Regulatory Impact Statement: Amending the Medicines Act 1981 to allow for off-label use of COVID-19 vaccinations

Coversheet

Purpose of Document	
Decision sought:	*Analysis to support the introduction of an amendment of the Medicines Act 1981 to allow for off label use of COVID-19 vaccinations*
Advising agencies:	*Ministry of Health*
Proposing Ministers:	*Hon Chris Hipkins, Minister for COVID-19 Response, Hon Andrew Little, Minister of Health*
Date finalised:	*27 May 2022*

Problem Definition

Currently, the Medicines Act 1981 does not allow the off-label use of COVID-19 vaccinations without a prescription, as the fourth dose is not approved by Medsafe. When large cohorts are recommended to have further vaccinations within a short timeframe, this can be challenging to implement, including raising significant equity issues. Previously used mechanisms to allow for off-label use (such as reducing the dose period between the second and booster doses from 6 months to 3 months) are no longer appropriate.

Executive Summary

The COVID-19 Technical Advisory Group recommended that people aged over 65 years, Māori and Pacific peoples aged over 50 years, people in aged residential care, and the severely immunocompromised should receive a fourth dose of Cominarty COVID-19 vaccine before winter 2022.

Currently a fourth dose is considered “off-label” as a fourth dose of Comirnaty has not been approved by Medsafe, due to the absence of an application from Pfizer. The only way for the approximately 834,000 at-risk people to access the fourth dose is on prescription via a General Practitioner (GP) on an individualised basis. This raises concerns over the ability to maximise uptake of the vaccine in these groups, due to equity of access, cost and timeliness of implementation.

An alternative to individuals seeking a prescription is to amend the Medicines Act 1981 to include the ability for the Director-General to make decisions regarding the administration and supply of COVID-19 vaccines in the absence of consent under the Act. This would ensure that the Ministry of Health can react quickly to any necessary changes to the vaccine dose or frequency as the pandemic develops. Whilst being outside of the established Medsafe regulations of medicines process, it would provide an enduring and sound legal basis for the provision of any further doses of COVID-19 vaccines, including fourth doses.

Limitations and Constraints on Analysis

This proposal was developed under time pressure due to the approach of winter, when it is expected that the continuing COVID-19 pandemic could increase due to people being indoors and with the increased risk of influenza and other respiratory illnesses.

Additionally, as the Omicron outbreak continues in New Zealand, immunity gained from the primary course and 'booster' doses of COVID-19 vaccines in the targeted groups is waning rapidly.

No application is expected from Pfizer for their Cominarty vaccine to receive approval as a fourth dose, and therefore normal regulatory approval processes are unable to be utilised.

No public consultation was undertaken with this proposal due to the time frame available. However, strong support for a fourth dose is considered likely as this has been consistently raised in the media and by members of the public to the Ministry of Health.

Responsible Manager(s) (completed by relevant manager)
Caroline Flora *Associate Deputy Director-General* *System Strategy and Policy* *Ministry of Health* *27 May 2022*

Quality Assurance (completed by QA panel)	
Reviewing Agency:	
Panel Assessment & Comment:	N/A – waiver obtained from QA assessment

Section 1: Diagnosing the policy problem

What is the context behind the policy problem and how is the status quo expected to develop?

International evidence has shown that immunity gained after a third COVID-19 dose wanes at a similar rate as after completion of a primary course of COVID-19 vaccination, and it wanes more quickly in the elderly and the immunocompromised.

In New Zealand, these groups and Māori and Pacific people are at higher risk of severe outcomes and many received their third COVID-19 vaccination (booster) in December 2021 and January 2022 when they became available. This means some people in these groups will have already passed four months since their booster dose and their immunity may have already waned significantly.

The Omicron outbreak in New Zealand appeared to be on the decline until recently, but case numbers have begun climbing again.. Notably, whilst case numbers in age groups under 50 years old continue to decline, case numbers in the older age groups have been increasing again. Hospitalisations and deaths in New Zealand during the Omicron outbreak have been high among the identified groups. For example, most people reportedly dying *with* COVID-19 have been in the older age groups (approximately 89 percent).

