Treatment of Psoriasis in Pregnancy

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PRACTICE **POINTS**

- Robust safety data often are lacking for the use of topical and systemic agents to treat psoriasis in pregnancy.
- Professional society guidelines on the use of systemic agents in pregnancy vary among dermatology, gastroenterology, and rheumatology organizations.

Many women report improvement in psoriasis during pregnancy; others report that psoriasis becomes worse during pregnancy. Balancing effective management of psoriasis against potential risk in pregnancy is important, especially because the severity of psoriasis can have an impact on the pregnancy experience and possibly the outcome. This article discusses current understanding of pregnancy risk profiles of medications used to treat psoriasis.

Cutis. 2020;106(suppl 2):15-20.

Historically, there have been limited data available on the management of psoriasis in pregnancy. The most comprehensive discussion of treatment guidelines is from 2012.[1] In the interim, many biologics have been approved for treating psoriasis, with slow accumulation of pregnancy safety data. The 2019 American Academy of Dermatology–National Psoriasis Foundation guidelines on biologics for psoriasis contain updated information but also highlight the paucity of pregnancy safety data.[2] This gap is in part a consequence of the exclusion and disenrollment of pregnant women from clinical trials.[3] Additionally, lack of detection through registries contributes; pregnancy capture in registries is low compared to the expected number of pregnancies estimated from US Census data.[4] Despite these shortcomings, psoriasis patients who are already pregnant or are considering becoming pregnant frequently are encountered in practice and may need treatment. This article reviews the evidence on commonly used treatments for psoriasis in pregnancy.

Background

For many patients, psoriasis improves during pregnancy[5,6] and becomes worse postpartum. In a prospective study, most patients reported improvement in pregnancy corresponding to a significant decrease in affected body surface area ($P<.001$) by 10 to 20 weeks'

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Dr. Flood has received fellowship funding from AbbVie; Janssen Biotech, Inc; and the National Psoriasis Foundation that went directly to her institution. Dr. Savage reports no conflict of interest. Dr. Porter is a consultant and/or investigator for AbbVie; Bristol-Myers Squibb; Eli Lilly and Company; Janssen Biotech, Inc; Novartis; Pfizer; and UCB. She gave a talk on psoriasis and pregnancy for an honorarium for the National Psoriasis Foundation. Dr. Kimball is a consultant and investigator for AbbVie; Bristol-Myers Squibb; Eli Lilly and Company; Janssen Biotech, Inc; Novartis; Pfizer Inc; and UCB. She serves on the University of California, San Diego, OTIS (Organization of Teratology Information Specialists) Pregnancy Study Scientific Advisory Panels for the Apremilast Pregnancy Exposure Registry (Amgen Inc) and the Ustekinumab Pregnancy Exposure Registry (Janssen Biotech, Inc). Her fellowship program receives funding from AbbVie; Janssen Biotech, Inc; and the National Psoriasis Foundation.
The eTables are available in the Appendix online at www.mdedge.com/dermatology.

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doi:10.12788/cutis.0103

gestation. Most patients also reported worsening of psoriasis postpartum; a significant increase in psoriatic body surface area (P=.001) was observed after delivery.[7] Despite these findings, a considerable number of patients also experience stable disease or worsening of disease during pregnancy.

In addition to the maternal disease state, the issue of pregnancy outcomes is paramount. In the inflammatory bowel disease and rheumatology literature, it is established that uncontrolled disease is associated with poorer pregnancy outcomes.[8-10] Guidelines vary among societies on the use of biologics in pregnancy generally (eTable 1[1,2,9,11-24]), but some societies recommend systemic agents to achieve disease control during pregnancy.[9,25]

Assessing the potential interplay between disease severity and outcomes in pregnant women with psoriasis is further complicated by the slowly growing body of literature demonstrating that women with psoriasis have more comorbidities[26] and worse pregnancy outcomes.[27,28] Pregnant psoriasis patients are more likely to smoke, have depression, and be overweight or obese prior to pregnancy and are less likely to take prenatal vitamins.[26] They also have an increased risk for cesarean birth, gestational diabetes, gestational hypertension, and preeclampsia.[28] In contrast to these prior studies, a systematic review revealed no risk for adverse outcomes in pregnant women with psoriasis.[29]

