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# Biologic Therapy for Severe Asthma During Pregnancy: Emerging Evidence on Maternal and Fetal Safety

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**Abstract** **Background:** Uncontrolled severe asthma during pregnancy is associated with maternal and fetal risks, whereas the pregnancy-specific safety evidence for biologic therapies remains limited. This narrative review considers pregnancy outcomes reported after exposure to omalizumab and newer biologics, distinguishing pregnancy-specific observations from efficacy evidence established in nonpregnant populations. **Methods:** PubMed, Scopus and Google Scholar were described as sources for English-language or other available publications from 2015 to 2025, including pregnancy registries, observational cohorts, case series and relevant reviews. **Results:** Pregnancy-specific observational evidence is most extensive for omalizumab, without a consistent signal of major congenital-malformation excess in the cited literature; however, selection bias, confounding and incomplete long-term follow-up limit causal inference. Data for mepolizumab, benralizumab, dupilumab, reslizumab and tezepelumab are substantially more limited. Benefits established in general severe-asthma trials should not be described as demonstrated pregnancy-specific effects. **Conclusion:** Decisions about continuing or initiating biologic treatment during pregnancy require individualized assessment of asthma severity, alternatives and the uncertainty of agent-specific reproductive safety data. Pregnancy registries, prospective comparative follow-up and coordinated maternal–fetal care are needed; this narrative review does not establish the safety or effectiveness of every agent in pregnancy.

**Key Words** Severe Asthma, Pregnancy, Biologic Therapy, Omalizumab, Pregnancy Registry, Maternal Outcomes, Fetal Safety

## INTRODUCTION

Pregnancy represents a special management issue with severe asthma: uncontrolled disease exposes both maternal and fetal conditions (preterm birth, low birth weight) and fetal development; most advanced therapies have no strong pregnancy-specific safety data. In the past 10 years, biologic therapies, including monoclonal antibodies targeting IgE (omalizumab), IL-5 (mepolizumab, reslizumab, benralizumab), IL-4/IL-13 signaling (dupilumab), and upstream alarmins Thymic stromal lymphopoietin TSLP (tezepelumab), have revolutionized the management of individuals with severe asthma by dramatically reducing exacerbations and corticosteroid dependence and also enhancing control and quality of life. The therapeutic revolution, thoroughly reported in current reviews and clinical trials, poses a practical question that clinicians increasingly encounter: how to balance the proven benefits of biologics in improving maternal respiratory health with inadequate, emerging evidence on pregnancy safety [1].

Biologic exposure data in pregnancy are sparse, but increasing. Omalizumab has the best experience with pregnancy (no apparent increase in the rate of significant congenital anomalies relative to background rates so far in the registry and in other observational studies, and a large number of professional reviews have considered omalizumab a reasonably well-characterized agent when used during pregnancy) [2]. Nonetheless, the findings are mainly based on observational studies rather than randomized trials, thereby retaining some uncertainty [3].

The most recently approved biologics targeting eosinophils (mepolizumab, benralizumab), IL-4/IL-13 pathways (dupilumab), and TSLP (tezepelumab) have limited evidence regarding use in pregnancy. Available data are largely derived from case reports, small case series, pregnancy registries with few exposures, and extrapolation from mechanistic pharmacology. These agents are mostly IgG antibodies, which can cross the placenta, particularly during the second and third trimesters. Separate case reports of the successful continuation of drugs like mepolizumab or

dupilumab during pregnancy with maternal benefit and no apparent significant neonatal harm have been reported. However, such reports cannot provide reliable estimates of the rate of rare adverse events or long-term outcomes. As a result, safety inferences should be reserved [4].

Clinical guidance is increasingly emphasizing a risk–benefit approach. Uncontrolled severe asthma, characterized by recurrent exacerbations or repeated courses of systemic corticosteroids, may pose greater overall risks to both mother and fetus than the continued use of targeted biologic therapy. In many patients, the goal is disease control with the least dose of systemic steroids. It is therefore advised that shared decision-making, multidisciplinary involvement (obstetrics, maternal-fetal medicine, respiratory/allergy specialists), and close monitoring be considered when deciding to initiate or continue biologics in pregnancy. Meanwhile, clinicians are advised to inform patients about the limitations of existing evidence and the importance of reporting outcomes to registries to build stronger knowledge in the future [5].

