Australian Government
Department of Health
Therapeutic Goods Administration

# Pharmacy Guild update
# 2 March 2022


**Adjunct Prof John Skerritt**

Deputy Secretary, Australian Department of Health

Head, Therapeutic Goods Administration


TGA Health Safety Regulation

# My last presentation - Oct 21 - opening up after the delta wave

# …. This presentation - Mar 22 - opening up after the omicron wave

- New vaccine approvals / boosters/ kids
- Vaccine safety
- New treatments
- RATs
- Omicron variants
- And more !


# COVID-19 vaccines

# COVID-19 vaccines – recent TGA approvals

- **Novavax** (2 doses at least 28 days apart)
  - Protein based vaccine may attract uptake from some vaccine-hesitant individuals
  - Not for booster or paediatric doses – still awaiting an application for this
  - Most common side effects in clinical trials - headaches, muscle pain and fatigue, some cases of hypertension and immunological adverse events
- **Pfizer booster for 16-17 year olds**
- **Astra Zeneca booster dose for 18 + years**
  - Decision to use must be made in consultation with a medical professional - may find greatest use if a significant adverse reaction occurred after a previous mRNA vaccine dose
  - mRNA vaccines recommended as a single booster dose, irrespective of the primary vaccine used
- **Moderna for 6-11 years** (2 doses at least 28 days apart, usually 8 weeks)
  - TGA is the first major regulator globally to approve for under 12s

# Moderna paediatric approval important

## because 5-11 vaccination rates hovering around 50 %

- **Rollout of Moderna vaccine (as well as Pfizer) provides wider access**
  - There are an additional 1600 sites - pharmacies and some GPs - with Moderna but not Pfizer
  - Mum and Dad can have boosters and their primary school age kids can have one visit
- **Differences with Pfizer paediatric vaccine**
  - Pfizer approval is 5- 11 – one year younger – reflects different clinical trial data
  - Moderna product – and the vials used - are the same for adults and children – just a different dose
- **Importance of vaccinating young children**
  - At least 6 deaths and a number of hospitalisations in under 10s
  - Almost 200,000 children under 10 have caught COVID in Australia – impact on transmission to parents and grandparents, over children with underlying health conditions, school participation
  - Serious paediatric multisystem inflammatory syndrome  - over 40 cases

# mRNA vaccine safety in young children

- **Most common reactions reported** include chest pain, vomiting, fainting, nausea and paleness
  - Active surveillance (AusVaxSafety) text message and follow up also shows fewer adverse reactions reported after vaccination in 5-11 year olds than in older Australians

- **Myocarditis is a rare adverse event** with mRNA vaccines
  - While rare, rates are highest after dose 2 in males older teenagers and young adults

- But **with 5-11 year olds myocarditis is extremely rare**
  - no confirmed cases from 10 reports of suspected myocarditis
  - one 10-year-old boy possibly had mild pericarditis
  - In the US rate of 1 in a million confirmed myocarditis in 5-11 year olds

- Myocarditis **also extremely rare in 12-15 year olds** for both Pfizer and Moderna
  - For any dose, per 100,000 doses - Pfizer – 3.6 (70 cases) vs Moderna  4.5 (11 cases)
  - For boys after the second dose -  Pfizer – 10 per 100,000 doses vs Moderna 13 per 100,000

# What further vaccines will be considered in 2022 ?

## Booster shots

- Pfizer for 12-15 year olds
- Novavax boosters for adults
- Others ?

## Vaccines for under 5 s

- Pfizer – 2-4 year olds may need a third low dose
- Others ?

## Other vaccines (two other provisional determinations)

- Vaccines against variants ? But will they arrive too late ?
- Multivalent vaccines ?
- Others – new mRNA/DNA/ other technologies, more protein vaccines

# Pharmacists can support vaccination after having a COVID-19 infection

- About 3 million Australians have reported COVID-19 infections
- **Boosters are just as important** for those who have had COVID-19 as reinfections occur in about 1 in 20 people, and are much more likely with omicron
- Vaccination after infection gives a **significant immunity boost**
- People who have had COVID-19 **can be vaccinated once they recover,** although it can be deferred up to 4 months
- For all, third dose is associated with **lower reported adverse event rates** than first 2 shots (1 myocarditis case per 100,000)

