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Medicine management for pregnant patients with COVID-19 – guidance for NSW Health clinicians

Introduction and principles of care

The purpose of this guidance is to outline pertinent COVID-19 medicine management information for the pregnant population. Guidance in this document is based on evidence and recommendations from the Australian guidelines for the clinical care of people with COVID-19, a rapid evidence review and international and Australian guidance.[1]

This evidence was considered by an expert group of NSW clinicians to inform the development of this document. They included a high-risk clinical midwifery consultant, maternal-fetal medicine specialists, obstetric physicians, intensivists, neonatologists and representatives from Mother Safe NSW, Agency for Clinical Innovation, Clinical Excellence Commission, the NSW Therapeutic Advisory Group and NSW Ministry for Health.

This document will be updated as required based on:

- changes in evidence or higher-level guidance
- the context in NSW
- the needs of patients and clinicians.

Principles of medicine use in this setting:

- Treatment should be considered on a case-by-case basis (factoring in gestational age and the woman's short and long-term health outcomes).
- Harm-benefit ratio of treatment for the pregnant woman and fetus **must** be considered.
- Clinicians are reminded to follow correct procedures if there is an intention to use a medicine for an indication other than those listed in the Therapeutic Goods Administration-approved product information.[2] The multidisciplinary team should consider and conduct a detailed discussion about potential benefits and risk of harms with use of the medicine in an individual patient. The discussion should include the patient and/or carer, and when relevant an interpreter.
- Patient consent processes should follow standard processes for the acute care environment. It is important to note that pregnant women are at risk of sudden respiratory deterioration. To ensure shared decision-making, discuss medicines that may be used before deterioration. The discussion and consent should take place alongside consent for other interventions e.g. expressing milk, Caesarean section.
- Urgent intervention for birth should not be delayed. When preterm birth is required, the administration of antenatal corticosteroids to promote fetal lung maturation and magnesium sulfate for neuroprotection should not delay delivery. See Appendix A for flowchart - guide for medicines management for pregnant women with COVID-19 with planned or expected preterm birth.
- NSW Therapeutic Advisory Group has developed supporting documents including drug guidance, patient information leaflets and consent guides and forms to assist clinicians, patients and carers when medicines are used for hospitalised adults with COVID-19.[3]
- For an overview of current recommendations for NSW, see also NSW Health interim guidance on use of antiviral and immunomodulation therapy in COVID-19.[4]
- The TGA pregnancy category should not be the sole basis of decision making in the use of a drug during pregnancy, because it does not provide information about the balance of harms and benefits for a particular woman and fetus. Furthermore, the category does not indicate the stage(s) of fetal development that might be affected by drug exposure and may not reflect the most up-to-date information about use of the drug in pregnancy.

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Corticosteroids

National COVID-19 Clinical Evidence Taskforce – Recommendation

Use dexamethasone 6mg daily intravenously or orally for up to 10 days in pregnant or breastfeeding women with COVID-19 who are receiving oxygen (including mechanically ventilated patients).[5]

The corticosteroid used will be determined by the likelihood of imminent birth and the need for fetal lung maturation. 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.

Prednisolone and hydrocortisone are suggested for pregnant women who require corticosteroid therapy for COVID-19, if there is no requirement to speed up fetal lung maturation. These medicines are much less likely to cross the placenta. Long courses of fluorinated corticosteroids may adversely impact on fetal physical and brain growth. When preterm birth with active neonatal care is anticipated within the next seven days, dexamethasone administered over two days can be used for lung maturation (see Table 1 for dose and route of administration). The remaining course of corticosteroid therapy for maternal health (treatment of COVID-19) can be completed with dexamethasone, prednisolone or hydrocortisone.

The decision regarding whether to complete a 10-day course of corticosteroids if the patient no longer requires oxygen should be made on a case-by-case basis, based on clinician discretion.

See Table 1 for dosing recommendations of corticosteroids.

Table 1: Corticosteroid choice and dosing recommendations

Indications	Corticosteroid medicines	Dosage
Corticosteroids indicated for fetal lung maturation (gestation <34 weeks) **AND** Maternal corticosteroid therapy indicated for COVID-19.	Dexamethasone	6mg intramuscular (IM) every 12 hours for four doses **THEN continue dexamethasone daily or switch to** prednisolone or hydrocortisone for the remainder of course (up to an additional eight days) per below dosage.
Maternal corticosteroid therapy indicated for COVID-19 **AND** Birth not expected within 7 days or corticosteroids for fetal lung maturation not indicated.	Prednisolone	50mg orally daily for up to 10 days.
	OR	
	Dexamethasone	6mg orally or intravenously (IV) daily for up to 10 days.
	OR	
	Hydrocortisone	50mg IV or orally every six hours for up to 10 days.
Corticosteroid therapy indicated for fetal lung maturation and **NO** maternal indication for steroids.	Betamethasone	11.4mg IM as a single dose; give second dose after 24 hours (unless delivery occurs).

