Record of the Ad Hoc Critical Care Advisory Group (CCAG)

Held via Zoom videoconference on 14 April 2020

Note that this document is not necessarily a complete record of the ad hoc CCAG meeting; rather it is a summary of the pertinent discussion at the meeting.

1. Welcome and introduction

1.1. Dr Ken Clark noted the purpose of this ad hoc Advisory Group was to enable PHARMAC to seek, where possible, nationally representative clinical advice on topics of relevance to supply management of critical care medicines and hospital medical devices, in the context of the national response to the COVID-19 pandemic. The primary purpose initially would be to provide advice related to *critical care medicines*; however, PHARMAC can foresee that advice regarding relevant hospital medical devices may be valuable as the situation evolves. PHARMAC also recognises the heavy overlap between those medicines used in critical care and those used in anaesthesia practice. Specific aims include:

- To provide clinical advice to PHARMAC on the medicines (and hospital medical devices) likely to be required in the critical care setting during the COVID-19 pandemic;
- To provide clinical advice to PHARMAC on potential therapeutic alternatives, including practice changes, that could be utilised in the event that stock supply becomes more challenging, and implementation-related activities that might be needed as a result;
- For PHARMAC to use this advice in its contract management work, and in its support to other sector partners including the Ministry of Health's National Crisis Management Centre and COVID-19 Technical Advisory Group (TAG)'s ICU subgroup.

1.2 The CCAG noted that at this time COVID-19 treatments (for example anti-viral agents) are considered outside of the scope of this Advisory Group, and that PHARMAC will seek advice via other clinical advice networks on these matters.

2. Critical care medicines in the context of COVID19

2.1. The Group reviewed a list of medicines that had been prepared by PHARMAC staff. The following feedback was provided by CCAG.

General anaesthetics:

2.2. The Group considered that propofol will be an essential medicine in the care of COVID-19 patients. In the critical setting the most suitable presentation would be the 100 ml vial, but any size would be acceptable. If propofol were unavailable the next best alternative is considered to be morphine with midazolam. Another option is methadone with phenobarbitone. A number of different agents are used as adjuncts to propofol. These include clonidine, ketamine and dexmedetomidine

2.3. The Group considered that volatile anaesthetics (i.e. desflurane, isoflurane and sevoflurane) are unlikely to be used in the critical care of COVID-19 patients, unless there was heavy demand on intensive care services. However, the group considered that there would be merit in practice moving away from total intravenous anaesthesia (TIVA) for procedural work in both ICU and in operating theatres should stocks of propofol need to be conserved and if there were safe alternatives. Were this to occur, then usage of volatile anaesthetics would likely increase. This would be particularly notable as elective procedures recommenced. Isoflurane/sevoflurane may be an option for maintaining sedation in the critical care setting. Desflurane is not generally preferred ahead of sevoflurane/isoflurane in the critical care setting. The ventilators used in the critical care setting generally are not used administer volatile anaesthetics (as distinct to those used in the operating theatre).

2.4. The Group considered that PHARMAC should ask the relevant Colleges and Societies (see Table Seven) to suggest guidance to membership on strategies for conserving propofol stock, should demand management be warranted.

2.5. The CCAG considered an essential list of general anaesthetics (in approximate priority order) could be as could be considered as shown in Table One.

Table One: General anaesthetics

Essential	
Propofol	Inj 10 mg per ml, 100 ml vial
Propofol	Inj 10 mg per ml, 50 ml vial
Propofol	Inj 10 mg per ml, 20 ml vial or ampoule
Highly desirable	
Ketamine	Inj 100 mg per ml, 2 ml vial
Clonidine	Inj 150 microgram per ml, 1 ml ampoule
Clonidine	Tab 25 mg
Dexmedetomidine	Inj 100 microgram per ml, 2 ml vial
Ketamine	Inj 10 mg per ml, 10 ml syringe
Ketamine	Inj 1 mg per ml, 100 ml bag
Etomidate	Inj 2 mg per ml, 10 ml ampoule

Neuromuscular blocking agents and reversal agents:

2.6. The Group considered that rocuronium and suxamethonium will be essential medicines in the care of COVID-19 patients. If these were unavailable the next best alternatives would be the common neuromuscular blocking drugs atracurium, vecuronium and pancuronium. Large doses of these increase speed of neuromuscular blockade, but increase duration of effect. Consequently, some patients may require additional neuromuscular monitoring.