On the basis of this information, the COVID-19 Technical Advisory Group (CV-TAG) have recommended that a fourth (and in some cases fifth) dose of Comirnaty (the Pfizer vaccine) should be given to the following at risk groups:

- people aged 65 years and over,
- Māori and Pacific peoples aged 50 years and over,
- residents of aged care and disability care facilities and
- severely immunocompromised people who received a three-dose primary course and a fourth dose as a first booster (noting this is a fifth dose for these people).

These groups cover approximately 834,000 people.

Currently, a fourth dose of Comirnaty has not been consented under the Medicines Act and would therefore be considered an “off-label” administration of the vaccine. That means it can only be accessed on prescription for an individual from an authorised prescriber. In many cases, an authorised prescriber will be a General Practitioner (GP).

Pfizer have not applied for approval of fourth doses in NZ (or other countries) and consider it best for local jurisdictions to find their own approval solutions.

What is the policy problem or opportunity?

At present the only way to implement the CV-TAG recommendation is by way of an off-label approach, requiring a prescription to be issued by an authorised prescriber. This would require over 800,000 New Zealanders to access a prescription in the next few months to ensure that their immunity to COVID-19 was maximised over the winter months. This poses siginificant access and equity issues.

International evidence

A number of other countries have been delivering fourth doses to their elderly and vulnerable populations, but at this early stage there is limited data and evidence available on the impact of fourth doses.

Preliminary data (and an early study) has shown that the risk of infection and severe illness appears to significantly reduce after a fourth dose (approximately 2-4 times less likely), and those aged 60-100 years old who have received a fourth dose of Pfizer, have had a 78 percent lower mortality rate from COVID-19 than those who only received a third dose.

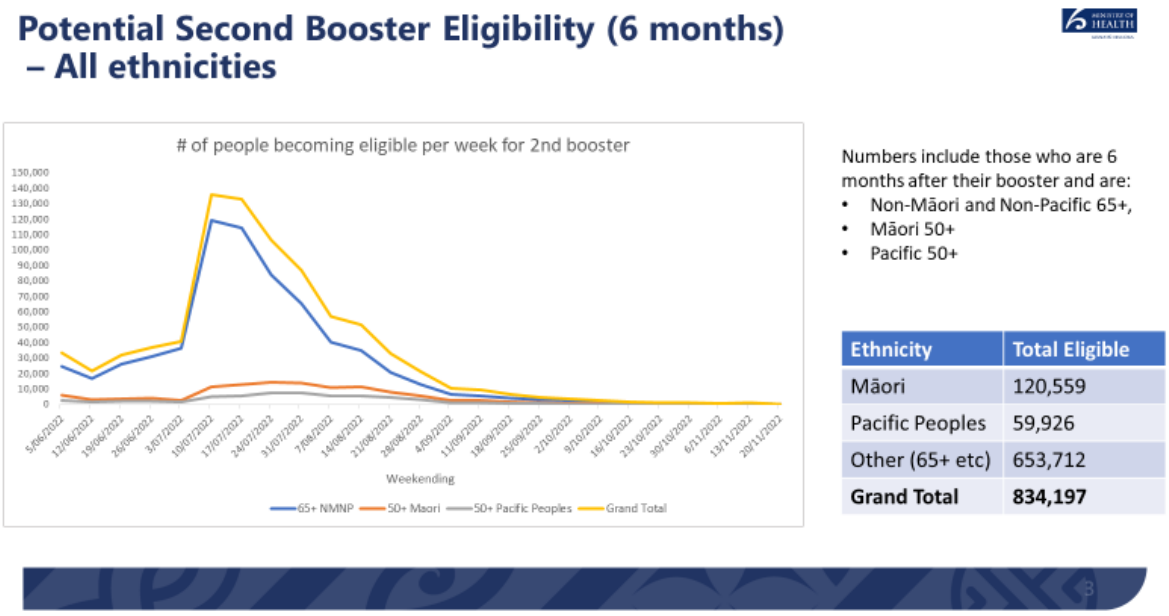
There are at risk groups in New Zealand who would benefit from a fourth dose

The Omicron variant coupled with waning immunity from either vaccinations or previous COVID-19 infection would disproportionately impact on the identified at-risk groups. We know that there is strong support for protecting these groups via vaccination, with vaccination rates especially high in the over-65s and the immunocompromised.