# Vaccine recognition and what it means

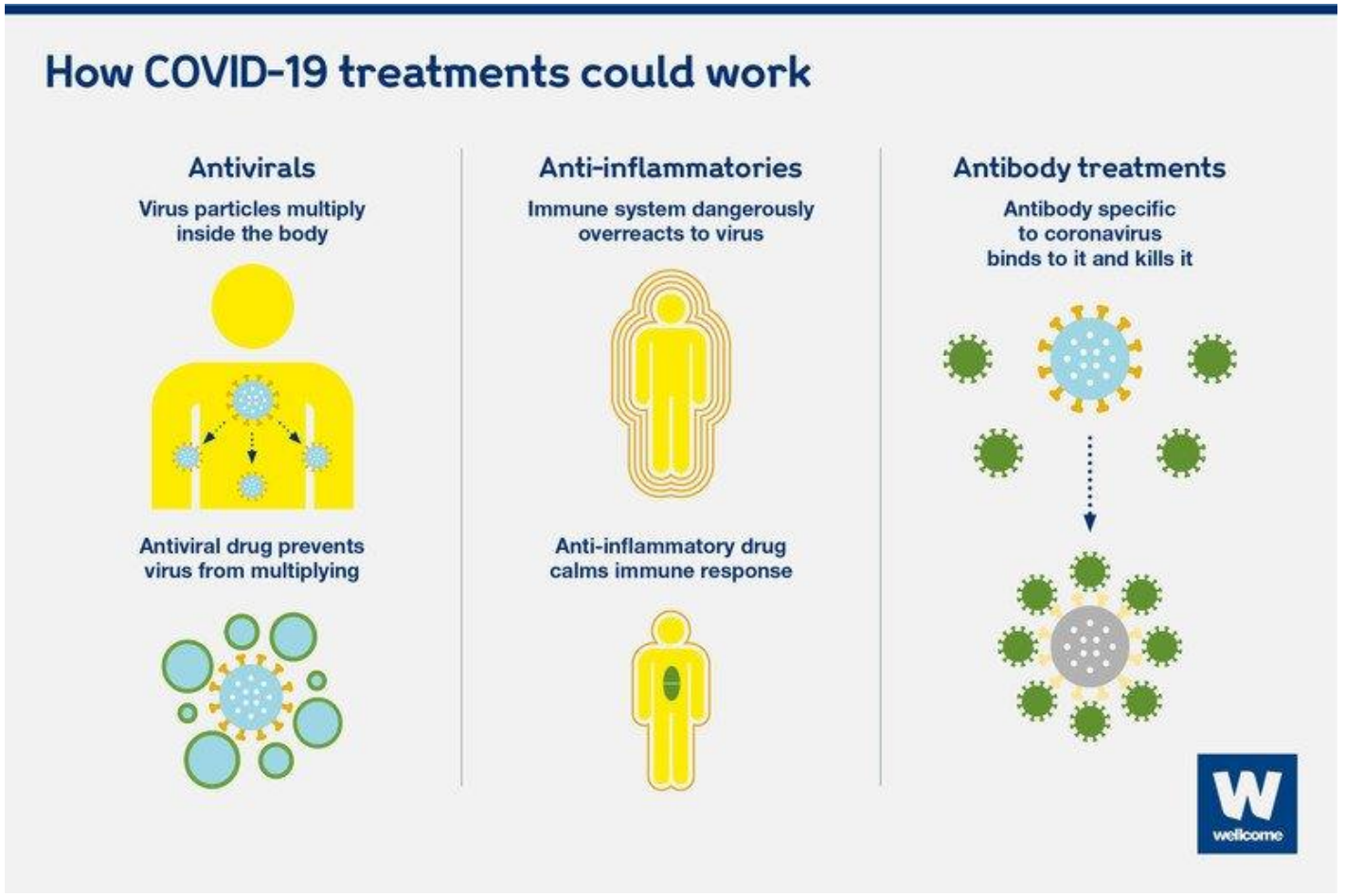
- **Not a TGA approval** – done to support inbound travel to Australia
- Based on both **efficacy data** (clinical trials / regulatory dossiers) and published real world **effectiveness data**
- Recognised vaccines **must be as effective as TGA-approved ones**
  - But many studies were conducted prior to the emergence of Omicron
- **Recognised vaccines include:**
  - Two dose course of Gamaleya (Sputnik, Russia)
  - Two Chinese vaccines - BBIBP-CorV (Sinopharm, for those under 60) and Coronavac (Sinovac)
  - Two Indian vaccines - Covaxin (Bharat Biotech) and Covishield (Serum Institute /AstraZeneca).
  - Two-dose protocols currently recognised, data emerging on third dose

# COVID-19 Therapeutics

# COVID-19 therapeutics

Being developed and used for different scenarios

- **Treatment of late stages of COVID-19** – reduction of deaths in ventilated patients
- **Prevention of disease progression** in high risk patients (hard to identify most suitable individuals)
- **Prophylaxis** (including pre- and post exposure)



