinumab, which targets IL-12 and IL-23, has been reported in 19 pregnant women showing stable placental transfer and antibodies in newborn serum up to 19 weeks, with uneventful outcomes. Despite no teratogenicity or embryotoxicity in animal studies, there are two case reports of ustekinumab use and miscarriage in the first trimester. For secukinumab, which targets IL-17α, manufacturer's global safety database of 238 maternal exposures reported that the rates of spontaneous abortion and congenital abnormalities were similar to the general population.

Human pregnancy exposure data is limited for the newest biologic agents targeting IL-23. A small ad-hoc analysis of clinical trial data for tildrakizumab in 14 pregnant women resulted in four elective abortions, seven full-term births, one late preterm birth, and two spontaneous abortions. In the analysis of clinical trial data of seven guselkumab-exposed pregnancies, there were no reported spontaneous abortions or premature births. There are limited human data on risankizumab, but preclinical animal studies at doses 10x the human AUC (Area Under the Curve), a measure of how much drug reaches a person’s bloodstream in a given period of time after a dose is given, were associated with increased fetal loss rates.

**BIOLOGIC AGENTS TARGETING TUMOR NECROSIS FACTOR (TNF)**

The monoclonal antibodies adalimumab, infliximab, and golimumab exhibit the highest rates of placental transfer compared to either etanercept or certolizumab. A prospective observational cohort study of adalimumab use in 257 women with rheumatoid arthritis or Crohn’s disease who received at least one dose in the first trimester has been associated with an increased risk of preterm delivery but not stillbirth or congenital disabilities. Similarly, a prospective manufacturer’s post-marking database of 1850 pregnancies exposed to infliximab was observed to have no increased risk of pregnancy or fetal complications compared to the general population except if also concomitantly exposed to methotrexate. Because of the placental transfer late in the third trimester, there is a potential concern for systemic immunosuppression in infants within the first 6 to 9 months of life. A single case was reported in 2010 of infant death in a mother taking infliximab 10 mg/kg every eight weeks for Crohn’s disease during pregnancy. In this case, the infant was healthy until receiving the BCG (Bacille Calmette-Guérin) vaccine at three months. He developed disseminated BCG and succumbed at 4.5 months of life.

Due to its lack of a fragment crystallizable (Fc) region, certolizumab is the only PEGylated (polyethylene glycol-modified) anti-TNF demonstrating low placental transfer. A study of 31 women with inflammatory bowel disease (IBD) exposed to certolizumab (n=10) showed low placental transfer compared to those exposed to infliximab (n=11) or adalimumab (n=10), which showed higher antibody concentrations in the infant serum for up to six months. In addition, the prospective post-marketing study of 16 third-trimester pregnancies showed no to minimal placental transfer of the drug, suggesting that the medication may be continued during pregnancy. Etanercept is a fusion protein that can cross the placenta by simple diffusion, and clinical information from the Organization of Teratology Information Specialists (OTIS) Enbrel Pregnancy Registry showed a more significant proportion of major congenital disabilities (9.4%) in etanercept exposed (n=314) compared to a non-exposed cohort (3.5%); however, these findings were found not to be statistically significant.

A post-marketing analysis from 2007 to 2019 of biologics in pregnant women with psoriasis showed overall birth outcomes resulted in 94.7% as healthy newborns, 4.1% with neonatal complications, one stillbirth (a drug not mentioned), and two congenital abnormalities (ustekinumab only). In summary, biologics with minimal placental transfer such as certolizumab pegol or etanercept should be favored. It is ultimately a decision between the medical provider and the patient to determine if the medical benefit for the mother outweighs the risks to the pregnancy and the fetus in the postpartum period due to possible immune alteration of the newborn.
PHOTOTHERAPY

In pregnant women, narrowband (NB) and broadband (BB) ultraviolet B (UVB) light treatment is generally considered the safest form of phototherapy in pregnant women. However, providers should be wary of the potential for the photodegradation of vitamins such as folic acid. Psoralen plus ultraviolet A (PUVA) has been shown to decrease serum folic acid, and psoralen is a potential mutagen that should be avoided. There are data to suggest that NBUVB also has the potential to reduce folate levels when used long-term in patients with psoriasis. Therefore, patients undergoing UVB will benefit from folic acid level monitoring and supplementation.

OTHER SYSTEMIC ANTI-INFLAMMATORY DRUGS

Apremilast is an oral phosphodiesterase-4 inhibitor for psoriasis. Because animal data have shown a dose-dependent increase in abortions/fetal deaths in monkeys at double the human dose, its package insert only encourages its use if the potential benefits outweigh the risks. More data on apremilast exposure is expected as the apremilast exposure registry at clinicaltrials.gov has a study completion date of July 2024.