### Aim of Work

This work is an attempt to critically evaluate the emerging evidence on biologic therapies of severe asthma in pregnancy. In particular, it will: (1) look for maternal and fetal safety data of registries, case reports, and pharmacokinetic studies; (2) enlighten regarding the benefits and risks of various biologic agents during pregnancy; and (3) offer practical clinical awareness to initiate or continue biologic treatment in pregnant patients, through a risk-benefit framework, to facilitate informed, shared decision-making by patients and multidisciplinary care teams.

## METHODS

This narrative review drew on publications from 2015 to 2025 indexed or located through PubMed, Scopus and Google Scholar, using combinations of asthma, pregnancy, biologic therapy and individual agent names (omalizumab, mepolizumab, benralizumab, dupilumab, reslizumab and tezepelumab). Pregnancy registries, observational studies, case series and relevant reviews were considered; evidence from non-pregnant severe-asthma trials was used only for = efficacy information.

## RESULTS

The papers in this review examine the multifaceted interplay between severe asthma and pregnancy, including disease control, maternal and fetal outcomes, and the emerging role of biologic therapies. They also assess the safety, efficacy, and potential adverse effects of FDA-approved biologic treatments for severe asthma in pregnant women whose symptoms remain inadequately controlled despite standard therapy. The articles included in this review were those written between 2015 and 2025. Results are presented in the discussion section, including: maternal and fetal risks of uncontrolled asthma; standard pharmacologic/non-pharmacologic management of asthma in pregnancy; placental transfer; safety data related to biologic therapies; and the advantages and risks of biologic treatments for severe asthma in pregnancy.

Evidence synthesis principle: pregnancy-exposed cohorts and registries inform observed reproductive outcomes, whereas severe-asthma clinical trials conducted outside pregnancy inform expected therapeutic mechanisms and general-population efficacy. Small case series and spontaneous safety reports cannot estimate absolute risks reliably; non-significant comparisons cannot establish equivalence or absence of harm.

### Asthma and Pregnancy

Asthma is one of the most prevalent of the chronic illnesses in pregnancy and has been estimated to affect 6.5% of adults in the UK [6]. It is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms, such as wheeze, shortness of breath, chest tightness, and cough, that vary over time and in intensity, together with variable expiratory airflow [7].

The physiological changes in the respiratory system during pregnancy are well documented and include: heightened oxygen requirements and an increase in minute ventilation during early pregnancy; later on, a rise in the diaphragm to accommodate the pregnancy, leading to a decrease in tidal volume. It is also worth noting that forced expiratory volume in 1 second, forced vital capacity, and peak expiratory flow rate (PEFR) are not influenced by pregnancy [8].

Pregnancy may also alter the severity of asthma, with a quarter of this deterioration believed to be due to several proposed mechanisms, including hormonal and mechanical pregnancy changes, greater vulnerability to viral infections, and poor treatment adherence. Women tend to blame dyspnoea on the pregnancy instead of the worsening of the asthma control, and under-treatment may result [9].

In most women, the adverse effects are not significant. However, when asthma is exacerbated and poorly controlled, there are observed relationships with low birth weight, preterm birth, and intra-uterine growth restriction. It is also related to elevated rates of pre-eclampsia, gestational diabetes, and caesarean section (CS). Asthma can be actively managed, and thus the risk of preterm birth can be reduced to insignificant levels, and if asthma is managed correctly, there is a low chance of worse outcomes [10].

Mechanistically, the aggravated asthma management in pregnancy can be due to hormonal and immunologic modifications, physiologic alterations, and the decline in adherence to medication [11]. Considering these risks, clinical guidance highlights that the overall maternal benefits of maintaining asthma control outweigh the risks of asthma medications.

## DISCUSSION

### Asthma Management in Pregnancy

Uncontrolled asthma in pregnancy is linked with poor maternal prognosis, pre-eclampsia, and gestational diabetes, and poor fetal prognosis, including preterm birth, low birth weight, and high rates of neonatal ICU hospitalization.

Asthma management during pregnancy focuses on symptom control, the prevention of exacerbations, and the preservation of maternal lung function to ensure the fetus receives adequate oxygen [12].

The assessment is important at an early age and regularly. Women are supposed to be assessed during early pregnancy to determine the control of asthma, inhaler use, and compliance with medication. Control can be measured using objective measures, including peak expiratory flow rate (PEFR) and fractional exhaled nitric oxide (FeNO). In contrast, individualized asthma action plans support self-management and enable timely intervention when symptoms worsen [13]. Regular follow-up enables dose adjustments and the introduction of other therapies as needed.