# COVID-19 injected therapeutics and omicron

- **Potency of antibodies affected by omicron**
  - Sotrovimab – slight decrease vs delta, greater decrease for BA 2 omicron variant
  - Casirivimab + Imdevimab (Ronapreve) – very low efficacy against omicron
  - Regdanvimab – not active against omicron
- **Antivirals (including Remdesivir) and steroids** seem to maintain potency
- **Evusheld – pre-exposure prophylaxis in people at high risk of severe COVID**
  - Combination of two long-acting monoclonal antibodies (tixagevimab and cilgavimab)
  - Clinical trials not done in immunosuppressed or vaccinated people, but expect it should be effective in immunosuppressed individuals with vaccine failure
  - Decreased activity against omicron but still valuable

# Paxlovid (2 Nirmatrelvir 150 mg tablets plus Ritonavir 100 mg – bd for 5 days)

- **Approved for patients who don't require supplemental oxygen**, at high risk of progressing to severe COVID-19, to be administered within 5 days of the start of symptoms
- Nirmatrelvir is a **peptidomimetic inhibitor of replication enzyme 3CL pro**
  - Ritonavir component inhibits CYP3A4 to maintain levels of the other drug
- **High efficacy** (including against omicron) but cannot be used in pregnancy or breastfeeding, and not recommended in women of childbearing potential
  - Must also not be used in patients with severely reduced kidney or liver function
- PAXLOVID **must not be used with a number of other medicines**, either because this may lead to potentially harmful increases in their blood levels, or for other medicines they may reduce the activity of PAXLOVID
  - Molnupiravir mainly being used in residential aged care as many residents take contraindicated medicines

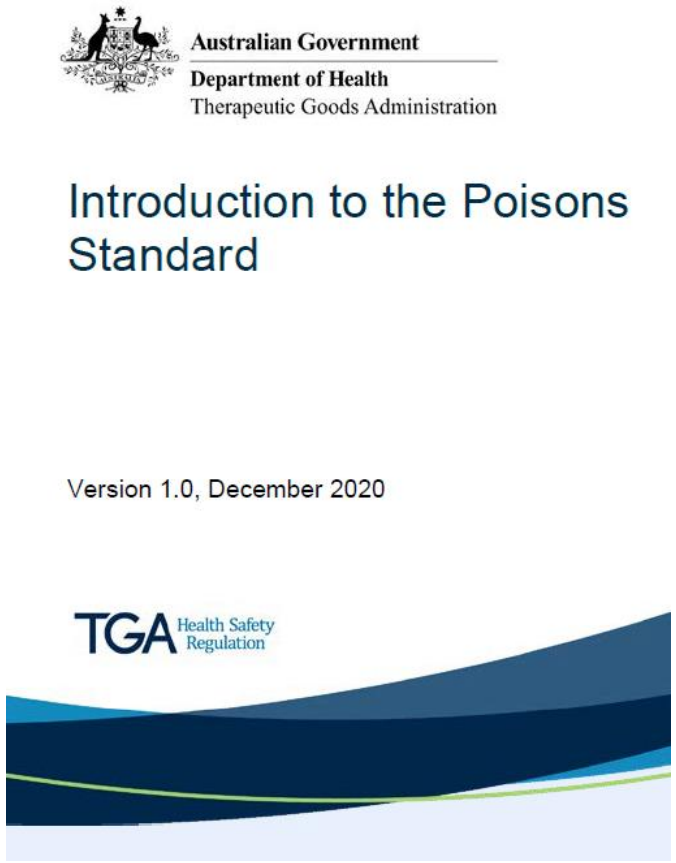
# Lagrevrio (Molnupiravir 4 x 200 mg capsules – bd for 5 days)

- **Approved for treatment of adults with COVID-19 who do not require initiation of oxygen** and are at increased risk for hospitalisation or death
- Molnupiravir works by **inhibiting replication of the SARS-CoV-2 virus**
- **Not recommended** in pregnancy and breastfeeding. Sexually active women of childbearing age should use contraception and men also use contraception during and 3 months after treatment
- **Lower efficacy** in published data than Paxlovid
  - But it has not been compared back to back against Paxlovid
  - There was differing disease pressures and differing hospitalisation criteria in the two trials
  - Lack of clinical trial data in vaccinated patients
- **PBS Streamlined Authority** from 1 Mar 2022 – first COVID-19 treatment on the PBS for:
  - People 65 and over with two risk factors for severe disease
  - People 75 years and over with one risk factor for severe disease
  - Aboriginal and Torres Strait Islanders 50 and over with two risk factors for severe disease
  - Those moderately to severely immunocompromised

# Why aren't the oral antivirals in schedule 3 ?

- Pregnancy warnings
- Strong recommendation for male partner contraception
- Significant drug interactions
- Use in liver and kidney function compromise

