

## In brief

### Budesonide and aspirin for pregnant women with COVID-19

25 February 2022

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#### 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.<sup>1</sup>
- Evidence prior to COVID-19 has shown inhaled corticosteroids, including budesonide, are safe in pregnant women.<sup>2</sup>
- The INTERCOVID prospective longitudinal study of over 2,000 women found an association between COVID-19 during pregnancy and preeclampsia.<sup>3</sup>
- 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.<sup>4-6</sup> One letter recommended that aspirin use may be stopped on diagnosis of SARS-CoV-2 infection and restarted after full recovery in pregnant women.<sup>7</sup>
- 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.<sup>8-10</sup>
- 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.<sup>11</sup>
- 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.<sup>10, 12</sup> 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.<sup>13, 14</sup>

#### 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.<sup>1</sup>
- 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.<sup>2</sup>
- During pregnancy the [placenta metabolises several corticosteroids](#) that are used in the treatment of COVID-19, however it does not metabolise budesonide and fluticasone.<sup>15</sup>

## 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.<sup>16</sup>
- The [INTERCOVID 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.<sup>3</sup>
- 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.<sup>4</sup>
- A [narrative review on aspirin use during COVID-19](#) found low-dose aspirin has multiple indications for use during the pandemic, including preeclampsia prevention.<sup>5</sup>
- 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.<sup>6</sup>
- 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.<sup>7</sup>

## Grey literature

**Table 1: Treatment recommendations from national and international guidance**

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

| Source   | Recommendation  |
|--|---|
| <a href="#">National COVID-19 Clinical Evidence taskforce</a> , 2022 <sup>8</sup>                                  | <ul style="list-style-type: none"> <li>• 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.</li> <li>• Budesonide is safe to use in pregnant and breastfeeding women.</li> <li>• 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.</li> <li>• General recommendations on aspirin do not recommend the use of aspirin for the treatment of COVID-19.</li> <li>• 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.</li> </ul> |
| <a href="#">What is the latest on COVID-19 treatments available in Australia?</a><br>Tsirtsakis, 2022 <sup>9</sup> | <ul style="list-style-type: none"> <li>• 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.</li> </ul>   |

| Source  | Recommendation   |
|---|--|
| <p><a href="#">COVID-19 rapid guideline: Managing COVID-19</a><br/>NICE UK, 2022<sup>11</sup></p>   | <ul style="list-style-type: none"> <li>• Only use budesonide to treat COVID-19 as part of a clinical trial.</li> <li>• People already on budesonide for conditions other than COVID-19 should continue treatment if they test positive for COVID-19.</li> </ul>  |
| <p><a href="#">Coronavirus (COVID-19) Treatment in pregnancy</a><br/>Monash Health, 2021<sup>10</sup></p>                                       | <p>Budesonide</p> <ul style="list-style-type: none"> <li>• Indication: Symptomatic COVID-19 infection not requiring oxygen in those with one or more risk factors for progression.</li> <li>• Pregnancy: can use if indicated</li> <li>• 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.</li> </ul> <p>Aspirin as prophylaxis for preeclampsia</p> <ul style="list-style-type: none"> <li>• 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.</li> <li>• Aspirin can be recommenced for preeclampsia prophylaxis after clearance of COVID-19 until 36 weeks gestation.</li> </ul> |
| <p><a href="#">Non-Communicable Diseases and COVID-19</a><br/>International Federation of Gynaecology and Obstetrics, 2020<sup>14</sup></p>     | <ul style="list-style-type: none"> <li>• It is important to consider the potential impact of pre-existing hyperglycaemia and hypertension on the outcome of COVID-19 in pregnant women.</li> <li>• The clinical management of these conditions must follow established protocols including screening for preeclampsia and initiation of aspirin prophylaxis.</li> </ul>  |
| <p><a href="#">Coronavirus (COVID-19) Infection in Pregnancy</a><br/>Royal College of Obstetricians &amp; Gynaecologists, 2022<sup>12</sup></p> | <ul style="list-style-type: none"> <li>• COVID-19 can be associated with thrombocytopenia. When aspirin has been prescribed as prophylaxis for preeclampsia or previous small-for-gestational-age baby it should be discontinued for the duration of the infection as this may increase the bleeding risk in women with thrombocytopenia.</li> <li>• While most patients with severe COVID-19 infection will have normal or even high platelet counts, COVID-19 can be associated with thrombocytopenia.</li> <li>• Women who take low molecular weight heparin thromboprophylaxis during pregnancy should discontinue this if their platelet count falls below 50x10<sup>9</sup>/L and their care should be discussed with a haematologist.</li> </ul>  |

| Source   | Recommendation   |
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|  | <ul style="list-style-type: none"> <li>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.</li> </ul> |
| <p><a href="#">COVID-19 and pregnancy: Questions and answers</a><br/>UpToDate, 2022<sup>13</sup></p> | <ul style="list-style-type: none"> <li>Low-dose aspirin for prevention of preeclampsia is safe throughout pregnancy.</li> </ul>  |