2.7. Members considered that some form of neuromuscular blockade reversal would be needed in the context of patients who have (or are suspected of having) COVID-19 undergoing potentially unrelated surgical procedures. Practice varies across the country, but options include neostigmine alone, or in a pre-mix with glycopyrronium or with atropine, or sugammadex (if rocuronium or vecuronium used). In general, sugammadex would only be used in patients refractory to the first line agents (in line with funding restrictions), and in the context of rocuronium use.

2.8. The CCAG considered an essential list of neuromuscular blocking agents and reversal agents (in approximate priority order) could be as follows in Table Two.

Table Two: Neuromuscular blocking agents and reversal agents

Essential	
Rocuronium	Inj 10 mg per ml, 5 ml ampoule
Suxamethonium	Inj 50 mg per ml, 2 ml ampoule
Highly desirable	
Neostigmine metilsulphate	Inj 2.5 mg per ml, 1 ml ampoule
Vecuronium bromide	Inj 10 mg vial
Pancuronium bromide	Inj 2 mg per ml, 2 ml ampoule
Sugammadex	Inj 100 mg per ml, 2 ml vial or 5 ml vial
Neostigmine metilsulfate with glycopyrronium bromide	Inj 2.5 mg with 0.5 mg per ml, 1 ml ampoule
Atropine sulphate	Inj 600 microgram per ml, 1 ml ampoule

Opioid analgesics:

2.9. The Group considered that fentanyl or other alternative opioids will be essential in the care of ventilated and sedated COVID-19 patients, particularly for procedures. Morphine and methadone are commonly used for longer term sedation/analgesia would also be alternative options for fentanyl should fentanyl be unavailable. The exception would be in people with compromised renal function where oxycodone may be preferred. Alternatives to fentanyl could include remifentanil and alfentanil. Alfentanil is not so commonly used in clinical practice in NZ as in the UK and so may require some implementation support. There are some UK data (from ICNARC) to suggest that a number of people with COVID-19 who are admitted to ICU have a BMI > 30 kg/m^2. It is possible that in the context of a large number of COVID-19 patients requiring critical care that alfentanil usage may increase.

2.10. The Group discussed the option of introducing diamorphine as a therapeutic alternative should other opioids become more challenging to procure. Members noted that diamorphine is licenced in the UK and been extensively used in ICUs and other settings in that country, with many CCAG members experienced in its use. PHARMAC staff noted that previously the PTAC and the Analgesic Subcommittee had previously expressed concerns about increasing the number of strong opioids available in New Zealand, and had considered that diamorphine should not be an option.

2.11. The CCAG considered, an essential list of opioid analgesics (in approximate priority order) could be as follows in Table Three.

Table Three: Opioid analgesics

Essential	
Morphine sulphate	Inj 5 mg or 10 mg or 15 mg or 30 mg per ml, 1 ml
Fentanyl	Inj 50 microgram per ml, 2 ml ampoule or 10 ml ampoule
Highly desirable (and necessary in the event of fentanyl or morphine out of stock)	
Methadone	Inj 10 mg per ml, 1 ml vial
Oxycodone	Inj 10 mg per ml, 1 ml amp or 2 ml amp or 50 mg per ml, 1 ml ampoule

Remifentanil	Inj 1 mg vial or 2 mg vial
Alfentanil	Inj 0.5 mg per ml, 2 ml ampoule

Sedatives:

2.12. The Group considered that midazolam will be essential in the care of COVID-19 patients, regardless of the availability of propofol. Usage would further increase if morphine with midazolam is used as a substitute for propofol. Alternatives to midazolam include clonidine, intravenous oral or nasogastric administration of diazepam (or other long-acting benzodiazepines), and phenobarbitone (used in combination with methadone).