IMMUNOSUPPRESSANTS

Mycophenolate mofetil (MMF) is used off-label for various dermatological autoimmune conditions, including bullous pemphigoid, dermatomyositis, discoid lupus, cutaneous lupus, vasculitis, and scleroderma. MMF carries a black box warning due to human pregnancy registry exposure data showing first-trimester pregnancy loss (up to 49%) and congenital malformations (up to 27%). There is a Risk Evaluation and Mitigation Strategy (REMS) drug safety program in place to avoid unintended drug exposure. Women of reproductive potential require a minimum of two forms of contraception for at least four weeks before therapy and six weeks after completion if planning a pregnancy. Patients should not use oral contraception alone, given MMF has been shown to influence the efficacy of oral contraceptive pills. Information about male fertility or pregnancy outcomes is limited. Still, according to the manufacturer, effective contraception should be in place for at least 90 days from the last dose to avoid sperm donation during this period.

Azathioprine is associated with preterm delivery and low birth weight in infants, and both hematologic toxicities have been reported. However, safety data support its use in organ transplant patients, autoimmune bowel disease, and rheumatic disease. There is a possible increased risk of congenital malformation, particularly atrial or ventricular septal defects. To prevent the development of leukopenia and thrombocytopenia in newborns, it is essential to halve the dose at 32 weeks gestation if the mother’s leukocyte count is less than one standard deviation below the mean.

Cyclosporine is not the first-line for psoriasis but may be used when clinically indicated for severe psoriasis in pregnancy when the anti-TNF biologic medications are contraindicated. A meta-analysis showed that the prevalence of congenital malformations was similar to that of the general population but may be associated with intrauterine growth restriction. Cohorts of children were followed throughout early childhood with no detectable long-term neurodevelopmental, nephrotoxic, or immunologic effects in the children. In addition, sexual dysfunction has been reported in men but there are no reports of effects on female fertility to date.

Intravenous immunoglobulin

Intravenous immunoglobulin (IVIG) is a safe therapy for recalcitrant pemphigus and pemphigoid gestationis in pregnancy. A study of anti-Ro/La pregnant women found IVIG was safe during pregnancy and prevented recurrent neonatal lupus. IVIG is not embryotoxic but has non-pregnancy-specific risks related to pooled human plasma, such as viral infections, anaphylaxis, and hypercoagulability.

ANTIHISTAMINES

Antihistamines are the treatment of choice in pruritus and urticaria in pregnant patients. First- and second-generation antihistamines have been studied in large numbers and there is no definitive teratogenic risk associated with the antihistamines. Exposure to hydroxyzine during the first trimester has been linked with a slightly increased risk (5.8%) of congenital abnormalities. However, there was no specific pattern identified, so chlorpheniramine, diphenhydramine, or second-generation antihistamines are preferred. In addition, antihistamine use should be limited in the last month of pregnancy due to withdrawals/seizures reported in two infants exposed near term to high dose antihistamines (self-medicating with 150 mg of hydroxyzine a day).

SURGERY, COSMETICS, HAIR, AND ACNE

Anesthetics and Cosmetic Therapy

Both lidocaine only and lidocaine with epinephrine...Continued on page 20
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are recognized as safe for use in pregnancy. Even high volumes (up to 48 ml) of lidocaine for local anesthesia have limited systemic absorption in non-pregnant patients. The addition of epinephrine reduces the placental transfer of lidocaine to the fetus due to localized vasoconstriction. No data indicate intravenous epinephrine or lidocaine are teratogenic or cause fetal harm in dermatological surgery.

Generally, therapy for cosmetic complaints should be avoided in pregnancy if not medically necessary.

**Clostridium botulinum toxin**

While the risk of systemic toxicity of toxin is remote, there are four case reports of mothers developing botulism in second and third trimesters. None of the exposed fetuses were affected due to a lack of placental transfer. In addition, up to 1200 units of botulinum toxin have been used for various medical conditions without adverse effects. An industry-sponsored study of botulinum toxin exposure in 16 first-trimester pregnancies reported no fetal malformations.

**Hydroquinone**

In Senegal, skin-lightening products are commonly used, and exposure to 4% to 8% hydroquinone has been reported in the third trimester. Despite reported studies of up to 35% to 45% systemic absorption in humans, there was no difference in pregnancy outcome with hydroquinone.

