

Current Evidence on IL-17 and IL-(12)/23 Inhibitor Safety during Pregnancy in Psoriasis: A Call for Harmonized Data Collection

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The onset of psoriasis often coincides with a patient's reproductive years (1). However, evidence regarding the safety of biologics during pregnancy, and effects of paternal exposure, remains limited. High disease activity during pregnancy is associated with an increased risk of adverse pregnancy outcomes (2), creating a dilemma in clinical practice: weighing the risks of continuing treatment to prevent disease flares against the uncertainty regarding the potential impact of medication exposure on perinatal health. Yet, information on using interleukin (IL)-12/23, IL-17 and IL-23 inhibitors during pregnancy is lacking in clinical guidelines due to limited available data (3, 4). Therefore, we aimed to determine which data on reproductive safety of these biologics are currently available and what additional evidence is still needed to develop guidelines for clinical practice.

METHODS

We performed a systematic literature review (May 2026), according to PRISMA guidelines, to identify publications assessing exposure to IL-12/23, IL-17 and IL-23 inhibitors before conception and during pregnancy (maternal and paternal exposure) and its effect on pregnancy and neonatal outcomes (PROSPERO registration #CRD420251080922). We included primary publications when pregnancy and/or neonatal outcomes were reported per biologic class, independent of the indication for which the IL inhibitor was prescribed. Animal or *in vitro* studies, abstracts and non-English publications were excluded (Appendix S1 and S2).

RESULTS

The search yielded 5,849 records; 144 full-text articles were retrieved to assess eligibility, of which 49 met the inclusion criteria. These included 21 case reports, 11 case series, 11 cohort studies and 6 studies using secondary data sources, reporting a total of 5,962 pregnancies after maternal exposure to IL-12/23, IL-17 and IL-23 inhibitors. Most studies involved ustekinumab (2,933 pregnancies) followed by secukinumab

(1,877 pregnancies), with fewer data available for risankizumab (589 pregnancies), ixekizumab (296 pregnancies), guselkumab (217 pregnancies), tildrakizumab (32 pregnancies), bimekizumab (11 pregnancies), brodalumab (6 pregnancies) and mirikizumab (1 pregnancy). Three studies reported on paternal exposure of either ustekinumab (133 pregnancies), ixekizumab (9 pregnancies) or secukinumab (54 pregnancies) (Appendix S3-S7).

DISCUSSION

At first glance, data on a considerable number of pregnancies appeared to be available. However, conducting a methodologically robust meta-analysis was not feasible for several reasons.

First, the included publications comprised data derived from heterogeneous sources that were collected using different study designs and data sources and are therefore hard to pool. A substantial number of exposures ($N=5,074$) originated from studies that relied on pharmacovigilance databases (Vigibase and Global Safety Databases from pharmaceutical companies), which contain spontaneous reports of adverse events. A strength of these databases is that they capture large real-world patient populations, enabling the detection of safety signals (5). However, exposed pregnancies without adverse outcomes are not reported, making it impossible to estimate incidence or prevalence rates or to establish whether the observed frequency of adverse pregnancy or neonatal outcomes differs from patients with psoriasis using no or other medication during pregnancy. Additionally, reported cases in these databases are often incomplete, unvalidated, and susceptible to bias due to under- or over-reporting of specific events (5, 6). Therefore, studies based on pharmacovigilance databases are not considered suitable for inclusion in a meta-analysis evaluating the safety of drug exposure during pregnancy. In addition, 2 studies combined data from pharmacovigilance databases with clinical trials and postmarketing registries, without clearly distinguishing which data originated from which source.

Second, included publications lacked important information on patient and clinical characteristics that

could bias the estimated effect of exposure during pregnancy on pregnancy and neonatal outcomes. This included information on the timing of exposure and confounders such as disease activity during pregnancy, comorbidities, intoxications and comedication. For example, for 11 of the 16 cohort studies and studies using secondary data sources, information on exposure timing was (partially) unknown.

In addition, among the studies identified, only one conducted a confounder-adjusted analysis and accounted for time-related biases (7). The included cohort studies and studies using secondary data sources compared outcomes following exposure to IL-12/23, IL-17 or IL-23 inhibitors with outcomes among patients exposed to other medication ($n=10$), patients not using medication ($n=2$), or the general population ($n=2$). In 5 studies no reference group was included. Lastly, generally insufficient numbers of exposed pregnancies were included to adequately assess (rare) adverse pregnancy and neonatal outcomes. This review predominantly included data from patients with inflammatory bowel disease (IBD), limiting the feasibility of conducting disease-specific analyses for psoriasis. Similarly, subgroup analyses by biologic class were constrained, particularly for IL-17 inhibitors. In contrast to several other biologic classes that are approved for multiple immune-mediated inflammatory diseases, IL-17 inhibitors are not approved for the treatment of IBD. Consequently, studies including patients with IBD do not contribute data on IL-17 inhibitors, resulting in a comparatively smaller body of evidence for this biologic class.