Assessment of Treatments for Psoriasis in Pregnancy

In light of these issues, treatment of psoriasis during pregnancy should be assessed from several vantage points. Of note, the US Food and Drug Administration changed its classification scheme in 2015 to a more narrative format called the Pregnancy and Lactation Labeling Rule.[30] Prior classifications, however, provide a reasonable starting point for categorizing the safety of drugs (Table[31]). Importantly, time of exposure to systemic agents also matters; first-trimester exposure is more likely to affect embryogenesis, whereas second- and third-trimester exposures are more prone to affect other aspects of fetal growth. eTable 2 provides data on the use of oral and topical medications to treat psoriasis in pregnancy.[1,8,22,32-45]

Topical Agents—Topical steroids are largely understood to be reasonable treatment options, though consideration of potency, formulation, area of application, and use of occlusion is important.[1,46] Risk for orofacial cleft has been noted with first-trimester topical steroid exposure, though a 2015 Cochrane review update determined that the relative risk of this association was not significantly elevated.[32]

The impact of topical calcipotriene and salicylic acid has not been studied in human pregnancies,[1] but systemic absorption can occur for both. There is potential for vitamin D toxicity with calcipotriene[46]; consequently, use during pregnancy is not recommended.[1,46] Some authors recommend against topical salicylic acid in pregnancy; others report that limited exposure is permissible.[47] In fact, as salicylic acid commonly is found in over-the-counter acne products, many women of childbearing potential likely have quotidian exposure.

Preterm delivery and low birthweight have been reported with oral tacrolimus; however, risk with topical tacrolimus is thought to be low[1] because the molecular

Prior System of Categorization Developed by the US Food and Drug Administration to Describe Pregnancy Risk Categories Associated With Various Drugs[31]

Category of Drug	Evidence
A	Adequate, well-controlled studies in pregnant women do not show any risk to the fetus in the first trimester
B	Animal studies did not demonstrate risk to the fetus; no well-controlled studies in humans exist; or animal studies demonstrated risk but well-controlled studies in pregnant women do not demonstrate adverse effects on the fetus
C	Animal studies demonstrate risk to the fetus (this category also applies to drugs for which no animal or well-controlled studies in humans exist)
D	There is evidence of risk to the fetus with these drugs, but their benefits may outweigh risks
X	There is positive evidence of risk that outweighs any possible benefit

size likely prohibits notable absorption.[47] Evidence for the use of anthralin and coal tar also is scarce. First-trimester coal tar use should be avoided; subsequent use in pregnancy should be restricted given concern for adverse outcomes.[1]

Phototherapy—Broadband or narrowband UVB therapy is recommended as second-line therapy in pregnancy. No cases of fetal risk or premature delivery associated with UVB therapy were found in our search.[1] Phototherapy can exacerbate melasma[47] and decrease folate levels[48]; as such, some authors recommend folate supplementation in females of childbearing age who are being treated with phototherapy.[49] Psoralen, used in psoralen plus UVA therapy, is mutagenic and therefore contraindicated in pregnancy.[1]

Oral Medications—Both methotrexate, which is a teratogen, abortifacient, and mutagen,[1] and systemic retinoids, which are teratogens, are contraindicated in pregnancy.[1,47] Acitretin labeling recommends avoiding pregnancy for 3 years posttreatment[50] because alcohol intake prolongs the medication's half-life.[22]

Apremilast use is not documented in pregnant psoriasis patients[51]; an ongoing registry of the Organization of Tetralogy Information Specialists has not reported publicly to date.[52] Animal studies of apremilast have documented dose-related decreased birthweight and fetal loss.[22]

Safety data for systemic steroids, used infrequently in psoriasis, are not well established. First-trimester prednisone exposure has been associated with prematurity, low birthweight, and congenital abnormalities.[38] A separate evaluation of 1047 children exposed to betamethasone in utero failed to demonstrate significant change in birthweight or head circumference. However, repeat antenatal corticosteroid exposure was associated with attention problems at 2 years of age.[39]

Data regarding cyclosporine use, derived primarily from organ transplant recipients, suggest elevated risk for prematurity and low birthweight.[53,54] A meta-analysis demonstrated that organ transplant recipients taking cyclosporine had a nonsignificantly elevated odds ratio for congenital malformations, prematurity, and low birthweight.[42] Cyclosporine use for psoriasis in pregnancy is not well described; in a study, rates of prematurity and low birthweight were both 21%.[43] Limited data are available for Janus kinase inhibitors, none of which are approved for psoriasis, though clinical trials in psoriasis and psoriatic arthritis are underway (ClinicalTrials.gov identifiers NCT04246372, NCT03104374, NCT03104400).