Pharmacologic care during pregnancy is usually similar to the non-pregnant care because the risks of drugs are less than the benefits of managing asthma. ICS are the primary controller therapy and have not been linked to higher risks of congenital malformations, preterm birth, and low birth weight when used at prescribed doses [14]. SABA (salbutamol) is also considered safe for symptom management (NCBI Bookshelf). The new GINA update preferred track is ICS-Formoterol as needed or as maintenance, or the alternative track with long-acting $\beta_2$-agonists (LABA) combined with ICS can be used in patients who need step-up therapy [15]. Long-acting muscarinic antagonists (LAMA) and Leukotriene receptor antagonists (LTRAs) can be considered in cases where additional control is required, and there is no evidence of high teratogenicity. Systemic corticosteroids such as prednisolone are not contraindicated in acute exacerbations when indicated, but some initial research has suggested a slight risk of cleft palate; overall, research supports their use when the benefit to the mother outweighs the potential risk to the fetus [16].

Biologic therapies targeting IgE or interleukins can be considered for patients with asthma that is not adequately controlled by standard therapy. Even though such studies in pregnancy have not been conducted in randomized controlled trials, pregnancy registries, case histories, and observational studies suggest that these agents may continue to be used following a personal risk-to-benefit evaluation [17].

Management also focuses on treating modifiable triggers and comorbidities. Gastro-oesophageal reflux, which is typical in pregnancy, must be treated to avoid aggravation of symptoms. It is highly recommended that smoking cessation be done, and tobacco consumption exacerbates the risk. Asthma is supposed to deteriorate during respiratory infections, which should be treated early. It is advisable that pregnant women with asthma receive vaccinations, especially influenza and COVID-19 vaccines, because infections may lead to severe exacerbation and impose unfavorable outcomes [18]. Recent research also indicates that gestational diabetes can lead to the increased likelihood of asthma exacerbations, which explains the significance of close observation in women with comorbidities [19].

Non-pharmacologic interventions complete medical therapy. Exacerbations are prevented by trigger avoidance, such as allergens, smoke, and irritants; the patient is educated on the proper inhaler technique and adheres to a written asthma action plan [20]. Obstetricians, pulmonologists, and primary care providers are advised to provide interdisciplinary care to achieve the best maternal and fetal outcomes [21].

Management of exacerbations follows conventional procedures but requires adjustments to accommodate pregnancy. Severe cases can be treated with oxygen supplementation, nebulized β-agonists, systemic corticosteroids, and magnesium sulfate, under the supervision of multidisciplinary personnel to secure maternal stabilization and fetal safety [22].

Despite having clear guidelines, research indicates a high level of poorly controlled asthma, inadequate inhaler use, and absence of written asthma action plans among pregnant women. Adherence, medication regimen optimization, and asthma self-management education are thus crucial for ensuring good pregnancy outcomes [18]. Conclusively, proper management of asthma during pregnancy focuses on controlling symptoms through regular treatment, avoiding triggers, and close observation. The health of the mother and the fetus is best preserved by reassuring patients about the safety of the medicines and by offering individualized management strategies.

## Biologic Therapy of Severe Asthma during Pregnancy and its Safety

The application of biologic therapies has transformed the treatment of severe, type 2 (T2) asthma by significantly reducing attacks, reducing the need for systemic corticosteroids, and improving quality of life (QoL) in patients who are unresponsive to conventional therapy [23]. Such benefits render biologics especially appealing to pregnant women with severe asthma that is hard to manage, but still, the issues of fetal exposure and safety are significant.

Asthma biologics are monoclonal antibodies composed of IgG molecules, which are known to cross the placenta via the neonatal Fc receptor (FcRn). The relatively early onset of placental transport, which rises during the third trimester, results in fetal IgG levels that are close to maternal levels at birth [24]. As a result, newborns of women exposed to biologics can possess meaningful levels of circulating drugs, which increases the hypothetical risks of harming and benefiting a newborn [25].

The EXPECT registry is one of the most informative sources of pregnancy exposure, as it enrolled more than 250 women with asthma treated with omalizumab. No significant major congenital anomalies, preterm births, or small-for-gestational-age (SGA) babies were observed in this cohort compared with disease-matched asthma controls [24]. One of the main areas of safety information is a global pharmacovigilance study that was based on the VigiBase database and included reports on multiple asthma biologics:

omalizumab, mepolizumab, reslizumab, benralizumab, and dupilumab between 1980 and 2023. In the research, 15,715 pregnancy-related reports were identified and examined using reporting odds ratios (RORs) to compare the frequency of adverse outcomes among women on biologics versus non-biologic asthma medicines [26].