- **Prioritisation for both Lagrevrio and Paxlovid for patients at highest risk**
  - Lagrevrio PBS conditions
  - Paxlovid - state and territory health unit allocation, aged care, aboriginal health services
  - Recognise need to get rapid access to patients in need



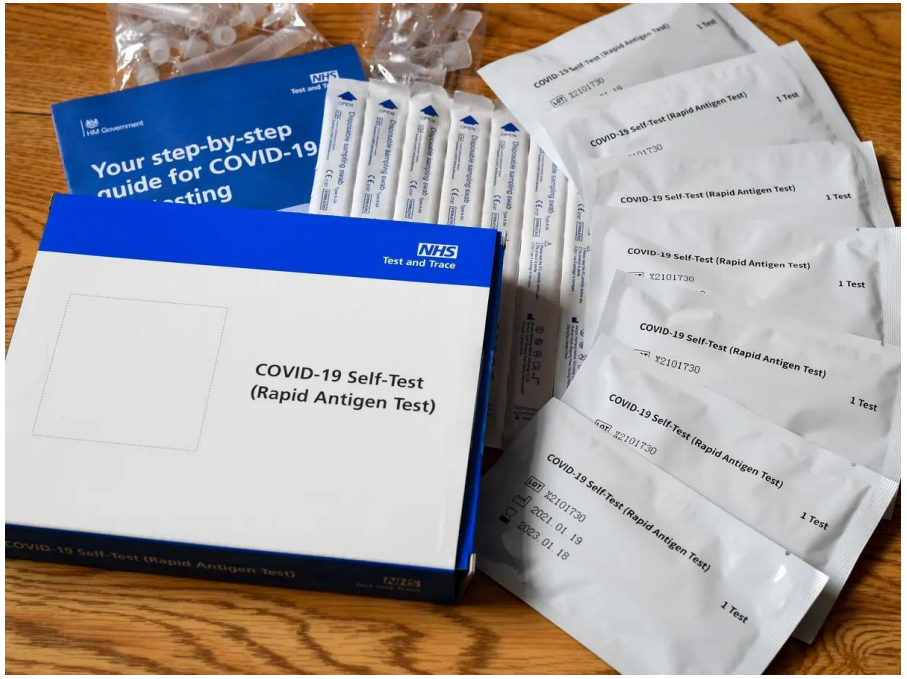
# Rapid antigen tests – and summing up

# Requirements for rapid antigen self tests

- **Simpler instructions for use**
- **Usability testing** with untrained users
- Contact centre for users (1800 number, interactive website)
- Confirm they detect the **delta** variant well – independent evaluation
- TGA regulation to enable **responsible advertising**
- **Pharmacists can also provide a testing service for the public** with point of care tests but need to consider infection management and other risks – limited take up ?

# What about RAT tests and omicron?

- Most **RATs were developed prior to omicron strain becoming predominant**
  - TGA requires manufacturers to provide available data on performance, including detection of omicron
  - Only some manufacturers have submitted omicron data – this is published on the TGA website
- However most **RATs are expected to detect omicron with similar sensitivity to other variants**
  - as they target a different (nucleocapsid) protein which has fewer mutations
- **We are testing the detection sensitivity for Omicron** of all RATs in collaboration with the Doherty Institute



# Omicron and new omicron variants

## Original BA1 Omicron (B.2.2529.1)

- Vaccine efficacy reduced, but third dose holds up well against serious illness – especially mRNA boosters
- T cell/ memory immune response also persists
- Antivirals retain efficacy
- Variable loss of efficacy of therapeutic monoclonal antibodies

## BA 2 sublineage

- 21 Different mutations to BA1, found in over 70 countries – now dominant in Denmark, India
- Possibly more infectious but no data on relative severity
- Vaccines may or may not be as efficacious
- Less efficacious against sotrovoimab and casirivimab/imdevimab (Regeneron)
- Betelovimab (Lilly MAb) remains efficacious

## BA 3 sublineage

- Little known about this subvariant so far

# Some of the many things we don't know

- **Will there be a new COVID wave in winter** ?
  - If so, a new variant or a resurgence of current variants ?
  - Will it be milder than the current variants ?
  - Will it coincide with a surge in flu cases ?
  - Will differential diagnosis of flu and COVID be important ? And what role will testing for both have ?
- Will **another booster or annual vaccination be needed** ?
- Will the **oral treatments** be effective enough to enable a combined vaccination/ treatment/ public health measures approach to be the longer term norm ?
  - A shift from prevention of transmission to prevention of severe disease ?
- How widely will RAT tests continue to be used ?