In brief

Budesonide and aspirin for pregnant women with COVID-19 25 February 2022

Summary

• While the early administration of budesonide has been shown to improve outcomes for people with COVID-19 more broadly, evidence is lacking on its use in pregnant women with COVID-19.1
• Evidence prior to COVID-19 has shown inhaled corticosteroids, including budesonide, are safe in pregnant women.2
• The INTERCOVID prospective longitudinal study of over 2,000 women found an association between COVID-19 during pregnancy and preeclampsia.3
• Narrative reviews and guidance for women with COVID-19, or during the COVID-19 pandemic, generally recommend low-dose aspirin as primary and secondary prophylaxis for pregnancy complications including preeclampsia.4-6 One letter recommended that aspirin use may be stopped on diagnosis of SARS-CoV-2 infection and restarted after full recovery in pregnant women.7
• Australian guidance, such as that from the National COVID-19 Clinical Evidence taskforce, states that budesonide is safe to use in pregnant and breastfeeding women.8-10
• The UK National Institute for Health and Care Excellence recommend budesonide to treat COVID-19 as part of a clinical trial. It recommends for people already on budesonide, for conditions other than COVID-19, treatment can continue following a positive test.11
• The Royal College of Obstetricians and Gynaecologists and Monash Health recommend to withhold aspirin prescribed for preeclampsia prophylaxis for the duration of COVID-19 infection.10, 12 While UpToDate and the International Federation of Gynaecology and Obstetrics state low-dose aspirin for prevention of preeclampsia is safe throughout pregnancy and that the clinical management of these conditions must follow established protocols.13, 14

Evidence

Budesonide for pregnant women with COVID-19

• While the early administration of budesonide has been shown to reduce the likelihood of needing urgent medical care and reduced time to recovery after early COVID-19 more broadly, evidence is lacking on its use in pregnant women with COVID-19.1
• A systematic review and meta-analysis on inhaled corticosteroids during pregnancy, prior to the COVID-19 pandemic, found inhaled corticosteroids, including budesonide, did not increase the risk of major malformations, preterm delivery, low birth weight and pregnancy-induced hypertension.2
• During pregnancy the placenta metabolises several corticosteroids that are used in the treatment of COVID-19, however it does not metabolise budesonide and fluticasone.15

In brief documents are not an exhaustive list of publications but aim to provide an overview of what is already known about a specific topic. This brief has not been peer-reviewed and should not be a substitute for individual clinical judgement, nor is it an endorsed position of NSW Health.
Aspirin prophylaxis for preeclampsia in pregnant women with COVID-19

- An article recommends that during the COVID-19 pandemic, pregnant women be screened for preeclampsia in the first trimester and offered low-dose aspirin if they become high-risk.\(^1\)
- The INTERCOV longitudinal study on the effect of COVID-19 during pregnancy found COVID-19 during pregnancy is strongly associated with preeclampsia, independent of any risk factors and pre-existing conditions. Whether aspirin administration reduces the risk for COVID-19 in women at high risk for preeclampsia is not known.\(^3\)
- A review of guidance on pharmacologic considerations for pregnant and lactating women with COVID-19 reports support for routine use of low-dose aspirin where clinically indicated and if not contraindicated for medical reasons.\(^4\)
- A narrative review on aspirin use during COVID-19 found low-dose aspirin has multiple indications for use during the pandemic, including preeclampsia prevention.\(^5\)
- A letter on giving aspirin to pregnant women during COVID-19 reported there are limited data to suggest that there is an association between low-dose aspirin prophylaxis and increased risk of progression of SARS-CoV-2 infection.\(^6\)
- A separate letter supported the continuous use of prophylactic aspirin for preeclampsia in pregnant women during COVID-19, however recommended stopping aspirin on diagnosis of SARS-CoV-2 infection and restarting after full recovery.\(^7\)

Grey literature

Table 1: Treatment recommendations from national and international guidance

Note: Recommendation wording has been copied directly from source material.

