This book is based on the sources believed to be reliable in providing information that is complete and generally in accordance with the standards accepted at the time of publication. Any change in the medical science may necessitate suitable modifications in the information contained herein. Every effort has been made to ensure that the drug doses and other information are presented accurately in this publication. However, the ultimate responsibility rests solely with the prescribing physician.
Pregnancy is one of the most beautiful and important phases in a woman’s life. As such, a pregnant woman with asthma wouldn’t want her asthma to put a damper on this period as she has to think not just about her health but also about her child’s health.

Asthma has been reported to affect about 7–8% of pregnant women in India. It is one of the most common problems in pregnancy and also, potentially, the most serious medical problem to complicate pregnancy.

Studies suggest that maternal asthma increases the risk of perinatal mortality, pre-eclampsia, preterm birth and low birth weight-infants, though the overall data is conflicting. Studies have shown that the number of women reporting worsening symptoms do so mainly during weeks 24–36 of the pregnancy. It has also been noted that one in ten women suffering from asthma has an attack during labour.

However, asthma that is better controlled is associated with decreased risks. Hence, the goal of treatment in a pregnant asthmatic is to provide the optimal asthma control therapy — for improved maternal health and quality of life as well as for normal foetal development.

Since inadequate control of asthma is a greater risk to the foetus than the asthma medications, it is safer for pregnant asthmatics to continue with their asthma medications than suffer asthma symptoms and exacerbations.

This booklet is an endeavour by Cipla and aims to provide some pointers on how a physician can ensure safe and favourable pregnancy for his/her asthmatic patients. It is intended as a quick reference guide to all physicians who want to know more about managing asthma in different practical scenarios.

August 2011
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PHYSIOLOGICAL CHANGES IN PREGNANCY

It is a well-known phenomenon that during pregnancy, there is an approximately 18% reduction in the functional residual capacity as well as a progressive decrease in the expiratory reserve volume due to the elevation of the diaphragm for the uterus growth.

Another physiologic change in pregnancy is a 20% increase in the maternal oxygen consumption to support the 15% increase in the maternal metabolic rate. There is also a relative increase in hyperventilation (i.e. 40–50% increase in minute ventilation) to compensate for the increased demands of pregnancy. This natural hyperventilation is a result of increasing tidal volume, and not an increased respiratory rate. Table 1 shows the lung volume descriptions and the respective changes during pregnancy:

<table>
<thead>
<tr>
<th>Lung Capacity Measurement</th>
<th>Description</th>
<th>Physiologic Change in Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional residual capacity</td>
<td>Volume of air left in the lungs after a tidal breath out. The amount of air that stays in the lungs during normal breathing</td>
<td>↓ 17–20% (300–500 mL)</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>Number of breaths per minute</td>
<td>Unchanged</td>
</tr>
<tr>
<td>Residual volume</td>
<td>Amount of air left in the lungs after maximum exhalation</td>
<td>↓ 20–25% (200–300 mL)</td>
</tr>
<tr>
<td>Tidal volume</td>
<td>Normal volume of air displaced between normal inhalation and exhalation with no extra effort</td>
<td>↓ 30–50%</td>
</tr>
<tr>
<td>Expiratory reserve volume</td>
<td>Amount of additional air that can be pushed out after the end expiratory level of normal breathing</td>
<td>↓ 5–15% (100–300 mL)</td>
</tr>
<tr>
<td>FEV₁</td>
<td>Volume of air exhaled during the first second of a forced expiratory manoeuvre</td>
<td>Unchanged</td>
</tr>
<tr>
<td>PEFR</td>
<td>Maximal flow (or speed) achieved during maximally forced expiration initiated at full inspiration; measured in L/s</td>
<td>Unchanged</td>
</tr>
<tr>
<td>Minute volume/ventilation</td>
<td>Volume of air that can be inhaled or exhaled in 1 minute</td>
<td>↓ 30–50%</td>
</tr>
</tbody>
</table>

Abbreviation: FEV₁ – forced expiratory volume in one second; PEFR – peak expiratory flow rate.
**Practice point**

*Keeping a check on the maternal PaCO₂ through an ABG* analysis: The maternal PaCO₂ should ideally be low, as an increase in the maternal PaCO₂ will affect the ability of the foetus to excrete acid and cause foetal acidosis. Hence, a normal maternal PaCO₂ rate in the ABG analysis is actually indicative of a degree of CO₂ retention and possible respiratory failure.