The success of Māori and Pacific health providers to promote vaccination cannot be overstated and it is likely that a fourth dose would also be highly supported and promoted, due to the awareness of the impacts of a COVID-19 infection on these population groups.

There is a time pressure to maximise immunity at a time when winter illnesses are at their peak

The graph below shows that the majority of the at-risk groups would be eligible for a further dose about mid-winter. Providing a fourth dose will maximise immunity for the at-risk groups, particularly when it coincides with the winter season where winter illnesses such as influenza and other respiratory infections cause significant increases in hospitalisations. The groups who are at risk of severe outcomes from COVID-19 are also at-risk of severe outcomes from other respiratory illnesses.



It would be ideal to enable broader delivery of fourth doses by early June 2022 as the majority of the at-risk group will become due for a fourth dose in June and July 2022.

Access can be improved

Off-label vaccination on prescription via GPs favours people who are enrolled with a general practice, have good access to health services, can afford the cost of the service, and knowledge of what they are eligible for and how to access it.

Administration via GPs is a slower, more costly and operationally challenging approach compared to having vaccination available from other community-based clinics, (including local pharmacies and via Māori and Pacific Health providers) where it is able to be administered by all COVID-19 vaccinators. It also places a large atypical workload on the GP network at a time when they are traditionally busy dealing with winter illnesses.

Ministry data shows that of the people in the recommended groups who have received a third (booster) dose, only 24 percent of them accessed this dose at a general practice. A large proportion (48 percent) accessed their third dose at their local pharmacy, and 28

percent accessed via a vaccination centre, pop-up, or mobile delivery clinic, with 5 percent via a marae, hospital, or residential care service. This means that of the approximately 834,000 people in the recommended groups who will become eligible for a fourth dose in the short-term, over 600,000 of them are likely to prefer vaccination somewhere other than a general practice.

COVID-19 vaccinations can be given at the same time as the influenza vaccine and many other vaccinations

Comirnaty is known to be able to be concomitantly administered with other vaccinations, such as the influenza vaccine. As mentioned above, these two viruses have similar at-risk groups and the influenza vaccine is free for these groups and available from pharmacies. Therefore, there is an opportunity to co-administer the vaccinations to maximise uptake and the protection of these groups if a person has not already received their influenza vaccine.

Maintaining trust and confidence in the health system

Experience from the COVID-19 vaccination programme has shown that alongside easy and equitable access to vaccinations, trust and confidence in the system and a good customer experience are also essential to encourage uptake. This includes the ease of booking, multiple available sites, and trustworthy local sites and providers. Through the delivery of the primary course and third (booster) doses, people have come to expect a certain experience. Adding additional steps into the customer journey could undermine the trust and confidence gained.

Futureproofing is required

During the pandemic, the Prime Minister put in place an Epidemic Notice under the Epidemic Preparedness Act. Once this Notice is revoked (expected within the next few months), a number of pathways to achieving COVID-19 health responses (including previous allowances for off-label vaccinations such as reducing the dose interval for third doses to 3 months) will fall away.

It is expected that COVID-19 will not disappear completely but will become an illness that can be managed, probably in a similar way that influenza is managed (regular vaccinations). However, there is the risk that further variants may arise that requires a change in the current vaccinations and their protocols, even if there is no Epidemic Notice in place. This could result in a need for large numbers of New Zealanders to access vaccinations without a prescription over a short period of time. Therefore, a flexible, proportionate and enduring solution is needed.

What objectives are sought in relation to the policy problem?

The desired outcome is for the recommended at-risk groups to get their fourth dose of Comirnaty to ensure that they have maximum immunity against COVID-19 going into winter 2022. The objectives are to:

- reduce hospitalisations and deaths from COVID-19 infection
- reduce the pressure on the health system over the busy winter period
- maximise uptake of the fourth dose in the at-risk groups recommended by CV-TAG
- maintain trust and confidence in the health system
- provide a permanent and future-proofed solution as COVID-19 vaccination activities move into a steady state.