## 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

- Ramakrishnan S, Nicolau DV, Jr., Langford B, et al. Inhaled budesonide in the treatment of early COVID-19 (STOIC): a phase 2, open-label, randomised controlled trial. *The Lancet Respiratory Medicine*. 2021;9(7):763-72. DOI: 10.1016/S2213-2600(21)00160-0
- Rahimi R, Nikfar S, Abdollahi M. Meta-analysis finds use of inhaled corticosteroids during pregnancy safe: a systematic meta-analysis review. *Hum Exp Toxicol*. 2006 Aug;25(8):447-52. DOI: 10.1191/0960327106het647oa
- Papageorghiou AT, Deruelle P, Gunier RB, et al. Preeclampsia and COVID-19: results from the INTERCOVID prospective longitudinal study. *Am J Obstet Gynecol*. 2021 Sep;225(3):289.e1-e17. DOI: 10.1016/j.ajog.2021.05.014
- D'Souza R, Ashraf R, Rowe H, et al. Pregnancy and COVID-19: pharmacologic considerations. *Ultrasound Obstet Gynecol*. 2021 Feb;57(2):195-203. DOI: 10.1002/uog.23116
- Sayed Ahmed HA, Merrell E, Ismail M, et al. Rationales and uncertainties for aspirin use in COVID-19: a narrative review. *Fam Med Community Health*. 2021 Apr;9(2). DOI: 10.1136/fmch-2020-000741
- Kwiatkowski S, Borowski D, Kajdy A, et al. Why we should not stop giving aspirin to pregnant women during the COVID-19 pandemic. *Ultrasound Obstet Gynecol*. 2020 Jun;55(6):841-3. DOI: 10.1002/uog.22049
- Gavillet M, Rolnik DL, Hoffman MK, et al. Should we stop aspirin prophylaxis in pregnant women diagnosed with COVID-19? *Ultrasound Obstet Gynecol*. 2020 Jun;55(6):843-4. DOI: 10.1002/uog.22063
- National COVID-19 Clinical Evidence Taskforce. Australian guidelines for the clinical care of people with COVID-19 [internet] Australia: National COVID-19 Clinical Evidence Taskforce; 3 Feb 2022 [cited 14 Feb 2022] Available from: <https://app.magicapp.org/#/guideline/L4Q5An/section/L6q73j>.
- Tsirtsakis A. What is the latest on COVID-19 treatments available in Australia? [internet] Australia: newsGP Royal Australian College of General Practitioners; 5 Jan 2022 [cited 14 Feb 2022] Available from: <https://www1.racgp.org.au/newsGP/clinical/what-is-the-latest-on-covid-19-treatments-availabl>.
- Monash Health. Coronavirus (COVID-19) Treatment in pregnancy [internet] Australia: Monash Health; 18 Jun 2021 [cited 14 Feb 2022] Available from: <https://app.prompt.org.au/download/144574?code=be488dbbd96df91cc630c6808fe5bad8>.

11. National Institute for Health and Care Excellence. COVID-19 rapid guideline: Managing COVID-19 [internet] United Kingdom: 8 Feb 2022 [cited 14 Feb 2022] Available from: <https://www.nice.org.uk/guidance/ng191/resources/covid19-rapid-guideline-managing-covid19-pdf-51035553326>.
12. Royal College of Midwives, Royal College of Obstetricians and Gynaecologists. Coronavirus (COVID-19) Infection in Pregnancy [internet] United Kingdom: 11 Jan 2022 [cited 14 Feb 2022] Available from: <https://www.rcog.org.uk/globalassets/documents/guidelines/2022-01-11-coronavirus-covid-19-infection-in-pregnancy-v14.3.pdf>.
13. UpToDate. COVID-19 and pregnancy: Questions and answers [internet] UpToDate; 9 Feb 2022 [cited 14 Feb 2022] Available from: <https://www.uptodate.com/contents/covid-19-and-pregnancy-questions-and-answers>.
14. International Federation of Gynecology and Obstetrics. Non-Communicable Diseases and COVID-19 Statement from the FIGO Committee on Pregnancy and NCDs [internet] FIGO; 30 March 2020 [cited 14 Feb 2022] Available from: <https://www.figo.org/sites/default/files/2020-04/FIGO%20statements%20-%20COVID%20NCDs%20English.pdf>.
15. Magala Ssekandi A, Sserwanja Q, Olal E, et al. Corticosteroids Use in Pregnant Women with COVID-19: Recommendations from Available Evidence. J Multidiscip Healthc. 2021;14:659-63. DOI: 10.2147/jmdh.S301255
16. Eslamian L, Ahmadi M, Ahmadi M. Prescribing Aspirin for Preeclampsia Prevention in Pregnant Women During COVID-19: Should or Shouldn't? Iran J Pharm Res. 2021 Winter;20(1):1-2. DOI: 10.22037/ijpr.2021.115076.15183

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