*Arterial Blood Gas*

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**EFFECT OF PREGNANCY ON ASTHMA**

Overall, the effect that pregnancy has on any one patient’s asthma is unpredictable. Some historical cohort and prospective studies have found that during pregnancy, the severity of asthma remains stable in a third of women, worsens in another third and improves in the remaining third; it is this widely used rule of thirds that makes asthma in pregnancy the very definition of unpredictable!

Some of the physiological factors affecting asthma in pregnancy are described below (Box 1):

<table>
<thead>
<tr>
<th>Box 1: Physiological factors affecting asthma in pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Increase in free cortisol levels may protect against inflammatory triggers</td>
</tr>
<tr>
<td>• Increase in bronchodilating substances (such as progesterone) may improve airway responsiveness</td>
</tr>
<tr>
<td>• Increase in bronchoconstricting substances (such as prostaglandin F2 alpha) may promote airway constriction</td>
</tr>
<tr>
<td>• Placental 11 beta hydroxysteroid dehydrogenase type 2 decreased activity is associated with an increase in placental cortisol concentration and low birth weight</td>
</tr>
<tr>
<td>• Placental gene expression of inflammatory cytokines may promote low birth weight</td>
</tr>
<tr>
<td>• Modification of cell mediated immunity may influence maternal response to infection and inflammation</td>
</tr>
</tbody>
</table>

Exacerbations are most likely to occur between weeks 24 and 36 of pregnancy. Some of the common triggers of exacerbations observed in some studies were respiratory viral infections (34%) and non-adherence to inhaled corticosteroids (29%).
Some studies have also shown that in pregnant women, the condition is more likely to deteriorate in those with severe asthma (52–65%) than in those with mild asthma (8–13%). Also, pregnant women with severe asthma were more likely to have respiratory or urinary tract infections than those with mild asthma or without asthma.

Practice point

Women with asthma need to be closely followed during pregnancy regardless of the severity of the disease.

**EFFECT OF ASTHMA ON PREGNANCY**

There is very little data on how asthma control before pregnancy affects pregnancy outcomes. Also, there is conflicting data on the effects of asthma on pregnancy.

In studies with a large number of pregnant asthmatics, an increased risk of pregnancy-induced hypertension has been seen, but only in those with moderate-to-severe daily symptoms. The pregnancy outcomes for asthmatics requiring corticosteroid therapy were associated with decreased gestational age at delivery, pre-eclampsia and small-for-gestational-age infants. However, this data indicates that the poor perinatal outcomes are due to poorly controlled asthma and not because of the treatment medications.

The exact effect of asthma on the developing foetus is poorly understood. Many studies have suggested that maternal hypoxia, inflammation, smoking and altered placental function may contribute to poor outcomes in pregnant asthmatics. However, it is clear that as the asthma worsens or gets more severe, it increases the risk of negative foetal and maternal outcomes.

Practice point

It is important that asthma is well-controlled before conception and that this control is maintained through continued asthma medication.
DIAGNOSIS AND CLASSIFICATION OF ASTHMA IN A PREGNANT PATIENT

Diagnosis of asthma in pregnancy is no different from that in the non-pregnant patient. Asthma is characterized by persistent symptoms of bronchoconstriction, including breathlessness, tightness in the chest, and cough and sputum production. As such, the diagnosis calls for an improvement in the symptoms as well as objective changes in pulmonary function tests such as the FEV₁ or PEFR reversibility.

The most common respiratory symptom during pregnancy is dyspnoea without the associated cough, tightness or obstructive signs as seen with asthma; the reason for this dyspnoea is mostly physiological. Hence, an alternate diagnosis such as GERD, pneumonia, post-nasal drip due to allergic rhinitis or bronchitis, etc., may also be considered (Box 2):