Biologics and Small-Molecule Inhibitors—Limited data on biologics in pregnancy exist[25] (eTable 3). Placental transport of IgG antibodies, including biologics, increases throughout pregnancy, especially in the third trimester.[82] Infants of mothers treated with a biologic with potential for placental transfer are therefore considered by some authors to be immunosuppressed during the first months of life.[2]

Looking globally across biologics used for psoriasis, limited safety data are encouraging. In a review of PSOLAR (Psoriasis Longitudinal Assessment and Registry), 83 pregnancies with biologic exposure resulted in 59 live births (71%); 18 spontaneous abortions (22%); 6 induced abortions (7%); no congenital abnormalities; and 7 reports of neonatal problems, including respiratory issues, ABO blood group mismatch, hospitalization, and opioid withdrawal.[83]

Use of tumor necrosis factor (TNF) inhibitors in pregnancy has the most data[25] and is considered a reasonable treatment option. Historically, there was concern about the risk for VACTERL syndrome (vertebral defects, anal atresia, cardiac defects, tracheoesophageal fistula, renal anomalies, limb abnormalities) with exposure to a TNF inhibitor,[25,84-86] but further reports have alleviated these concerns. Active transplacental transport occurs for adalimumab, infliximab, and golimumab,[87] but given structural differences, transport of certolizumab and etanercept is substantially less.[88,89] In the CRIB study of placental transfer of certolizumab from mother to infant (N=14), pharmacokinetic data demonstrated no quantifiable certolizumab levels in 13 infants and minimal levels in 1 infant at birth.[88] There are fewer data available on the use of other biologics in pregnancy, but for those in which active placental transport is relevant, similar concerns (ie, immunosuppression) might arise (eTable 3).

Concern over biologics largely involves risk for newborn immunosuppression. A case report detailed a Crohn disease patient treated with infliximab who gave birth to an infant who died of disseminated bacille Calmette-Guérin infection at 4.5 months after receiving the vaccine at 3 months.[90] This case underscores the importance of delaying live vaccination in infants born to mothers who were treated with a biologic during pregnancy. Authors have provided various data on how long to avoid vaccination; some state as long as 1 year.[91]

In pregnant females with inflammatory bowel disease treated with a biologic, no correlation was observed among maternal, placental, and infant serum biologic levels and neonatal infection. However, an association between preterm birth and the level of the biologic in maternal and placental (but not infant) serum and preterm birth was observed.[92]

In another report from the same registry, combination therapy with a TNF inhibitor and another immunomodulator led to an increased risk for infection in infants at 12 months of age, compared to infants exposed to monotherapy[89] or exposed to neither agent.[93] A strategy to circumvent this potential problem is to avoid treatment with actively transported molecules in the third trimester.

Conclusion

Limited data exist to guide providers who are treating pregnant women with psoriasis. Our understanding of treatment of psoriasis in pregnancy is limited as a consequence of regulations surrounding clinical trials and inadequate detection of pregnancies in registries. Further efforts are necessary to better understand the relationship between psoriasis and pregnancy and how to manage pregnant women with psoriasis.

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APPENDIX

eTABLE 1. Recommendations on Using Biologics in Pregnancy Differ Across Specialty Societies