**Minoxidil**

Use of oral minoxidil during pregnancy can cause diffuse fetal hypertrichosis that disappears after the first three months of life. However, case reports of topical minoxidil have been associated with teratogenicity, including cases of heart, gut, brain, skeletal, and renal defects; it is recommended that its use be avoided during pregnancy.

**Acne medications**

Topical medications are generally considered safe in pregnancy, and oral antibiotics such as amoxicillin for acne and rosacea patients or cephalosporins for acne vulgaris are well tolerated. Systemic absorption of glycolic acid, salicylic acid, and benzoyl peroxide in pregnancy are limited and unlikely to pose a risk to the fetus. Oral spironolactone has been relatively contraindicated in pregnancy due to its theorized mechanism to cause the feminization of male fetuses. However, a systematic literature review of spironolactone-exposed male fetuses had no evidence of feminization at birth; though animal studies showed feminization at high dosages. Animal data for topical clascoterone, a novel androgen receptor inhibitor, showed congenital deformities and increased rates of spontaneous abortion, so its use during pregnancy should be avoided due to lack of human data. Oral isotretinoin is absolutely contraindicated in pregnancy due to its known teratogenicity in human fetuses; its use in women of reproductive age requires adherence to a strict risk evaluation and mitigation strategy program. Over 25% of isotretinoin-exposed pregnancies develop multiple severe central nervous system (e.g., cerebellar abnormalities, cerebellar malformation, microcephaly), craniofacial (e.g., anotia, absent external auditory canals, cleft palate), cardiac, thyroid, or parathyroid gland abnormalities. These abnormalities can occur up to one month following drug discontinuation. For topical tretinoin, 1% to 2% has been shown to percutaneously absorb with plasma concentrations unchanged after one month of use. Several studies indicate no increased risk of birth defects with topical tretinoin. There are case reports in the literature indicating ear, cerebral, and cardiac malformations, but it is unclear if these were related to the use of tretinoin. Providers should seek to document clearly and carefully in all instances of dermatological treatment during pregnancy.

**ANTIBIOTICS**

In pregnant women, the first line of oral antibiotics includes penicillin, first-generation cephalosporins, and dicloxacillin due to their long history of favorable side effect profiles showing a minimal risk of teratogenicity during pregnancy and safety during breastfeeding. In terms of macrolide-type antibiotics, erythromycin is preferred over azithromycin and clarithromycin due to the latter causing atrial/ventricular septal defects and pyloric stenosis with first-trimester use. In addition, it is vital to use erythromycin base or erythromycin ethylsuccinate formulations, given that erythromycin estolate can cause hepatotoxicity in 10% of second-trimester cases. Clindamycin used either orally or topically is considered safe during pregnancy and used to treat life-threatening peripartum infections such as chorioamnionitis. Rifampin is the choice of therapy in both latent and active pulmonary tuberculosis during pregnancy. In the US, it is standard practice for newborn infants to receive vitamin K injections if exposed to rifampin in the peripartum period due to an increased risk of hypercoagulability; however, a meta-analysis found only low-quality evidence supporting the supplementation of maternal and fetal vitamin K prophylactically.

Multiple smaller retrospective studies have implicated an increased risk of congenital malformations or spontaneous abortion during the first-trimester exposure to trimethoprim and/or sulfonamide. In addition,
sulfamethoxazole-trimethoprim exposure has also been associated with low birth weight and prematurity. However, in 2016, a cohort study of 1.2 million mother-infant pairs found no associated increased risk in mothers compared to others exposed to penicillin or cephalosporin group antibiotics. Conventionally, using folic acid antagonists can increase the risk of neural tube defects. Therefore, it is still recommended that exposure during first trimester should be supplemented with greater than 1 gram of folate.

Quinolone and tetracycline-class antibiotics are generally contraindicated after week 15 of gestation due to previous animal studies and case reports demonstrating permanent damage to cartilage and bone. A meta-analysis of quinolone use during the first trimester found no increased association with miscarriage, preterm birth, or low birth weight. Similar studies of tetracycline-class antibiotic use in the first trimester have not demonstrated a genetic malformation risk.

**ANTIFUNGALS**

**Topical Antifungals**

Safe topical antifungals in pregnancy include nystatin, clotrimazole, miconazole, and ketoconazole due to their poor uptake by skin or mucous membranes; whereas, topical terbinafine, naftifine, and ciclopirox have limited human data, but have not been shown to exhibit teratogenic potential. In addition, over-the-counter products such as zinc pyrithione or topical benzoyl peroxide soap are generally considered safe with limited systemic absorption.