Immunomodulating drug use in pregnancy

Sotrovimab

National COVID-19 Clinical Evidence Taskforce – Conditional recommendation

Consider using sotrovimab for the treatment of COVID-19 within five days of symptom onset in pregnant women in the second or third trimester who do not require oxygen and who have one or more additional risk factors for disease progression.[6]

Within the population of pregnant women for which sotrovimab is conditionally recommended for use (as listed above), decisions about the appropriateness of treatment with sotrovimab should be based on; the patient's individual risk of progression to severe disease, the presence of risk factors and COVID-19 vaccination status. Please refer to the ACI Model of care for the use of sotrovimab in adults in NSW and NSW TAG Drug Guidance for further advice.[3, 7]

Tocilizumab

National COVID-19 Clinical Evidence Taskforce – Conditional recommendation

Consider use in pregnant women with COVID-19 who are receiving supplemental oxygen, particularly if there is evidence of systemic inflammation.[8]

Dosages in pregnant women are based on their current body weight (not pre-pregnancy weight).

Please refer to the NSW Therapeutic Advisory Group tocilizumab guidance for further information including recommended dosing.[3]

In accordance with the RECOVERY trial, tocilizumab should be administered as an intravenous infusion over 60 minutes. **Only a SINGLE DOSE of tocilizumab should be used (see Safety Alert 002/21 for further information).[9]**

Important note about use of live vaccinations for infants

When tocilizumab is administered after 20 weeks of gestation, rotavirus and Bacille Calmette–Guérin (BCG) vaccines should be avoided during the first six months of life. Non-live vaccines as per the National Immunisation Program Schedule can be given.[10] Ensure appropriate communication of maternal tocilizumab administration and the implications for the infant's vaccine administration. This includes documentation in the infant's *Primary Healthcare Record (Blue Book)* upon birth and communication to the primary healthcare providers of the patient and infant.

Not recommended for use in pregnant women outside a clinical trial

- Baricitinib
- Sarilumab

Antiviral drug use in pregnancy

Remdesivir

National COVID-19 Clinical Evidence Taskforce – Conditional recommendation

Consider use in pregnant women hospitalised with moderate to severe COVID-19 who do not require ventilation.[11]

Despite the National Taskforce recommendations, controversy about remdesivir's efficacy remains.[12, 13] From the evidence available, if remdesivir is effective, it appears to be more likely to be of benefit when used within 10 days of symptom onset. See NSW TAG Drug Guidance and ACI Critical Intelligence Unit's rapid evidence check Initiation of remdesivir treatment for COVID-19 for further information.[3, 14]

Note: Contraindicated in women with significant renal impairment, ALT>5x upper limit of normal (ULN) or ALT>3x and bilirubin>2xULN. Consider interactions with other medicines as remdesivir is metabolised by cytochrome P450 and non-cytochrome P450 (CYP) enzymes. Can cause abnormal liver function tests.

Fetal neuroprotection or eclampsia prevention

Magnesium sulfate

National COVID-19 Clinical Evidence Taskforce – Conditional recommendation

The use of magnesium sulfate in pregnancy for the management of severe pre-eclampsia or eclampsia is supported as part of standard care, independent of the presence of COVID-19.[15]

Magnesium sulfate is recommended for women between 24+0 to 30+0 weeks' gestation, where preterm birth is expected or planned within 24 hours.

Recommendations for fetal neuroprotection

- When birth is planned, commence administration as close to four hours prior to birth as possible.
- Best effect when given for at least four hours and within the six hours prior to birth.
- If birth is expected to occur within four hours, give magnesium sulfate immediately, as there may still be benefit from administration.
- In situations where urgent birth is necessary, **do not** delay birth to administer magnesium sulfate.
- Magnesium sulfate can be used in patients with COVID-19. It has not been associated with respiratory compromise (such as pulmonary oedema).
- For women with increasing oxygen requirements or where there may be renal dysfunction, the harm to-benefit ratio should be considered before using.
- Renal function and fluid balance should be monitored. If renal impairment develops, the dose of magnesium sulfate may need to be adjusted or withheld accordingly.