Box 2: Main differential diagnoses in pregnant women with dyspnoea

- **Asthma**: Acute or progressive dyspnoea with wheezing and cough, more often with a history of asthma and precipitating factors; diagnosis confirmed by pulmonary function tests.
- **Physiological dyspnoea of pregnancy**: Hyperventilation due mainly to increased progesterone; may occur early in pregnancy and does not interfere with daily activities.
- **Pulmonary embolism**: Acute respiratory distress or gradually progressive dyspnoea with or without tachycardia, cough, chest pain, haemoptysis, or signs of deep venous thrombosis; diagnosis established by scintigraphic ventilation perfusion scan, computed tomographic angiography, or pulmonary angiography.
- **Pulmonary oedema**: Acute or progressive respiratory distress in the presence of heart disease, hypertension, embolic disease, tocolytic therapy, aggressive fluid replacement, or sepsis; diagnosis confirmed by chest radiography.
- **Peripartum cardiomyopathy**: Dyspnoea caused by dilated cardiomyopathy occurring during the final month of pregnancy to six months after delivery; signs and symptoms of heart failure confirmed by echocardiographic evaluation.
- **Amniotic fluid embolism**: Acute respiratory distress occurring more often during the evacuation of the uterus and which may be complicated by hypotension, seizure, disseminated intravascular coagulation, and cardiac arrest.
If the clinical picture is consistent with asthma but reversibility of airway obstruction cannot be demonstrated, then a trial of asthma treatment can be used for diagnosis in pregnancy.

Once a diagnosis of asthma has been established, it is also important that the asthma severity is classified in a similar way as is usually done in adult asthmatics to help predict the possible risk of severe exacerbations and to establish a regular maintenance therapy. The general principles for the management and treatment of asthma are the same in pregnant women as in non-pregnant women and in men. Knowing and applying the classification system is essential to selecting the appropriate management route as well as anticipating complications during pregnancy.

MANAGEMENT OF ASTHMA IN PREGNANCY

The ultimate goal of asthma therapy in a pregnant patient is to achieve optimal asthma control for improved maternal and perinatal outcomes. This is expected to be met by preventing hypoxic episodes and preserving continuous foetal oxygenation. Thus, effective asthma management revolves around these four basic components of asthma therapy:

1. Assessment and close monitoring of asthma
2. Patient education
3. Trigger avoidance
4. Pharmacotherapy according to severity and control

Since one-third of women with asthma develop worsening of control during pregnancy, it is important that all pregnant asthmatics be closely monitored and re-evaluated.
1. **Assessment and close monitoring of asthma**

Since subjective measures used by the patient or physician to gauge the asthma severity are not reliable, objective measurement of the FEV₁ with a spirometer (if not available, then measurement of the PEFR with a peak flow meter) is a dependable criterion of airway obstruction and correlates with pregnancy outcomes.

- Women who have sub-optimally controlled asthma or moderate-to-severe asthma (starting at 32 weeks) or who are recovering from a severe asthma exacerbation may be considered for additional foetal surveillance in the form of ultrasound examinations.
- Antenatal surveillance of foetal well-being should be considered in women who have persistent asthma during pregnancy and the intensity of this surveillance should be based on the severity of asthma as well as any other high-risk features of pregnancy that may be present (such as the risk of intrauterine growth retardation and pre-eclampsia).
- Patients should also be instructed to be attentive to foetal activity.

**Point to ponder: Spirometry during pregnancy**

The measurement of the FEV₁ after a maximal inspiration (using a spirometer) is the single best measure of pulmonary function even though it is an effort-dependent test. When adjusted for confounders, a mean FEV₁ less than 80% predicted has been found to be significantly associated with an increased preterm delivery less than 32 weeks and less than 37 weeks, and a birth weight less than 2,500 gm. Spirometry with pre- and post-bronchodilation is recommended to evaluate the airflow obstruction and reversibility. However, if the spirometry is normal but asthma is highly suspected, a trial of asthma therapy can be initiated for the purpose of diagnosis.

2. **Patient education**

Controlling asthma during pregnancy is important for foetal well-being and, hence, it is recommended that the pregnant asthmatic be imparted more information about asthma.
Practice point

Patient education should begin at the first prenatal visit and include the following:

- The patient should be made to understand that it is safer to be treated with asthma medications than it is to have asthma symptoms and exacerbations.
- She should be able to recognize and promptly treat the signs of worsening asthma and have prompt access to her clinician in case of uncontrolled symptoms.
- She should be taught how to do peak flow measurements, how to record the results and which values should be of concern, as well as who to contact in emergency.
- She should have a basic understanding of medical management during pregnancy and should be observed using her inhalers as well as peak flow meters, with correct use being reinforced if needed.
- She should also understand what contributes to her asthma severity, i.e. asthma triggers, and how to reduce her exposure or control them.

3. Trigger avoidance

Identifying and avoiding triggers that contribute to asthma severity can lead to improved maternal well-being, along with less need for medications.