Section 2: Deciding upon an option to address the policy problem

What criteria will be used to compare options to the status quo?

The options have been assessed against the following criteria:

- *Effectiveness*

  The option should provide for reasonable protections against COVID-19 in the at-risk groups and reduce hospitalisations, deaths, and the pressure on the health system

- *Equity*

  Access should be fair, just and proportionate for all in the at-risk groups

- *Simplicity*

  The option should be simple to implement and clear and understandable to those it seeks to engage with. This enhances trust and confidence in the health system

- *Timeliness*

  The option should be able to be initiated and implemented within the desired timeframe

- *Futureproofed*

  The option should be enduring and flexible to be able to be used for other scenarios related to COVID-19 vaccination proposals

What scope will options be considered within?

While a number of other options are available for the administration of a vaccine for the purposes of promoting public health during pandemic conditions, these are determined to be limited to the two options proposed.

For recent off-label changes such as reducing the dose interval from 6 months to 4 months and then to 3 months, an Immediate Modification Order (IMO) under the Epidemic Preparedness Act is currently in place. Consideration was given to replacing the current IMO with one that also allows for the delivery of a fourth dose, but Ministers decided that this was not an option due to its temporary nature and vulnerability of being tied to the temporary Epidemic Notice. An IMO can only be made:

a. while an epidemic notice is in force (one is currently in force for COVID-19);

b. on the recommendation of the Minister of Health;

c. on the written recommendation of the Director-General of Health that the modifications are or are likely to be necessary to enable the effective management of COVID-19 or its effects (or both).

There are two non-legislative options that were taken forward were:

- Pfizer submitting an application for Comirnaty to be approved as a fourth dose. Medsafe cannot procure an application from a company for medicine approvals and as stated, Pfizer has indicated that they are encouraging countries who wish to provide their populations with fourth doses to find their own legal ways of providing this route.
- Standing Orders cannot be made for an unconsented medicine (a “new medicine” under the Act). Treating a fourth dose as other than “new medicine” undermines the scheme and purpose of the Medicines Act and the consent process under the Act.

Additionally, liability for standing orders ultimately sits with the issuer and the person acting in reliance of the standing order.

What options are being considered?

Option One – *Status Quo*

Section 25 of the Medicines Act permits authorised prescribers to administer new medicines and medicines for an off-label use. Option 1 allows anyone to seek a prescription for a fourth dose and obtain maximum immunity against COVID-19.

However, it is known that a number of people in the recommended groups will experience inequities in access to the vaccine if provided only through authorised prescribers on prescription. Some may not be enrolled with a GP (and there is clear evidence that this is especially true in rural areas and certain regions), the cost of seeking a prescription, and if they do have a GP, the ability to receive a timely appointment can be a barrier to seeking what is essentially a recommended course of action. While some elderly and immunocompromised are more likely to have an existing relationship with an authorised prescriber, Māori and Pacific people aged over 50 are likely to find access significantly more difficult. This may mean that some will choose not to get the fourth dose as access is too problematic.

The implementation of Option 1 can be relatively simple if messaging is to seek access through a GP. This is, however, very different from the messaging that has occurred with previous doses of COVID-19 vaccinations and may be confusing for those who fall into the recommended groups, who have expectations of widespread providers and flexible booking times.

GPs are already under pressure, and workload increases over the winter period. Finding available time for a GP appointment can be challenging and therefore a person may not be able to obtain their vaccine in a timely manner.

Section 25 is able to be used for many medicines and is a permanent feature of the Medicines Act, although it is limited in its use to only authorised prescribers. Most of the COVID-19 vaccinating workforce are currently not authorised prescribers so are unable to rely on section 25 to administer an off-label dose.

Option Two – Amendment of the Medicines Act 1981

An amendment to the Medicines Act 1981 would enable the usual rules that restrict administration of medicines to be explicitly overridden in the case of COVID-19 vaccines.