Class and Agent	Dermatology	Rheumatology	Gastroenterology	Other Societies (Including Recommendations from Obstetrics-Gynecology and Various Joint Societies)
Biologics generally	SPGSADV: exposure of the fetus to biologics should be avoided from the second trimester onward[11]; Italian Delphi consensus statement: for women who are going to procreate in the medium term, use etanercept[12]; CDA: consensus statement notes minimal transfer of biologics in the first trimester with increasing placental transport throughout pregnancy, with exception of certolizumab[13]	TRAR: biologics should not be prescribed in pregnant patients; assess risks and benefits[14]	None found	None found
TNF inhibitors	NPF: may be used with caution as a third-line agent, given limited experience[1]; NPF-AAD: safe in pregnancy[2]; CDA: studies have not revealed teratogenicity or increased risk of poor maternal-fetal outcomes[13]	BSR, BHPR: can be continued through the end of the second trimester[15]	TCS: recommend continuing TNF inhibitor maintenance therapy; in women at low risk of relapse and a compelling reason to discontinue TNF inhibitor therapy, administer last dose at 22–24 WGA[9]; in women who have a steroid-resistant flare, start anti-TNF treatment[9]; ECCO: low risk, consider stopping at 24 WGA in patients who are in sustained remission[16]; SIGE: women of childbearing potential should avoid pregnancy while on TNF inhibitor therapy; if necessary to control disease activity, benefit of treatment outweighs risk in the first 2 months of pregnancy[17]	ASGHRR: treatment is feasible throughout pregnancy; if a patient is in stable remission, TNF inhibitor therapy may be stopped at the end of the second trimester to decrease exposure to infant[18]; ACOG: low to moderate teratogenic risk, no obstetric complications reported[19]; BSG: counsel on risks; it may be advisable to continue anti-TNF therapy in patients at high risk of relapse or with active disease; in patients with inactive disease who want to stop therapy, it may be reasonable to do so at the beginning of the third trimester[20]; FNAH: after pregnancy occurs, TNF inhibitor therapy should be stopped but may be continued on a case-by-case basis, depending on disease activity, though it should not be used in the third trimester[21]

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eTABLE 1 CONTINUED

Class and Agent	Dermatology	Rheumatology	Gastroenterology	Other Societies (Including Recommendations from Obstetrics-Gynecology and Various Joint Societies)
Adalimumab	APC: limited data, but expert opinion is that it is safe; if washout is desired, stop 10 wk before conception[22]	BSR, BHPR: may continue through the end of the second trimester[15,a]	AGA IBD PPWG: plan last injection 2–3 wk before estimated date of confinement, resume postpartum[23]; WCOG: low risk in pregnancy during first and second trimesters[24]; ECCO: use beyond the second trimester results in neonatal levels greater than maternal levels; to limit exposure, stop treatment approximately 24–26 WGA, when considered appropriate[16]	None found
Certolizumab	APC: limited data, but expert opinion is that it is safe; if washout desired, stop 10 wk before conception[22]; CDA: can be used throughout pregnancy (all trimesters)[13]	BSR, BHPR: may continue throughout pregnancy[15]	AGA IBD PPWG: may continue throughout pregnancy[23]; WCOG: considered to be low risk and compatible during pregnancy[24]	None found
Etanercept	APC: limited data, but expert opinion is that it is safe; if washout desired, stop 15 d before conception[22]	BSR, BHPR: may continue through the end of the second trimester[15,a]	Not used for inflammatory bowel disease	None found
Golimumab	None found	BSR, BHPR: unlikely to be harmful in the first trimester[15]	AGA IBD PPWG: plan last injection 4–6 wk before estimated date of confinement[23]	None found
Infliximab	APC: limited data, but expert opinion is that it is safe; if washout is desired, stop 7 wk before conception[22]	BSR, BHPR: may continue until 16 wk[15,a]	AGA IBD PPWG: plan last infusion 6–10 wk before estimated date of confinement (for dosing every 4 wk, plan 4–5 wk before EDC)[23]; WCOG: considered to be of low risk in the first and second trimesters[24]; ECCO: use beyond the second trimester results in neonatal levels greater than maternal levels; to limit exposure, stop treatment approximately 24–26 WGA, when considered appropriate[16]	None found

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eTABLE 1 CONTINUED

Class and Agent	Dermatology	Rheumatology	Gastroenterology	Other Societies (Including Recommendations from Obstetrics-Gynecology and Various Joint Societies)
IL-12/IL-23 agent: ustekinumab	NPF: no recommendation[1]; NPF-AAD: safety during pregnancy is uncertain[2]; CDA: studies on IL-12/IL-23 inhibitors have not revealed teratogenicity or increased risk of poor maternal-fetal outcomes; data on IL-23 inhibitors is limited[13]; APC: likely safe; limited human data; stop 15 wk before conception as a precautionary approach[22]	None found	AGA IBD PPWG: plan final dose 6–10 wk before estimated date of confinement (if dosing every 4 wk, then 4–5 wk before estimated date of confinement)[23]; TCS: no guidance provided, given limited data[9]	ASGHRR: avoid in pregnancy, given insufficient data[18]
IL-23 agents	NPF-AAD: safety in pregnancy unknown[2]	None found	None found	None found
Risankizumab, tildrakizumab, guselkumab	None found	None found	None found	None found
IL-17 agents	NPF-AAD: guidelines only mention that no human studies exist[2]; CDA: data on IL-17 inhibitors is limited[13]	None found	Not used for inflammatory bowel disease	None found
Secukinumab	APC: likely of low risk, though no human data exist; stop 19 wk before conception as a precautionary approach[22]	None found	Not used for inflammatory bowel disease	ASGHRR: avoid in pregnancy, given insufficient data[18]
Ixekizumab	APC: likely of low risk, though no human data exist; stop 9 wk before conception as a precautionary approach[22]	None found	Not used for inflammatory bowel disease	None found
Small-molecule inhibitors	None found	None found	None found	None found
Tofacitinib	None found	None found	AGA IBD PPWG: recommends considering other options, given limited human data[23]	None found