Despite the limitations described above, it is important to note that the findings of the included cohort studies and studies using secondary data sources are reassuring about maternal exposure to IL-12/23, IL-17

and IL-23 during pregnancy. No signal for an increased risk of adverse pregnancy or neonatal outcomes was detected, except for one study that reported an increased risk of infants being born small for gestational age following ustekinumab exposure in pregnancy.

Data regarding paternal exposure to IL-12/23, IL-17 and IL-23 inhibitors is scarce (3 studies, 281 pregnancies). Paternal use of these medications may impact pregnancy outcomes via (epi)genetic changes in sperm or immunological changes in the composition of seminal plasma (8, 9). As existing data is reassuring, although limited, current guidelines recommend to continue biologics during spermatogenesis/when planning a pregnancy (4).

Our systematic literature search provides valuable insight into the current state of knowledge in this field. However, it also shows that high-quality epidemiological studies are scarce, despite being essential to inform clinical decision-making regarding the safety of these medications during pregnancy (7, 10–12). Robust research strongly depends on the availability of valid and detailed longitudinal data. Collecting prospective data on a sufficient number of pregnancies with rare exposures (and appropriate reference groups) are inherently challenging and require a standardized manner of data collection and international collaboration. Several initiatives actively collect data on medication exposure, pregnancy outcomes and disease characteristics, like MotherToBaby (13).

However, given the importance of detailed disease characteristics for evaluating medication safety in pregnancy, we additionally advocate for an expanded role of existing psoriasis registries (e.g. BADBIR, BIOBADADERM, BioCAPTURE, DermBio, PsoBest, PsoReg), which are established in many countries.

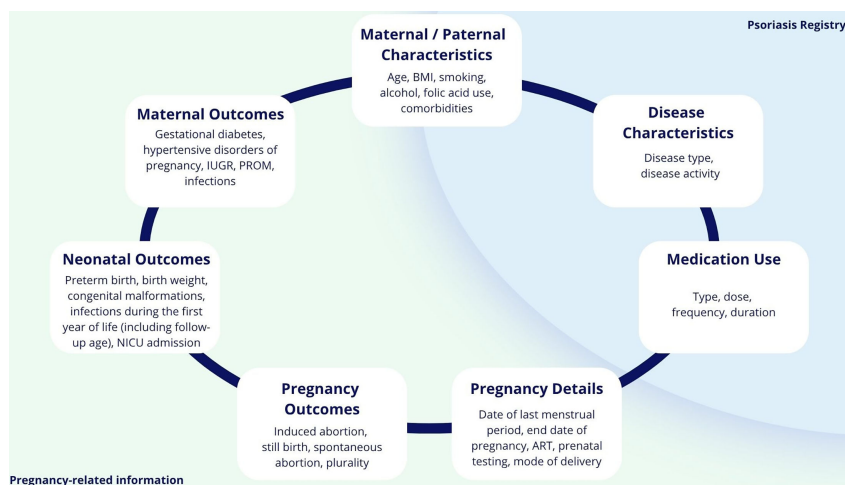


Fig. 1. Schematic overview of psoriasis registry and pregnancy-related variables required for reproductive safety studies in patients with psoriasis. This figure is based on the framework proposed by Richardson et al., in which these variables are described in greater detail (14). BMI: Body Mass Index; ART: Assisted Reproductive Technology; NICU: Neonatal Intensive Care Unit; IUGR: Intra-Uterine Growth Restriction; PROM: Premature Rupture of Membranes.

Such registries often already collect data at regular intervals on patient, disease and treatment characteristics. In particular, disease activity represents a critical confounding variable when studying the safety of biologics during pregnancy, given its association with adverse pregnancy and neonatal outcomes. To ensure the reliability of statistical analyses, it is essential to adjust for this factor. Since clinical information on disease activity is often insufficient in pregnancy registries, disease-specific registries could play an important role in providing this information. With the addition of a minimal standardized dataset on pregnancy and infant health, in combination with the clinical information that is already captured in the registry, existing psoriasis registries could efficiently be used to study the safety of biologics during conception and pregnancy (**Fig. 1**). A list of the minimum required variables for conducting robust studies on medication safety in the preconceptional period and during pregnancy has been extensively described previously (14). Alternatively, efforts could be made to integrate data from psoriasis registries with existing prospective pregnancy outcome registries (e.g. registries from teratology information services or birth cohorts).

Overall, although we identified a substantial body of evidence on IL-12/23, IL-17 and IL-23 inhibitor safety during pregnancy, definitive conclusions were too difficult to draw because of important methodological limitations and heterogeneity in the existing data. It is therefore crucial to bring together data on psoriasis and pregnancy through standardized data collection and international collaboration. This can facilitate meaningful progress in generating evidence on the safety of medications during this critical life stage for patients with psoriasis.

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