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| National COVID-19 Clinical Evidence taskforce, 2022\(^8\) | • Consider using inhaled budesonide within 14 days of symptom onset in adults with COVID-19 who do not require oxygen and have one or more risk factors for disease progression.  
• Budesonide is safe to use in pregnant and breastfeeding women.  
• In pregnant women, the use of antenatal corticosteroids for women at risk of preterm birth is supported as part of standard care, independent of the presence of COVID-19.  
• General recommendations on aspirin do not recommend the use of aspirin for the treatment of COVID-19.  
• There are not recommendations on the use of aspirin prophylaxis for the treatment of preeclampsia in pregnant women. However, there are general recommendations that aspirin may still be considered for other evidence-based indications in people who have COVID-19. |
| What is the latest on COVID-19 treatments available in Australia? Tsirtsakis, 2022\(^9\) | • Budesonide is also safe for use in pregnant or breastfeeding women and is recommended for use in children and adolescents who do not require oxygen and who have one or more paediatric complex chronic conditions. |
## COVID-19 Critical Intelligence Unit: Budesonide and aspirin for pregnant women with COVID-19

<table>
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| **COVID-19 rapid guideline: Managing COVID-19**                       | • Only use budesonide to treat COVID-19 as part of a clinical trial.  
• People already on budesonide for conditions other than COVID-19 should continue treatment if they test positive for COVID-19. |
| NICE UK, 2022\(^1\)                                                  |                                                                                                                                                                                                               |
| **Coronavirus (COVID-19) Treatment in pregnancy**                    | Budesonide  
• Indication: Symptomatic COVID-19 infection not requiring oxygen in those with one or more risk factors for progression.  
• Pregnancy: can use if indicated  
• Dose: 800μg inhaled (by breath actuated inhaler) twice a day for up to 14 days. If patient is already on inhaled corticosteroid, patient receives equivalent or higher doses of their existing therapy – a change to budesonide is not required. Discuss questions with respiratory team. If patient deteriorates despite budesonide and is commenced on dexamethasone, cease budesonide. |
| Monash Health, 2021\(^10\)                                           |                                                                                                                                                                                                               |
| **Non-Communicable Diseases and COVID-19**                           | Aspirin as prophylaxis for preeclampsia  
• COVID-19 can be associated with thrombocytopenia. All women admitted with COVID-19 who are taking aspirin as prophylaxis for preeclampsia, should have this discontinued for the duration of the infection. This is to mitigate risk of bleeding in women with thrombocytopenia, and disseminated intravascular dissemination, and also to minimise bleeding risk in deterioration and need for birth.  
• Aspirin can be recommenced for preeclampsia prophylaxis after clearance of COVID-19 until 36 weeks gestation. |
| International Federation of Gynaecology and Obstetrics, 2020\(^14\)   |                                                                                                                                                                                                               |
| **Coronavirus (COVID-19) Infection in Pregnancy**                    | • It is important to consider the potential impact of pre-existing hyperglycaemia and hypertension on the outcome of COVID-19 in pregnant women.  
• The clinical management of these conditions must follow established protocols including screening for preeclampsia and initiation of aspirin prophylaxis. |
| Royal College of Obstetricians & Gynaecologists, 2022\(^12\)         |                                                                                                                                                                                                               |

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COVID-19 Critical Intelligence Unit: Budesonide and aspirin for pregnant women with COVID-19

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<tr>
<td>COVID-19 and pregnancy: Questions and answers UpToDate, 2022</td>
<td>• The use of mechanical aids (such as intermittent pneumatic compression) should be used if low molecular weight heparin therapy is contraindicated or paused secondary to thrombocytopenia.</td>
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<tr>
<td>Low-dose aspirin for prevention of preeclampsia is safe throughout pregnancy.</td>
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Method
To inform this brief, PubMed and Google searches were conducted using terms related to (Budesonide AND pregnan* AND COVID-19) and (aspirin AND preeclampsia AND COVID-19) on 14 February 2022.

References


Evidence checks are archived a year after the date of publication