Medicine Shortages Working Party

National demand model for ICU medication for COVID-19 treatment

3 June 2020

Background

Since the emergence of COVID-19 in Australia the Therapeutic Goods Administration (TGA) within the Department of Health has been closely monitoring supply of critical medicines used in the intensive care setting, and working with health professional, pharmaceutical industry and wholesaler groups and State and Territory health departments to identify and respond to medicine supply issues as they arise.

Concerns have been raised that available supply of intensive care medicines may not meet an increase in demand resulting from a rise in COVID-19 cases requiring intensive care and ventilation as elective surgery recommences. These concerns also include that access to increased quantities of these medicines may be impeded by the international impacts of the pandemic on manufacturing workforces, freight availability and export restrictions, combined with very high demand for these medicines from countries with much higher numbers of infections than Australia.

Pharmaceutical industry sponsors have reported supplying significantly increased quantities of critical intensive care medicines in March and April as hospitals have sought to build reserve stocks to operate a planned significant increase in the number of ventilated intensive care unit (ICU) beds. In response to the dramatically increased demand for ICU medicines, manufacturers and wholesalers constrained supply to facilitate equitable allocation. This approach, and the substantial increase in volumes ordered, resulted in some hospitals not receiving the quantities of stock ordered, which had caused significant concerns in the sector over the last two months.

Medicine sponsors have indicated to the TGA that they can seek increased supply of critical medicines from their international supply chains, but that proposed quantities to obtain are difficult to estimate based on current ordering patterns from hospitals and states and territories. Sponsors seeking increased allocations from their international headquarters must be able to demonstrate a reasonable level of certainty about Australian demand, particularly when multinational companies must make decisions on supply for different markets, some of which may have very limited supplies to treat much higher numbers of current COVID-19 patients.

Medicine sponsors, state and territory health departments and hospitals have also expressed concerns about the variation in supply nationally, with some hospitals being expected to hold much larger stocks than others, and the lack of a mechanism to identify and rapidly redistribute available supply to meet a shortfall at another location.

Purpose of the state/territory demand forecast working group

The TGA, in collaboration with state and territory health departments, convened a working group to estimate the national medicines requirements for ICU management of COVID-19 patients to:

- facilitate the supply in Australia of additional quantities of these medicines where needed, by providing medicine sponsors with reliable estimates of demand
- inform the development of strategies to address any gap between anticipated supply and demand, such as redistribution of stock, conservation, and/or the use of alternative therapeutic options.

The working group includes representatives of state and territory health departments, pharmacists, anaesthetists, intensivists and the TGA and is chaired by Professor Michael Dooley, Director of Pharmacy at the Alfred Hospital, Melbourne.

Methods

Medicines in scope

Medicines to be included:

- sedatives – midazolam, propofol, clonazepam, ketamine, dexmedetomidine
- opiates – fentanyl, morphine, oxycodone
- neuromuscular blocking agents (NMBA) – cisatracurium, rocuronium, suxamethonium, vecuronium, atracurium

Other medicines, including those for sepsis and pneumonia, will be incorporated in the demand forecasting should this be required.

Inputs

The following information has been used to inform the demand forecasting:

- historical national medication distribution data, provided by the TGA from a dataset purchased from IQVIA
- historical medication distribution data for public and private hospitals, provided by state and territory health departments, a major wholesaler and a major private provider
- medication distribution data within hospitals (ICU/emergency department/operating theatres/other) provided by state and territory health departments
- medicines use data for > 95% COVID-19 ICU admissions in Australia to date, including length of stay, proportion ventilated, duration of neuromuscular blockade and medicines use per admission
- clinician preferences available from various surveys
- historical data on private and public elective surgery provided by the Australian Institute of Health and Welfare
- state and territory estimates for COVID-19-related ICU occupancy

Aggregated, de-identified data on current stock held by medicine sponsors and expected deliveries to sponsors was also provided in confidence to estimate anticipated supply. Average supply per month aggregated across all presentations (data not shown) was calculated from the sum of current stock held by sponsors and deliveries to sponsors anticipated from May to October 2020. Average supply per month was compared with the demand estimates for different levels of surgical activity and ICU occupancy to determine the level of ICU occupancy that could be accommodated.

Modelling assumptions

Projected demand for medications will be dependent upon:

- ICU activity (non COVID-19 related)
- ICU activity (COVID-19 related)
- surgical activity
- activity in other areas of use (e.g. emergency department, palliative care)

Due to the limited access to historical patient usage data the modelling is based on previous 2019 medicine demand and assumes:

- ICU beds (non-COVID-19) remain at 2019 levels
- Emergency Department and other usage remains at 2019 levels
- ICU beds for COVID-19 patients are additional and modelled on different monthly occupancy levels of ventilated ICU beds, from 10 beds per month to 2400 beds per month.
- Operating theatre requirements projected on elective surgery rates 25%, 50%, 75% and 100% and 125% of 2019 activity

Supply of medicines is assumed to occur at a constant rate, based on the average of current stock and future deliveries from May to October.