The reslizumab was identified as one of the results with a lower overall reporting frequency of adverse events (ROR = -0.19, 95% CI: 0.05-0.67), and there were no strong safety signals in spontaneous reports [27]. Conversely, omalizumab, mepolizumab, and dupilumab were found to have an increased number of original cases of fetal death than other drugs. In particular, the omalizumab ROR was approximately 3.88, mepolizumab approximately 1.87, and dupilumab approximately 5.34 [26]. Nevertheless, the same agents demonstrated lower rates of late-pregnancy complications, including preterm birth: omalizumab ROR = -0.22, mepolizumab = -0.10, and dupilumab = -0.07 [24]. Conversely, benralizumab showed a somewhat different trend: it was less frequently reported to have spontaneous fetal death (ROR 0.69) and spontaneous abortion (~0.47), but higher rates of delivery complications, such as preterm birth (ROR 0.46). The authors clearly interpret these as associations rather than evidence of causality, and their data indicate that future mechanistic and registry-based research is necessary to elucidate risk [28].

In addition to accumulating pharmacovigilance data, there is an increasing international professional consensus supporting the use of biologic therapies during pregnancy. A Modified-Delphi study of 141 severe-asthma experts in 32 countries found that biologics could be continued or initiated during conception and pregnancy, provided joint decisions were made (shared decision-making) and care was integrated, preferably through obstetric and respiratory teams [15]. This agreement also proposes continuing biologics even during breastfeeding, suggesting that the clinical benefits tend to outweigh the hypothetical risks.

In addition to the pharmacovigilance and consensus data, a literature review of atopic-disease pregnancies (including asthma) of some 313 pregnancies exposed to biologics (omalizumab, mepolizumab, reslizumab, benralizumab, dupilumab, tezepelumab, and tralokinumab) did not show any evidently increased rates of preterm birth, stillbirth, low birth weight, or congenital malformations [29]. With that said, the authors point out that evidence is limited: the majority of available evidence is presented in case reports or small observational series, rather than randomized controlled trials.

In the case of omalizumab, country-based cohort studies are reassuring. As an example, a retrospective study comparing 20 pregnant women who received omalizumab (and their 23 newborns) reported no congenital abnormalities; some infants were found to have low birth weights (13%), or were preterm (22%), but these events also might have been due to the severity of maternal asthma and not a drug effect [30]. Also, case reports dating back to older times report about two women with highly severe asthma who used omalizumab during pregnancy and gave birth to healthy children at term without exacerbations during pregnancy [31]. More recently, a larger case series (22 pregnancies) reported that approximately one-third of patients experienced exacerbations, although overall delivery outcomes were satisfactory and no significant teratogenic effects were observed [32].

Biologics have strong evidence of reducing exacerbations and sparing systemic corticosteroid use in non-pregnant patients. A systematic review with supporting evidence for EAACI guideline recommendations found that benralizumab, dupilumab, mepolizumab, omalizumab, and reslizumab were all associated with a significant reduction in exacerbation rates (high-certainty evidence). Some of them (benralizumab, mepolizumab) were associated with a significant reduction in oral corticosteroid use [23].

According to safety, outside of the outcome of pregnancy, it is also worth mentioning that biologics are associated with an anaphylaxis possibility. In an FDA Adverse Event Reporting System-based pharmacovigilance study, positive signals were identified in anaphylaxis with omalizumab, benralizumab, reslizumab, and mepolizumab, but not dupilumab [33]. This risk must be included in clinical decision-making, particularly during pregnancy, when maternal and fetal stability are most important.

Clinical practice recommends that biologics should not be discontinued during pregnancy, but should be used cautiously. In a case in point, Canadian expert advice indicates further use of biologic therapy in those patients who are already on it, since their chances of exacerbation are increased with the discontinuation of the treatment [34]. Since all therapeutic antibodies are IgG-based and can cross the placenta to varying degrees, no credible signal of teratogenicity has been detected in humans [35]. However, it requires long-term follow-up and more robust research; current registries on benralizumab and mepolizumab, such as the one, are continuing to gather additional data [34]. A more comprehensive safety review based on VigiBase (not pregnancy-related) also indicated uncommon yet relevant potential risks of biologics like autoimmune diseases, cancer, and thromboembolic processes [36]. Although these are not specific to pregnancy, they signify the need to exercise caution whenever these therapies are used in any patient group particularly during gestation.