Abbreviations: SPGSADV, Spanish Psoriasis Group of the Spanish Academy of Dermatology and Venereology; CDA, Canadian Dermatology Association; TRAR, Thai Rheumatism Association Recommendations; TNF, tumor necrosis factor; NPF, National Psoriasis Foundation; AAD, American Academy of Dermatology; BSR, British Society of Rheumatology; BHPR, British Health Professionals in Rheumatology; TCS, Toronto Consensus Statements; WGA, weeks' gestational age; ECCO, European Crohn's Colitis Organization; SIGE, Italian Society of Gastroenterology; ASGHRR, Austrian Societies of Gastroenterology and Hepatology and Rheumatology and Rehabilitation; ACOG, American College of Obstetrics and Gynecology; BSG, British Society of Gastroenterology; FNAH, French National Authority for Health; APC, Australian Psoriasis Collaboration; AGA IBD PPWG, American Gastroenterological Association IBD Parenthood Project Working Group; WCOG, World Congress of Gastroenterology; EDC, estimated date of confinement.

[a]To ensure a low level or no level of drug in cord blood.

eTABLE 2. Data on Using Oral and Topical Medications to Treat Psoriasis in Pregnancy

Agent (Pregnancy Category)	Risk Profile		
	Indication Studied	Study Type	Results
Topical agents			
TCS (C)	Various (dermatologic conditions, pregnant patients)	Cochrane review	No association between TCS (all potencies) and mode of delivery, premature birth, low Apgar score, or birth defects; potent or highly potent TCS are associated with LBW; mild to moderate TCS might be protective against newborn death[32,33]
Topical calcipotriene (C)	Mice	Animal studies	Skeletal abnormalities (abnormal ossification, enlarged fontanelles, development of extra ribs[1,34])
	No well-controlled studies exist in pregnant women[34]		
Coal tar (no category)	Psoriasis	Retrospective study	No change in birth outcomes[35]
Topical salicylic acid (no category)[1]	Not studied in pregnant women[1]		
Anthralin (C)	Not studied in humans or animals[1]		
Topical tacrolimus (C)	Not studied in pregnant women, though adverse outcomes have been observed with oral tacrolimus		
Phototherapy			
UVB (no category)	No cases of risk to the fetus or premature delivery found in our search (limited data)[1]		
PUVA therapy (specifically, psoralen is contraindicated); formulation of psoralen used in psoriasis (C)[1]	Known mutagen; contraindicated in pregnancy		
	Psoriasis	Review of data from the European Network of Teratology Information Services	Of 41 women with PUVA exposure periconception or during pregnancy or both, these pregnancies resulted in 31 LB (1 set of twins), 4 SA, 6 IA, no CM, and 2 LBW infants[36]

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eTABLE 2 CONTINUED

Agent (Pregnancy Category)	Risk Profile		
	Indication Studied	Study Type	Results
Systemic agents			
Corticosteroids (C or D, depending on the label)[1,37]	All indications for corticosteroids	Prospective cohort	Unclear association of LBW, prematurity, and CM,[38,39] especially at higher potencies
	Women at risk of preterm birth	Australasian Collaborative Trial of Repeat Doses of Corticosteroids registry	Increased risk of attention problems at 2 y of age[39]
	Rheumatoid arthritis	MotherToBaby Autoimmune Diseases in Pregnancy study	Increased daily dosage of prednisone associated with increased risk of prematurity[40]
Cyclosporine (C)[1]	All indications for cyclosporine	Meta-analysis	No increased risk of MC or CM[8]
	Mice	Animal studies	Increased prenatal and postnatal mortality and LBW[41]
	Transplant recipients	Meta-analysis[42,43]; registry[44]	Human studies found no statistically significant increased risk for CM[42-44]; human studies suggest increased incidence of LBW and prematurity[43,44]
Acitretin (X)	Contraindicated in pregnancy[1] because it causes retinoid syndrome (318 cases reported[22])		
Methotrexate (X)	Contraindicated in pregnancy[1]		
Apremilast (C)	Human data not available[45]		
	Animal studies	Animal studies	Increased risk for fetal loss in animal studies[22]