Practice point

- Identification of triggers in patients can be done either by using skin prick tests or through in vitro tests such as the radioallergosorbent test (RAST) or the enzyme-linked immunosorbent assay (ELISA).
- For exercise-induced asthma, the use of a bronchodilator, 5–60 minutes before exercise, may reduce the symptoms.
- All patients should be strongly encouraged to stop smoking as maternal smoking may be associated with an increased risk for wheezing and development of asthma later on in the offspring.
Point to ponder: Allergy treatment and immunotherapy

Immunotherapy may be continued if the patient is stable on the medication and receiving maintenance doses. Starting immunotherapy or advancing the dose is not recommended during pregnancy due to the risk of anaphylaxis. Allergic rhinitis is a potent trigger of asthma symptoms; pregnancy can worsen the symptoms of allergic rhinitis, resulting in uncontrolled asthma. Allergic rhinitis is generally treated with antihistamines and/or an intranasal corticosteroid. The preferred corticosteroid is budesonide because of the availability of sufficient safety data. However, the overall safety profile of intranasal corticosteroids supports continuing any corticosteroid effective in controlling the patient’s symptoms. Recommended antihistamines include first-generation diphenhydramine and second-generation loratadine, cetirizine and levocetirizine. Decongestants have been associated with an increased occurrence of gastroschisis when taken during the first trimester and should be avoided.

4. Pharmacotherapy according to severity and control

The stepwise approach to therapy, which remains similar to the asthma management in the adults, in which the dosage, number of medications and the frequency of administration are increased as necessary and decreased when possible, is used to achieve and maintain asthma control.

Many pregnant women and their doctors are concerned about the potential effects of the asthma drugs on their babies as well as on the women themselves. It is, however, safer to take asthma drugs during pregnancy than to leave the asthma uncontrolled.

In addition to the animal studies, prospective as well as case-control studies and systematic reviews have shown that asthma drugs such as inhaled corticosteroids, short-acting beta₂-agonists and leukotriene-receptor antagonists (such as montelukast) and theophylline, do not increase the risk of foetal congenital malformations, pre-eclampsia, preterm delivery or low birth weight. Long-acting beta₂-agonists should always be used together with an inhaled corticosteroid, just as in cases other than pregnancy. In addition, the doctor should not refrain from using oral corticosteroids in severe asthma and life-threatening situations.
It is assumed that asthma medications are as effective in the pregnant asthmatic as in the non-pregnant one; however, there may be physiological changes in pregnancy that affect many aspects of the pharmacokinetics of these medications.

**Practice point**

At least twice during the pregnancy, the treatment should be reviewed and stepped up if symptoms are persistent; if they are well-controlled, therapy can be maintained or even decreased.

**Point to ponder: Use of inhaled corticosteroids in pregnant women**

Inhaled corticosteroids are preferred for the management of all levels of persistent asthma in pregnancy. Corticosteroids are the most effective treatment for the airway inflammation of asthma and reduce the hyper-responsiveness of the airways to allergens and triggers. They also decrease the incidence of exacerbations by more than threefold in users, compared with those who do not use inhaled corticosteroids. A concern about the risks of congenital malformations with inhaled corticosteroid exposure in the first trimester has proved unfounded; multiple studies have confirmed their safety regardless of dose. In fact, it has been proven that patients with inadequate inhaled anti-inflammatory treatment during pregnancy run a higher risk of an acute attack of asthma, which would then warrant treatment with oral/systemic corticosteroids, thus increasing the risk of pre-eclampsia. Budesonide is considered the preferred medication because of the availability of sufficient safety data regarding its use in pregnant asthmatics and in the pregnancy category B. All other corticosteroids are category C. However, if a woman’s asthma is well-controlled on a different inhaled steroid, it is recommended that the regimen be continued.

**MANAGEMENT OF ACUTE ATTACKS IN PREGNANCY**

An asthma exacerbation in a pregnant woman places her as well as her foetus at increased risk of severe hypoxaemia during these events. The most important part of managing such an event is prevention, but it has also been noted that 52% of patients with severe asthma have an exacerbation during pregnancy and many of them require hospitalization.
A decrease in foetal movement may be an early manifestation of an asthma exacerbation.