However, despite the positive statistics, there are still critical gaps. Biologics for pregnant asthma patients lack randomized controlled trials (RCTs); the available evidence comprises case reports, observational registries, and pharmacovigilance studies. With newer agents, especially mepolizumab, benralizumab, and dupilumab, there is limited data on human pregnancy. Some of these biologics (including mepolizumab and benralizumab) have not shown any fetal harm in animal reproductive studies, although only short-term human follow-up has been done [37]. There are also pregnancy exposure registries being planned (e.g., OTIS / VAMPSS registries of mepolizumab and benralizumab), although a number of these are not yet finished [24].

Confounding is another vulnerability of pharmacovigilance data, such as VigiBase: most reports do not include detailed clinical information, such as asthma severity, comorbid conditions, or adherence, and it is hard to separate the drug effect from the disease risk [26]. Further, biases in reporting and underreporting of some outcomes might bias the results. Moreover, even though spontaneous reporting systems may indicate the presence of signals, they cannot establish causality. Based on the available evidence, there is consensus among experts to maintain the use of biologics such as omalizumab during pregnancy in circumstances where they have been used (pre-pregnancy) with success [34]. The use of biologic therapy in pregnancy is more debatable. It must be approached on a case-by-case basis, balancing maternal interests of avoiding severe exacerbations against the possible but unproven risks in the fetus [37].

Organizations such as the Asthma Pregnancy Toolkit recommend a shared-decision model that incorporates asthma specialists, obstetricians, and the patient [38]. Moreover, because of the possibility of drug transfer to the fetus and the newborn, there are some recommendations to be cautious when using live vaccines in infants exposed in utero, especially those who were exposed during the third trimester, as an extrapolation of rheumatology practice [39].

## The benefits and Adverse Effects of FDA-Approved Biologic Agents for Severe Asthma in Pregnancy

Biologic therapies have played a critical role in asthma management, especially in patients with severe uncontrolled asthma. Biologics have the potential to be of use in the context of pregnancy, such as asthma control, which is essential to the health of the mother and the fetus. Uncontrolled asthma in pregnancy has been shown to lead to poor outcomes, including preterm delivery, low birth weight, small for gestational age, pre-eclampsia, and maternal morbidity. Thus, the risks can be minimized with the help of effective asthma management, including biologics, which underlines the significance of personalized therapy in pregnant patients with severe asthma [40,41] (Table 1).

### Benefits of Biologic Therapy in Pregnancy

Omalizumab is the strongest biologic with the most pregnancy data regarding asthma. The EXPECT study involved 250 pregnant women with asthma who were treated with omalizumab either prenatally or during pregnancy. The findings showed that the incidence of significant congenital anomalies did not differ from that of disease-matched controls, with live births at 99.1, premature births at 15, and small-for-gestational-age babies at 9.7 [40]. These results imply that omalizumab can achieve disease control without posing a high teratogenic risk, which is why it may be continued during pregnancy.

Other biologics data- mepolizumab, benralizumab, and dupilumab- are limited but becoming more encouraging. Case reports and observational studies suggest that these agents do not seem to predispose to adverse maternal or fetal outcomes, but the sample sizes are small and heterogeneous [42]. There is no published pregnancy outcome of reslizumab or tezepelumab. Current pregnancy exposure registries, such as OTIS registries of mepolizumab, benralizumab, and dupilumab, strive to gather safety information systematically and monitor any risks of a drug [43].

### Risks and Considerations

Biologics use in pregnancy presents theoretical risks based on their mechanism of action and placental transfer. The majority of monoclonal antibodies are IgG-based and increasingly infiltrate the placenta in the second and third trimesters. As a result, the fetus is most exposed to it during late pregnancy, which may affect neonatal immune responses. Although animal research often shows no teratogenicity, human data remain insufficient for most biologics [40].