This approach would:

- provide a basis for administration of a fourth dose to protect from serious outcomes from a COVID-19 infection
- provide for equitable access to vaccinations through a range of vaccinators
- provide a vaccination experience similar to that with previous vaccinations, ie using the same technology and at similar venues
- provide a mechanism to more readily enable future doses of COVID-19 vaccines to be administered if emerging scientific evidence demonstrates this is required (such as fourth doses for the wider population).

The key risk with this option is that an amendment such as this would not be in keeping with the scheme of the rest of the Act. It singles out COVID-19 vaccines from a regulatory regime that is intended to set requirements for the safety, quality and efficacy of all medicines.

To mitigate this risk, we need to ensure the amendment is narrowly applied, although not so narrow as to create problems for administering COVID-19 vaccines in future. Finding the right balance between an amendment that is overly broad or overly restrictive will be crucial to ensure we are not restricting any future doses that may be required, such as a fifth dose, or further doses for the broader population. This can be achieved by providing for the Director-General of Health to be satisfied that it is an appropriate measure to manage the risks associated with a COVID-19 outbreak or spread.

To enable the bespoke amendment to be enacted in time for the recommended June 2022 roll out (to align with most of the recommended groups' six-month dose interval, as well as being in time for winter), this option requires Ministers to act under urgency.

What option is likely to best address the problem, meet the policy objectives, and deliver the highest net benefits?

Option 2 is the preferred approach

An amendment to the Medicines Act is the preferred option as it provides for a permanent and future proofed pathway in case further changes are needed to meet future COVID-19 challenges. These may include further vaccine doses, changes to dose intervals, or targeting different population groups in response to future variants where evidence supports its use. This is similar to the approach taken in the IMO providing for a third (booster) dose (Epidemic Preparedness (Medicines Act 1981—COVID-19) Immediate Modification Order 2022). It provides for the Director-General of Health to specify a class of authorised vaccinators who can administer doses of COVID-19 vaccines contrary to the usual rules, in addition to a number of other conditions not included in the section 20 or section 23 consent processes.

Option 2 is also the preferred option to ensure equitable access for the at-risk groups as the data shows that the majority prefer to receive their vaccinations from a pharmacy or other health provider.

This Option is expected to promote a higher uptake of the fourth dose resulting in better health outcomes of the at-risk groups vulnerable to COVID-19 over the winter period, and reduced pressure on the health system. The higher uptake would also help consume the current supplies of vaccine that otherwise could expire before they are used.

The Therapeutic Products Bill will provide regulatory mechanisms to ensure such issues may be more easily dealt with in the future

Section 3: Delivering an option

How will the new arrangements be implemented?

The preferred option would be given effect through an amendment to the Medicines Act. The Bill would be introduced on 7 June 2022 and passed by mid-June 2022 under urgency. This would result in an additional section of the Medicines Act that only applies to COVID-19 vaccinations and only on the recommendation of the Director-General of Health.

Provision of fourth doses to the CV-TAG recommended groups will be on a voluntary uptake basis and will not have any impacts on other COVID-19 legislation, such as the COVID-19 Public Health Response (Vaccinations) Order 2021.

The Ministry of Health would be responsible for the implementation of the roll out of the fourth dose, utilising all existing delivery settings, processes and technology that have been developed and used for previous COVID-19 vaccination roll outs.

How will the new arrangements be monitored, evaluated, and reviewed?

The Ministry of Health would monitor the impacts of the new arrangements through existing comprehensive data collection processes. The uptake of COVID-19 vaccinations is currently reported publicly and regularly, and therefore the application of the amendment to the fourth dose would be included and be available for analysis.

The amendment is to the Medicines Act 1981, which is currently under review and expected to be replaced with the Therapeutic Products Bill (intended to be introduced later in 2022). It is expected that the Bill will be fit for purpose and be better able to manage situations such as those that required the proposed amendment.

In the meantime, the Ministry will monitor the application of the amendment to ensure its ongoing use does not undermine the usual consenting processes under the Act.