Admission to an intensive care unit, or intubation, is indicated in those with life-threatening asthma, in those with a PaCO$_2$ higher than 40–45 mm Hg on arterial blood gas, mental status changes, maternal exhaustion, respiratory acidosis or foetal distress.

Early recognition of worsening asthma is important so that prompt home rescue treatment may be instituted to avoid maternal and foetal hypoxia; the principles for managing an acute exacerbation of asthma during pregnancy remain the same as in a non-pregnant patient. The goal of hospital management is reversal of bronchoconstriction with inhaled beta$_2$-agonists and corticosteroids, prevention and correction of hypoxaemia, or reduction of hypercarbia. However, there are some precautions to be taken in managing asthma exacerbations in pregnancy (Box 3):

**Box 3: Management of acute asthma in pregnancy**

- To intervene rapidly
- To closely monitor the woman and assess foetal well-being continuously
- To maintain oxygen saturation >95%
- To avoid PaCO$_2$ >40 mm Hg
- To place the patient in a left lateral position
- To provide ample hydration with an intravenous fluid (isotonic saline 125 ml/h) if unable to swallow fluids
- To avoid hypotension with adequate position, hydration, and treatment
- To use adrenaline (epinephrine) only in the context of an anaphylactic reaction
- To consider intubation earlier than usual and calling an expert if intubation is required as it can be more difficult in pregnant women owing to the oedema of the oropharyngeal mucosa

Refractory status asthmaticus is defined as a severe exacerbation of asthma that is unresponsive to bronchodilators and corticosteroids; it requires admission to an intensive care unit and, typically, mechanical ventilation.
Improvement in a severe asthma exacerbation after delivery (if it is being considered) may result from several physiological factors, including reduced pressure on the diaphragm and decreased oxygen consumption.

Practice point
- Pregnant asthmatics should be taught to recognize the signs and symptoms of early exacerbations, such as coughing, chest-tightness, dyspnoea, wheezing, or a 20% decrease in their PEFR rate.
- Additionally, they should be given an individualized guide for decision making and rescue management.
- However, they should seek further medical attention promptly if the response is incomplete or if foetal activity is decreased.
- In pregnant patients with refractory status asthmaticus, delivery should be considered as a therapeutic option; however, this is rarely required. A caesarian delivery is most likely necessary where there is an urgent need for the delivery.
- Vaginal delivery may be possible during an acute exacerbation in a setting of progressive active labour, normal maternal oxygenation, absence of hypercapnoea, adequate neuraxial anaesthesia, and the use of operative vaginal delivery.
- If delivery is being considered for maternal reasons at a gestational age between 24 and 34 weeks, then betamethasone should be given before the delivery for foetal lung maturity, if at all possible.

**MANAGEMENT OF ASTHMA DURING LABOUR AND DELIVERY**

- Asthma medications should not be discontinued or delayed during labour and delivery.
- Although asthma during labour is typically quiescent, consideration should be given to obtaining a peak flow measurement on admission and then every 12 hours or as needed to monitor for asthma exacerbation. Monitoring is, more likely, only necessary in those women who have a history of exacerbations during pregnancy.
• Neuraxial anaesthesia decreases the oxygen requirements and minute ventilation and, thus, can be helpful in controlling asthma symptoms during labour.

• If systemic (oral or intravenous) corticosteroids have been used for treatment in the previous 4 weeks, then the patient should receive stress-dose steroids to prevent an adrenal crisis. Usually, this regimen begins with hydrocortisone 100 mg every 8 hours, continued for 24 hours postpartum, and then stopped. Tapering of the dose of stress-steroids is not necessary.

• Medications typically used for tocolysis, induction of labour and during delivery can have an influence on asthma symptoms, especially in the most severe or medication-sensitive asthmatic patients. Prostaglandins E2 or E1 can be used for cervical ripening, for postpartum haemorrhage or to induce abortion without significant adverse reactions. In these cases, the respiratory status of the patient should be routinely monitored. Carboprost (prostaglandin F2-alpha), ergonovine and methylergonovine can cause bronchospasm, especially in the aspirin-sensitive patient. For these patients, choosing a medication such as misoprostol, which is an E1, may be more appropriate.

• Magnesium sulphate is a bronchodilator and should not have a deleterious effect on asthma, but indomethacin can induce bronchospasm in an asthmatic patient with known aspirin sensitivity.

• No formal studies on calcium channel blockers in the gravid asthmatic have been published, but bronchospasm has not been observed with the wide clinical use of these medications for tocolysis.