Data has been provided in various formats with varying degrees of detail. All information has been provided confidentially to develop the model. The model has been constructed in Excel. An example of the data used for the models is shown in Figure 1.

Results

The working group identified that five medicines were to be modelled as highest priority. Initial estimates developed for the medicines below are included in Attachment 1:

- sedatives – midazolam, propofol
- opiates – fentanyl
- NMBA – cisatracurium, rocuronium

Each figure shows the medicine requirement (expressed as the % change from usual demand defined as historical 2019 demand) for varying levels of surgical activity (25%, 50%, 75%, 100% and 125% 2019 activity) and varying numbers of ICU beds occupied by ventilated COVID-19 patients per month.

Medicines demand has been estimated for monthly ventilated bed occupancy from 10 beds to 2400 beds, to accommodate a range of scenarios on which different jurisdictions have indicated they are basing their planning. Data on Australian admissions shows that the average duration of ventilation for COVID-19 patients is 17 days and length of stay in ICU slightly longer. Therefore, monthly occupancy of 10 beds equates roughly to 17 individual patients, and 2400 beds per month equates roughly to 4080 patients.

For reference, there were 21 COVID-19 ventilated patients in ICU in Australia on 1 May 2020 and only 2 ventilated patients on 3 June 2020. To 17 May 2020 a total of 50 patients with COVID-19 in Australia had been admitted to ICU and received ventilation.[1]

Additional propofol requirements for COVID-19 patients are relatively modest compared with usual demand. This is reflective of the large use of propofol in ICU and OT historically. Approximately 200 COVID-19 ventilated ICU beds per month (approximately 350 individual patients) could be accommodated with an increase in propofol supply of around 25% above usual levels and 100% elective surgery activity.

Increases in midazolam and fentanyl supply to 50% above usual levels would accommodate 200 ventilated ICU beds per month.

Demand for NMBAs for ventilated COVID-19 patients is proportionally higher than for sedatives and opioids due to the larger quantities of NMBAs administered to these patients. Internationally, supply of NMBAs has been more problematic than for other medicines for countries with high numbers of infections.

Cisatracurium is the preferred NMBA for most Australian intensive care units for continuous infusion and has been used in the majority of COVID-19 cases in ICU. An increase in supply of cisatracurium to 150% above usual levels would be required to accommodate 200 COVID-19 ventilated ICU beds (approximately 350 individual patients) per month.

Demand for rocuronium has been estimated as it is the second most preferred agent. The model for rocuronium has been undertaken for two scenarios, one based on usage seen to date, and one if cisatracurium is unavailable. If cisatracurium was completely unavailable, then quantities of rocuronium of 50% above usual supply would be required to manage 200 COVID-19 ventilated ICU beds per month (approximately 350 individual patients).

Average supply per month of cisatracurium, rocuronium, midazolam, fentanyl and propofol is anticipated to be sufficient to accommodate 200 ventilated ICU beds per month for COVID-19 patients from June to October. Anticipated supply depends on future deliveries arriving in time and in full. Supply over the next few months for some critical medicines is dependent on future deliveries. Unforeseen problems with manufacturing or increases in demand from other markets could affect the size or timing of these deliveries.

Next steps

The working group is modelling demand for further medicines, and working with state and territory health departments to develop estimates to inform sponsors' future orders.

[1] https://www1.health.gov.au/internet/main/publishing.nsf/Content/1D03BCB527F40C8BCA258503000302EB/$File/covid_19_australia_epidemiology_report_16_reporting_week_ending_23_59_aest_17_may_2020.pdf

Figure 1: example of data input for demand forecast model

1. 2019 HISTORIC DISTRIBUTION DATA	
Historic PRIVATE hospital usage: %	Derived from major private provider, representing approx 25% private activity in Aust
Private ICU use:	%
Private OT use:	%
Private ED use:	%
Other use:	%
Historic PUBLIC hospital usage: %	Derived from hospital distribution data: comprehensive data from some jurisdictions; large samples from other states
Public ICU use:	%
Public OT use:	%
Public ED use:	%
Other use:	%

Annual sales (2019)	Derived from IQVIA via Commonwealth
Annual sales: medication x (g)	**X grams**
2. COVID scenario: patient treatment	Derived from Australian COVID ICU admissions requiring ventilation (39pts) [represents >95% of COVID ventilated pt]*
% COVID patients receiving MEDICATION X	%
Average daily dose: X g day	X g
Average no. of days treatment	X days
Ave TOTAL dose received per episode (g)	X g
Duration of ventilation per patient (days)	X days
Ave daily dose PER DAY of VENTILATION	X g
3. COVID ICU Activity:	Approximating multiples of National COVID-19 ICU ventilated bed occupancy @1st May 2020 (n=21)#
10 patients	10
20 patients	20
40 patients	40
100 patients	100
200 patients	200
400 patients	400
600 patients	600