2.13. The CCAG considered, an essential list of sedatives (in approximate priority order) could be as follows in Table Four.

Table Four: Sedatives

Essential	
Midazolam	Inj 5 mg per ml, 3 ml ampoule
Highly desirable	
Phenobarbitone	Inj 200 mg per ml, 1 ml ampoule
Diazepam	Tab 2 mg or 5 mg or inj 5 mg per ml, 2 ml ampoule
Lorazepam (or other long-acting benzodiazepine)	Tab 1 mg or 2.5 mg
Clonidine	PO, IV, transdermal

Vasopressors/sympathomimetics

2.14. The Group considered that noradrenaline and adrenaline will be essential in the care of COVID-19 patients. In the event of noradrenaline being unavailable, alternatives would be phenylephrine, metaraminol, dopamine or dobutamine.

2.15. The CCAG considered, an essential list of vasopressors/sympathomimetics (in approximate priority order) could be as follows in Table Five.

Table Five: vasopressors/sympathomimetics

Essential	
Noradrenaline	Inj 1 mg per ml, 4 ml ampoule
Adrenaline	Inj 1 in 1,000, 1 ml ampoule
Highly desirable	
Phenylephrine hydrochloride	Inj 10 mg per ml, 1 ml ampoule
Metaraminol	Inj (not specified)
Argipressin [vasopressin]	Inj 20 units per ml, 1 ml ampoule
Terlipressin	Inj 1 mg in 8.5 ml
Desmopressin	Inj 4 microgram per ml
Dobutamine	Inj 12.5 mg per ml, 20 ml ampoule

Vasodilators:

2.16. The Group considered that, in the context of care of ventilated COVID-19 patients, some use of vasodilators is likely to be nebulised. The rationale would be to reduce the pulmonary shunt that may be associated with intravenous administration of these agents.

2.17. The Group considered that iloprost will be essential in the care of COVID-19 patients. In the event of iloprost being unavailable, alternatives would be milrinone or epoprostenol.

2.18. The CCAG considered, an essential list of vasodilators (in approximate priority order) could be as follows in Table Six.

Table Six: vasodilators

Essential	
Iloprost	Nebuliser soln 10 microgram per ml, 2 ml
Highly desirable	
Milrinone	Inj 1 mg per ml, 10 ml ampoule
Epoprostenol	Inj (not specified)

Other

2.19. Members noted the following medicines that may need to be considered, as supply issues have been reported in overseas jurisdictions;

- Potassium chloride injection
- Phosphate injection
- Magnesium Sulphate injection
- Omeprazole injection
- Insulin Actrapid
- Antibiotics for secondary infections
- Anticoagulants (heparin, LMWH, warfarin/NOACs)
- Fluids for continuous venovenous hemodiafiltration (CVVHDF)
- IV fluids (e.g., dextrose 5%, normal saline, compound sodium lactate, Plasmalyte)
- Paracetamol injection

3. Communications with the sector

3.1. Members provided the following list (Table Seven) of possible groups to keep informed of any supply issues and any need for national demand management approaches. The Group considered that the Anaesthetics stakeholders would likely be most critical group with respect to demand management, particularly once elective surgical procedures resume.

Table Seven: Key Contacts

Discipline	Organisation/contact group
Intensive Care	ICU Directors Group
Intensive Care	ANZICS
Intensive Care	CICM
Anaesthesia	ANZCA
Anaesthesia	NZSA
Anaesthesia	NZ Anaesthetic Technicians Society
Pharmacy	Chief Pharmacists
Pharmacy	PSNZ
Pharmacy	NZHPA
Nursing – Critical Care	NZCCCN
Nursing	NZNO
Nursing	Nursing Council