Note: Magnesium sulfate may be extremely hazardous in the following circumstances: renal failure, severe renal compromise or if oliguria is present (as elimination of magnesium is predominantly renal).

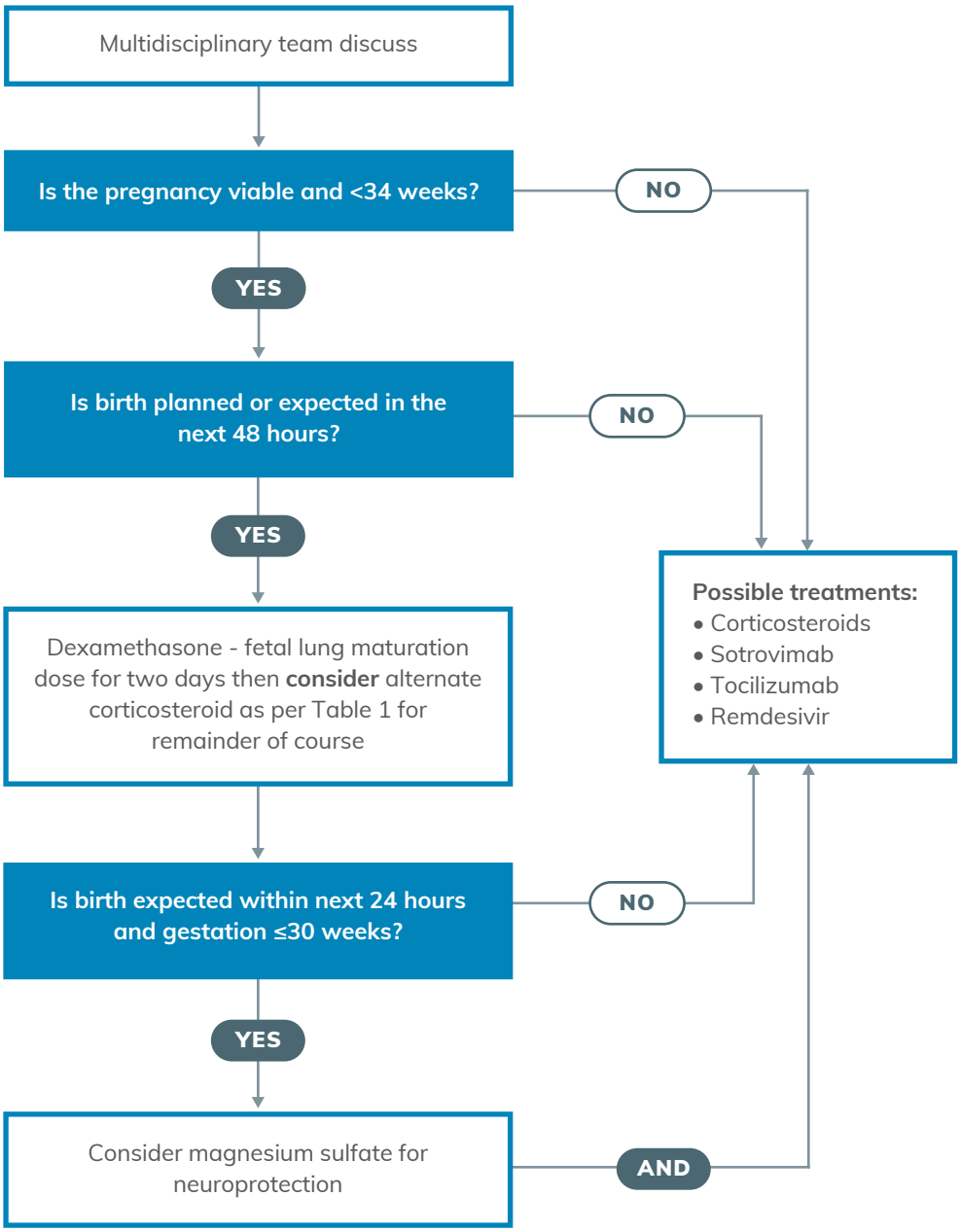
Note: In intensive care unit (ICU) patients that are intubated and/or sedated, the signs of toxicity may be masked. The first sign may be arrhythmia and/or cardiac arrest.

Please refer to GL2020_009 Management of Threatened Preterm Labour for dosage, administration, care and observations during infusions for fetal neuroprotection and maternal preeclampsia or eclampsia.[16]

Appendices

Appendix A

Flowchart: Guide for medicines management for pregnant women with COVID-19, with planned or expected preterm birth



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