MANAGEMENT OF ASTHMA DURING POSTPARTUM AND BREASTFEEDING

• It is important to continue asthma medications in the postpartum period.

• Peak flow values should be monitored on the days following delivery in women with moderate-to-severe asthma.

• Breastfeeding should be encouraged since it has been reported that breastfeeding between 1 and 6 months reduces the later prevalence of atopy in 17-year-olds by about 30–50%. However, it does not appear to protect the offspring from developing asthma.
Even though asthma medications are excreted in small and varying amounts into the breast milk, most asthma medications, including oral prednisone, are considered compatible with breastfeeding.

Prednisone, theophylline, cromolyn, antihistamines, inhaled corticosteroids or inhaled beta-agonists are not contraindicated during breastfeeding.

**SUMMARY: SPECIAL CONSIDERATIONS IN PREGNANT WOMEN WITH ASTHMA**

- To ensure optimal asthma control throughout pregnancy
- To manage asthma exacerbations aggressively
- To avoid delay in diagnosis and treatment
- To assess medication needs and response to therapy frequently
- To ensure adequate patient education and acquisition of self-management skills
- To treat rhinitis, gastric reflux and other comorbidities adequately
- To encourage smoking cessation
- To assess pulmonary function (expiratory flow) with spirometry at least monthly
- To offer a multidisciplinary team approach
- To do not give flu vaccination until after 12 weeks of pregnancy
- To be aware of the risk of pre-eclampsia and intrauterine growth retardation

Asthma is a chronic illness that can complicate a significant number of pregnancies since exacerbations and poor asthma control can have proven negative effects on the pregnancy outcomes. However, with effective treatment and an emphasis on the importance of good asthma control, women with asthma can expect good pregnancy outcomes by ensuring not only their own health but also the health of the growing foetus.
## Information about daily controller medications

<table>
<thead>
<tr>
<th>Drug</th>
<th>Category</th>
<th>Potential Adverse Effects</th>
<th>Recommended Use</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inhaled Corticosteroids</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Budesonide</td>
<td>B</td>
<td>Cough, dysphonia, thrush; potential systemic effects at high doses; local side effects decreased with valved holding chamber (spacer) for metered-dose inhalers that are not breath-actuated and with washing of the mouth and spitting after inhalation (however, spacer devices are not recommended with ciclesonide, which is a prodrug activated only in the lungs and not the pharynx, thus reducing oropharyngeal deposition)</td>
<td>Preferred controller therapy</td>
</tr>
<tr>
<td>2. Beclomethasone</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Fluticasone</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Ciclesonide</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Mometasone</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Long-acting β₂-agonist</strong></td>
<td></td>
<td>Tachycardia, skeletal-muscle tremor, hypokalaemia, possible increase in the risk of severe life-threatening or fatal exacerbation</td>
<td>Preferred add-on therapy to medium- or high-dose inhaled corticosteroids</td>
</tr>
<tr>
<td>1. Salmeterol</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Formoterol</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Leukotriene-receptor antagonist</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Montelukast</td>
<td>B</td>
<td>No major adverse effects identified</td>
<td>Alternative for mild asthma or as add-on therapy to inhaled corticosteroids, especially in patients with good response before pregnancy</td>
</tr>
<tr>
<td>2. Zafirlukast</td>
<td>B</td>
<td>Cases of hepatitis reported</td>
<td></td>
</tr>
<tr>
<td><strong>Cromolyn</strong></td>
<td>B</td>
<td>Cough</td>
<td>Alternative for mild asthma</td>
</tr>
<tr>
<td><strong>Theophylline</strong></td>
<td>C</td>
<td>Insomnia, gastric upset, aggravation of gastro-oesophageal reflux</td>
<td>Alternative for mild asthma or as add-on therapy to inhaled corticosteroids</td>
</tr>
</tbody>
</table>

**Key:**
- Category A: Studies have failed to show a risk to the foetus in all trimesters.
- Category B: Animal studies do not show risk, but there are no adequate human studies or animal studies in all trimesters.
- Category C: Animal studies have shown risk, but the benefits may outweigh the risks or there are not enough animal or human studies.
- Category D: There is potential risk to the foetus but the benefit may outweigh the risk.
- Category X: Toxicity or foetal abnormalities known, and risk outweighs the benefit.
REFERENCES