Abbreviations: TCS, topical corticosteroid; LBW, low birthweight; PUVA, psoralen plus UVA; LB, live birth; SA, spontaneous abortion; IA, induced abortion; CM, congenital malformation; MC, miscarriage.

eTABLE 3. Data on Use of Biologics and Small-Molecule Inhibitors in Pregnant Patients With Autoimmune Disease

Agent (Pregnancy Category)	Risk Profile		
	Indication Studied	Study Type	Results
TNF inhibitors, generally (B)	IBD	Retrospective cohort study	Increased risk of maternal complications and maternal infections; no increased risk of infection in children; maintenance of TNF inhibitor therapy past 24 WGA did not increase the risk for maternal complications[55]
	IBD, RA, AS, PsA, psoriasis	Registry study	Nonstatistically significant elevated OR for any birth defect, cardiovascular defect, or urinary defect in exposed pregnancies[56]
	Arthritic disease	Meta-analysis	TNF inhibitors were associated with a higher risk of LBW (although the CI included a null value) and lower rate of LB; no significant difference was seen for birth defects, IA, SA, or PTB[57]
	IBD	Meta-analysis	OR for adverse pregnancy outcomes, PTB, LBW, or CA was nonsignificantly increased compared to disease-matched controls[58]
	All indications for TNF inhibitors	Meta-analysis	No significant difference in MC or CM[8]
	IBD, RA, AS, PsA, psoriasis	Prospective study	Significantly higher odds ratio for PTB and C-section and nonsignificant trend for SGA neonates compared to controls treated with nonbiologic systemic treatment; on subgroup analyses the OR for SGA neonates was significant in the RA, AS, PsA, psoriasis group but not the IBD (UC and CD) group[59]
	Autoimmune disease	Prospective study	No elevated risk of MCA compared to disease-matched controls and nonteratogen-exposed pregnancies[60]
Adalimumab (B)[61]	Indication not specified	Review of case reports, cohort studies, case-control studies	No increase in MC or CM[62]
	RA	Prospective cohort study through OTIS	No significant difference in adverse pregnancy outcomes; no pattern of major or minor CM identified[22,63]
	All indications	Meta-analysis	No difference in MC; study demonstrated an increased rate of CM but not when compared to disease-matched controls[8]

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eTABLE 3 CONTINUED

Agent (Pregnancy Category)	Risk Profile		
	Indication Studied	Study Type	Results
Certolizumab (B)[61]	Rheumatic disease, CD, other	UCB Pharma Safety Database	Of 538 known pregnancies outcomes, 459 LB, 47 MC, 27 IA, 5 stillbirths, 8 CM, 2 neonatal deaths[64]
	Indications not specified	Review of registry data and case reports	No increase in malformations or MC was detected[62]
	All indications	Meta-analysis	Nonelevated risk for CM and MC[8]
Etanercept (B)[61]	All indications	Meta-analysis	No difference in MC or CM[8]
	Psoriasis, CIA	Retrospective claims-based study	Prevalence estimates for 1 MCM were 2.0% in psoriasis and 6.0% in CIA with etanercept exposure and 4.2% and 5.5% without exposure, respectively (compared to 4.7% and 5.7% in the general population, respectively)[65]
	Indication not specified	Case reports, cohort studies, case-control studies, registry data	No increase in MC or CM[62]
Golimumab (B)[66]	All indications	Meta-analysis	No evidence of increased risk of CM (though evidence is limited); use alternative agent first[8]
	Indications not specified	Registry data	Overall, data were inconclusive[62]
Infliximab (B)[61]	All indications	Meta-analysis	No increased evidence of MC or CM[8]
	Psoriasis, PsA	Janssen safety database	59 pregnancies resulted in 43 LB (72.9%), 5 SA (1 case with concomitant azathioprine), 11 IA, 4 CA (1 case with concomitant MTX)[67]
	Indications not specified	Case reports, cohort studies, case-control studies, registry data	No increase in MC or malformations identified[62]