### Drug-Specific Considerations

- **Omalizumab:** Uncommon anaphylaxis (approximately 0.1-0.2% of patients) and serum sickness-like reactions, generally very well-tolerated. Cardiovascular events and eosinophilic granulomatosis with polyangiitis (EGPA) are rare but known. It is a good choice because it provides vast pregnancy information, making it preferred in cases of a biologic indication [41,44]
- **Mepolizumab:** No anaphylaxis with randomized trials; mild hypersensitivity reactions are observed in 12-2%. There is no increase in malignancy and severe infections. Pregnancy data are scanty, and registry monitoring is in place (OTIS VAMPSS) [45]
- **Benralizumab:** Rare allergic events, no serious risk of infections or malignancy; however, eosinopenia is to be monitored due to the potential immune effects. There is limited data on pregnancy, which lacks significant adverse outcomes [46]
- **Dupilumab:** Mild to moderate hypersensitivity reactions, transient eosinophilia (up to 14% of patients), and conjunctivitis. The cardiovascular risk is not dangerous. Data on early pregnancy indicate no significant teratogenic risk, but no extensive cohort studies are available [47]
- **Reslizumab and Tezepelumab:** Inadequate pregnancy-specific data. The risk of anaphylaxis is low (reslizumab 0.3%), malignancy is not clearly increasing, and the long-term impact on the fetal immune system is unknown for both; caution is necessary [24]

### Clinical Implications

Biologic therapy should be initiated in pregnancy based on balancing maternal gains and possible fetal harm. Optimal asthma control is the key objective, and uncontrolled disease is riskier than most biologics. Good safety data suggest that omalizumab could be the first-line biologic in pregnant patients. For other biologics, shared decision-making and

Table 1: The Benefits and Adverse Effects of the Biologic Agents for Severe Uncontrolled Asthma in Pregnancy

| Biologic Agent | Benefits in Pregnancy | Reported Adverse Effects / Risks |
|---|---|---|
| Omalizumab | • Reduces asthma exacerbations<br>• Improves lung function<br>• Reduces need for oral corticosteroids<br>• Generally well-tolerated in pregnancy (EXPECT study: no increased risk of significant congenital anomalies, preterm birth, or low birth weight compared to disease-matched cohort) | • Anaphylaxis (~0.1–0.2%)<br>• Serum sickness-like reactions<br>• Rare reports of eosinophilic granulomatosis with polyangiitis (EGPA)<br>• Cardiovascular/cerebrovascular events (possible increased risk in patients with baseline risk factors)<br>• No clear evidence of increased malignancy or infection risk |
| Mepolizumab | • Reduces exacerbations in severe eosinophilic asthma<br>• Reduces corticosteroid use<br>• Safe in animal studies; ongoing pregnancy registry (VAMPSS) | • Rare hypersensitivity reactions (rash, headache, myalgia)<br>• No evidence of increased malignancy<br>• Low rates of herpes zoster and opportunistic infections reported<br>• Eosinophilia risk not reported |
| Benralizumab | • Reduces exacerbations and steroid dependence in severe eosinophilic asthma<br>• Long half-life allows extended dosing intervals<br>• No evidence of harm in animal studies; ongoing pregnancy registry (VAMPSS) | • Mild hypersensitivity reactions (urticarial rash)<br>• Rare malignancy reports (not increased over placebo)<br>• Minimal infection risk, rare herpes zoster<br>• Eosinopenia; theoretical immunomodulation concern |
| Dupilumab | • Reduces exacerbations in moderate-to-severe asthma<br>• Improves lung function and quality of life<br>• May reduce corticosteroid use<br>• Safe in animal studies; ongoing pregnancy registry (OTIS) | • Hypersensitivity reactions (1%) including rash, serum sickness, erythema multiforme<br>• Transient blood eosinophilia (mostly asymptomatic, 4–14%)<br>• Rare cardiovascular events (0.2–0.6%)<br>• Conjunctivitis and ocular surface disorders (mostly in atopic dermatitis)<br>• Arthralgia/arthritis (mainly in atopic dermatitis)<br>• No significant increased infection or malignancy risk |
| Reslizumab | • Reduces exacerbations and steroid dependence in severe eosinophilic asthma | • Anaphylaxis (0.3%)<br>• No reported malignancy increase<br>• No specific vaccination restrictions or infection risk noted<br>• Limited pregnancy data available |
| Tezepelumab | • Reduces exacerbations in severe asthma, independent of phenotype<br>• Improves lung function<br>• Reduces corticosteroid use | • Rare hypersensitivity reactions in postmarketing reports<br>• No increased malignancy risk in trials<br>• Minimal infection risk; live vaccines should be avoided<br>• Potential cardiovascular risk listed on product label<br>• No pregnancy data available |

enrollment in pregnancy registries are advised to track outcomes and contribute to safety data. During pregnancy, clinicians should consider timing (preferably continuation if it has already been controlled), patient history (e.g., prior hypersensitivity), and monitoring for adverse events (e.g., eosinophilia, infection).