**Systemic Antifungals**

Systemic antifungals in the imidazole class, such as fluconazole, ketoconazole, and itraconazole, are not advised during pregnancy due to the risk of craniosynostosis, congenital heart defects, and skeletal anomalies. In particular, in 2011, the FDA released a safety communication on the potential association of congenital disabilities with long-term fluconazole use due to a trend in case reports. However, in a pharmacoepidemiologic study of over 1 million northern European women, fluconazole use was not significantly associated with an increased risk of stillbirth or fetal demise. The risk remains relatively low in studies evaluating low doses and short-term incidental exposure to fluconazole during the first trimester. Oral griseofulvin is not recommended in pregnancy due to its teratogenic and embryotoxic effects in animals. However, a case-control cohort published in 2015 of approximately 23,000 Hungarian birth defects did not reveal an association between birth defects with griseofulvin use. For oral terbinafine, a sizeable registry-based study of over 1.5 million pregnancies in Denmark over 20 years showed no increased risk of major malformations or spontaneous abortions.

**Antiviral medications**

Acyclovir is the drug of choice during pregnancy to prevent significant herpes simplex virus (HSV)-related neonatal morbidity, and both famciclovir and valacyclovir are likely safe and effective as well. Primary HSV must be treated but routine prophylaxis is not recommended throughout the pregnancy. Prophylaxis can be started at 36 weeks gestation to minimize the risk of transmission through vaginal delivery. For genital warts induced by human papilloma virus (HPV), liquid nitrogen is the treatment of choice, and trichloracetic acid is the preferred medication for condylomata acuminata. For periungual verruca, squaric acid is a non-toxic, non-mutagenic alternative, and injections with intralesional Candida albicans are considered safe. Topical salicylic acid is also a well-tolerated choice for warts and has not been shown to bind platelets or cause Reye’s syndrome. Providers should avoid treating warts with imiquimod, podofilox, and cantharidin during pregnancy. Unsupervised use of imiquimod has been shown to cause poor weight gain and dysfunctional bone ossification in the developing fetus. Topical podophyllin was generally known to be contraindicated in pregnancy due to case reports of fetal death and congenital malformations; however, a cohort study published in 2020 found no association with spontaneous abortion or birth defects in 170 podophyllin-exposed pregnancies.

**Antiparasitics**

For scabies, the drug of choice in the US is permethrin (5% cream). Permethrin is safe for use during pregnancy due to its low systemic absorption (<2%). However, lindane is contraindicated due to its higher potential for systemic absorption (~10%) and strong evidence supporting fetal neurotoxicity and hepatotoxicity in humans and animals.

For lice infestations, first-line treatment is non-medicated occlusive therapy. However, in recalcitrant cases, pyrethrins 0.33% shampoo or benzyl alcohol 5% may be safe and effective. Though unavailable in the US, a study evaluating 25% benzyl benzoate lotion in 444 second- and third-trimester southeast Asian women showed no increased risk of congenital disabilities.

**CONCLUSION**

In summary, providers should avoid roflumilast during labor and delivery, PUVA, all formulations of minoxidil, topical clascoterone, some systemic antifungals, and cosmetic procedures during pregnancy. Preferred therapies during pregnancy include second-
generation antihistamines for itch, topical salicylic acid or oral acyclovir for genital warts, permethrin for parasitic infestations, and certolizumab pegol as biologic therapy for psoriasis. Newer topical and systemic dermatologic drugs lack robust evidence for safe use during pregnancy (e.g., crisaborole, tapinarof, JAK inhibitors, risankizumab, apremilast). For drugs on the market with extensive post-marketing experience but limited to moderate evidence for safety during pregnancy (e.g., oral calcineurin inhibitors, dupilumab, ustekinumab, secukinumab, spironolactone, topical antifungals), the benefits and risk should be carefully weighed before initiation. 

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**Thu M. Truong, PharmD,** is from the School of Medicine, Rutgers New Jersey Medical School, in Newark, New Jersey, and Department of Dermatology, Rutgers Robert Wood Johnson Medical School, in Somerset, New Jersey.

**Marita Yaghi, MD,** is from the Dr. Philip Frost Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, in Miami, Florida.

**Jenny E. Murase, MD,** is from Palo Alto Foundation Medical Group, Department of Dermatology, in Mountain View, California, and University of California San Francisco Department of Dermatology, in San Francisco, California.

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**Address for Correspondence:** Thu Minh Truong, PharmD; Email: tmtruong11@gmail.com