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eTABLE 3 CONTINUED

Agent (Pregnancy Category)	Risk Profile		
	Indication Studied	**Study Type**	**Results**
IL-12/IL-23 agent: Ustekinumab (B)[61]	All indications	Meta-analysis	No elevated risk of MC or CM[8]
	Psoriasis	Case series	10 pregnancies resulted in 2 MC and 8 LB including 1 PTB; no birth defects were reported[68]
	Psoriasis, psoriatic arthritis	Company safety database	57 LB resulted in 3 PTB and 1 CA; SA rate (18.4%) was similar to what is seen in the general population[69]
IL-23 agents			
Tildrakizumab[a]	Healthy volunteers, psoriasis, CD	Phase 1 through phase 3 clinical trials	13 pregnancies resulted in 2 SA, 4 IA, and 7 LB without identifiable CM[70]
Guselkumab[a]	No data available in humans[71]		
	Monkeys	Animal studies	No adverse effects in infants; neonatal deaths observed at 6–30 times the MRHD[71]
Risankizumab[a]	Limited data in humans[72]		
	Monkeys	Animal studies	No maternal toxicity; no effects on fetal growth, development, or malformations; dose-dependent increase in fetal and infant loss noted at 20 times the MRHD[72]
IL-17 agents			
Brodalumab[a]	No data available in humans[73]		
	Monkeys	Animal studies	No adverse effects in infants[73]
Ixekizumab[a]	Indications not specified	Lilly Safety System	Outcomes were similar to the Psoriasis Longitudinal Assessment and Registry and US epidemiologic data; 18 pregnancies resulted in 8 LB (44.4%), 5 SA (27.8%), and 5 IA (27.8%)[74]
	Monkeys[75]; not specified[2]	Animal studies	No evidence of teratogenicity[75]; higher rate of neonatal death[2]

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eTABLE 3 CONTINUED

Agent (Pregnancy Category)	Risk Profile		
	Indication Studied	Study Type	Results
Secukinumab (B)[61]	Psoriasis, PsA, AS	Novartis safety database	292 pregnancies (maternal exposure, 238; paternal exposure, 54; known data for 153 pregnancies) resulted in 3 CA and rate of SA similar to that of the general population[76]
	Not specified	Animal studies	No harm[2]
	Psoriasis	Case report	Patient who had hysteroscopic tubal sterilization with microinserts and was treated with secukinumab became pregnant and subsequently had an SA[77]
Small-molecule inhibitor			
Tofacitinib (C)[78,79,b]	All indications	Meta-analysis	High rate of MC with concomitant MTX and tofacitinib exposure; no sign of increased risk of CM[8]
	UC	Tofacitinib safety database	25 pregnancies, 19 with known outcomes (maternal exposure, 11; paternal exposure, 14) resulted in 15 LB, 2 SA, and 2 IA[80]
	RA, psoriasis	Review of randomized controlled trials	47 pregnancies (33 on tofacitinib, 13 on combination tofacitinib and MTX, 1 with blinded therapy) resulted in 7 SA, 8 IA, and 1 case of pulmonary valve stenosis; the remainder were healthy LB (n=25) or lost to follow-up or pending results (n=6)[81]

Abbreviations: TNF, tumor necrosis factor; IBD, inflammatory bowel disease; WGA, weeks' gestational age; RA, rheumatoid arthritis; AS, ankylosing spondylitis; PsA, psoriatic arthritis; OR, odds ratio; LBW, low birth weight; CI, confidence interval; LB, live births; IA, induced abortion (or medication termination or therapeutic abortion); SA, spontaneous abortion; PTB, preterm birth; CA, congenital abnormality; MC, miscarriage; CM, congenital malformation; SGA, small for gestational age; UC, ulcerative colitis; CD, Crohn disease; MCA, major congenital anomalies; OTIS, Organization of Teratology Information Specialists; CIA, chronic inflammatory arthritis; MCM, major congenital malformation; MTX, methotrexate; MRHD, maximum recommended human dosage.

[a]No pregnancy category.

[b]Per 2012 product insert. 2018 product insert did not have a pregnancy category.