Overall, biologic therapy has significant maternal advantages because it helps to cut down on the exacerbations, enhances the control of asthma, and reduces corticosteroid exposure in pregnant women. Existing data show that omalizumab, and probably other biologics, do not predispose to congenital malformations or adverse pregnancy outcomes, but the data are scarce on many agents. Long-term safety of biologics in pregnant populations requires continued pharmacovigilance through the use of pregnancy registries and additional research. The use of biologics should be personalized, with a focus on shared decision-making, risk-benefit assessment, and close monitoring.

## CONCLUSIONS

Emerging evidence suggests that biologic therapies are a promising option for managing severe asthma in pregnancy, offering substantial maternal benefits by reducing exacerbations, minimizing systemic corticosteroid use, and improving quality of life. Registry reports and observational data, especially for omalizumab, indicate no significant increase in adverse fetal outcomes, but high-quality randomized trials remain unavailable. Individualized patient counseling, careful risk-benefit assessment, and multidisciplinary care should guide clinical decisions. Further data gathering using pregnancy registries is required to support safety evidence and maximize treatment approaches in both the mother and child.

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## APPENDIX

Table 2: Summary of Key Studies on Biologic Therapy for Severe Asthma in Pregnancy

| Author and Publication Year | Study Design | Main Points | Results and Main Findings |
|---|---|---|---|
| Gyawali B, Georas SN, Khurana S. [1] | State-of-the-art review | Overview of biologic therapies (omalizumab, mepolizumab, benralizumab, dupilumab, reslizumab) | Biologics reduce exacerbations, hospitalizations, systemic steroid use; improve quality of life. Evidence from RCTs, extensions, meta-analyses, and real-world studies; supports personalized asthma management. |
| Georgakopoulou VE, Taskou C, *et al.* [3] | Narrative review | Assessed maternal-fetal outcomes and asthma management during pregnancy | Poorly controlled asthma increases risk of preeclampsia, gestational diabetes, cesarean delivery, preterm birth, low birth weight. Biologics and personalized medicine improve outcomes; digital monitoring recommended. |
| Al-Lehebi RO, *et al.* [4] | Multi-country, self-controlled observational cohort study | Evaluated real-world effectiveness of mepolizumab | Significant reduction in clinically significant exacerbations (76%), oral corticosteroid use (from 52.8% to 16.6%), hospitalizations (22.5% to 6.9%), improvement in lung function (FEV1 62.8% → 73%) and asthma control (ACT well-controlled 15% → 64.5%). |
| Vyawahare AP, Gaidhane A, Wandile B. [11] | Critical review | Examined prevalence, physiological changes, impact on maternal-fetal outcomes | Proper asthma diagnosis, medication management, personalized action plans, lifestyle modifications, and trigger avoidance improve maternal and fetal outcomes; emphasizes precision medicine and early intervention. |
| Naftel J, *et al.* [15] | International consensus (Delphi study) | Recommendations on asthma biologics use during pregnancy | Consensus: biologics can be used during conception, pregnancy, and breastfeeding; initiation guided by standard criteria; risk-benefit discussions emphasized; registry data collection needed for guideline development. |
| Javorac J, *et al.* [18] | Narrative review | Evaluated pharmacological therapy safety, including biologics | Medications including biologics justified maintaining asthma control and preventing exacerbations; GINA recommends continuation; benefits outweigh potential risks; individualized assessment required. |
| Agache I, *et al.* [23] | Systematic review | Assessed efficacy and safety of benralizumab, dupilumab, mepolizumab, omalizumab, reslizumab | All biologics reduce exacerbations (IRR 0.43–0.56), improve asthma control, QoL, FEV1; benralizumab, dupilumab, mepolizumab reduce oral corticosteroid use; slight increase in drug-related adverse events; cost-effectiveness above willingness-to-pay threshold. |
| Dorscheid DR, *et al.* [34] | Guidance document | Provided recommendations for biologic administration in various health contexts | Biologics can be continued during pregnancy, post-surgery, respiratory infections (including COVID-19), and vaccination; maintaining asthma control reduces severe infection risk; individualized clinical assessment recommended. |