Medicines Assessment Advisory Committee

Minutes of the 109th meeting held on Tuesday 2 February 2021

Ministry of Health
Wellington

Minutes of the 109th meeting
of the Medicines Assessment Advisory Committee
by videoconference
on 2 February 2021 at 9:30am

s 9(2)(g)(ii)

[redacted]

1 Welcome

The Chair opened the 109th meeting at 9:30am and welcomed members and guests to this extraordinary meeting to consider a recommendation on the approval of Comirnaty (COVID-19 mRNA vaccine) (Pfizer-BioNTech) 0.5 mg/mL concentrate for injection submitted by Pfizer New Zealand Limited. The Committee members introduced themselves.

2 Apologies

Apologies were received from s 9(2)(g)(ii) [redacted] s 9(2)(g)(ii) [redacted] as unavailable over the duration of the meeting.

4 Declaration of conflicts of interest

Members submitted their conflicts of interest forms to the Secretary.

The following new conflicts of interest were declared:

a. s 9(2)(g)(ii) [redacted] before accessing the meeting documentation, had declared that she had shares in Pfizer, Moderna, Johnson & Johnson and Vitalis. This precluded her from accessing the meeting documentation and from attending the 109th meeting.

b. s 9(2)(g)(ii) [redacted] declared he had shares in Ergomed and BLIS Technologies

All other members declared they had no additional interests that would pose a conflict with any of the items on the agenda.

The Committee agreed that, other than s 9(2)(g)(ii) [redacted], there were no potential conflicts of interest that were considered likely to influence the discussion or decisions of the Committee at this meeting.

5 Applications for consent to distribute a new medicine under section 20/23 of the Medicines Act 1981 (referred by the Minister of Health under section 22(2))

5.1 Comirnaty (COVID-19 mRNA vaccine) (Pfizer-BioNTech) 0.5 mg/mL concentrate for injection (TT50-10853) Pfizer (NZ) Ltd

The Pfizer-BioNTech Covid-19 mRNA vaccine has been developed in response to the global pandemic of the SARS-COV-2 virus that causes Covid-19. This is the first application to market a Covid-19 vaccine in New Zealand and the first Covid-19 vaccine to be granted emergency use authorisations in the UK and the US. Australia provisionally approved this vaccine on 25 January 2021. Due to the continued global spread of the virus and its variants, availability of a vaccine is an important part of the New Zealand Government's Covid-19 strategy.

New Zealand does not have an emergency use authorisation pathway and currently does not have the public health emergency situation of many other countries, but this situation can change.

A new medicine application was submitted by Pfizer New Zealand Limited for Comirnaty (COVID-19 mRNA vaccine) (Pfizer-BioNTech) 0.5 mg/mL concentrate for injection (TT50-10853) under section 20 of the Medicines Act 1981.

The application is being considered for provisional consent under section 23 of the Medicines Act 1981 for the following indications:

> *Active immunisation to prevent coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2, in individuals 16 years of age and older.*
>
> *The use of the vaccine must be in accordance with official recommendations.*

The application has been submitted via an expedited rolling review process and has been assessed under urgency due to the significant clinical need for a COVID 19 vaccine with a positive benefit risk profile. The initial application was received on 13 November 2020, after which a total of eight tranches of supporting information were submitted to Medsafe. Following assessment of these data packages, a request for additional information was issued on 15 January 2021 and response from Pfizer was received on 22 January 2021. Additional responses and data to support a change in the number of deliverable doses per vial were received on 27 January 2021. All additional data has since been assessed and a final recommendation has been made on 28 January 2021.

Given the rapid development of this medicine and the urgent clinical need that exists in New Zealand, there are several aspects of the data required to support quality, safety and efficacy that are not available at the time of completion of the evaluation. It is also proposed that any provisional consent be granted for a period of nine months, before which time all additional data should be received.

It was requested that the Committee focus on the specific aspects in their consideration of the application:

- The conditions and consent time period proposed for provisional consent under section 23 of the Medicines Act 1981. Specifically, whether these are appropriate and sufficient given the data provided up to the time of referral, as well as whether any additional conditions should be applied.
- Whether the proposed indications for the medicine are appropriate and supported by the clinical data available, as well as whether any additional restrictions should be applied.

The following is the full list of evaluation reports and supporting documentation that were provided:

- Final evaluation report – Quality (includes final recommendation)
- Final evaluation report – Novel excipients
- Final evaluation report – Non-clinical
- Final evaluation report – Clinical
- Final evaluation report – RMP
- Application dossier composed of iterative rolling review tranches and RFI responses and additional data
- TGA assessment documentation

- Advice from the Ministry of Health Science and Technical Advisory Group (STAG) on new SARS-CoV-2 virus strains and the implications for COVID-19 vaccines

Pfizer New Zealand was informed of the referral on 29 January 2021.

Medsafe Presentation

Medsafe presented an overview of what is known about Comirnaty to the Committee.

Pre-clinical discussion

The Committee considered the following documentation:

- Final evaluation report Non-clinical

The Committee noted that the pre-clinical questions raised in the report were addressed satisfactorily by the company. The Committee noted that pre-clinical observations such as hepatoxicity are not apparent in the clinical data. The reactogenicity seen in the clinical data does not appear to be a concern in the pre-clinical data. The data on long terminal half-life of the lipid nanoparticles was considered unusual but unlikely to be a safety concern, as only two doses are intended to be administered. The pre-clinical data did not suggest safety concerns in pregnancy.

The Committee considers that generally the pre-clinical data has been superseded by the clinical data. The Committee had no safety concerns based on the preclinical data.

The Committee adopted the report and agreed with the conclusions.

Evaluation

- **Quality evaluation report (including Novel Excipients evaluation report)**

The Committee considered the following documentation:

- Final evaluation report Quality (includes final recommendation)

The Committee noted that the Medsafe evaluation report was detailed and comprehensive. It was noted that many of the questions posed by Medsafe had been resolved and unresolved questions were included as conditions for the provisional consent.

The number of quality conditions was noted and that these conditions addressed instances where usual data was missing due to the developing nature of the vaccine. The quality conditions align with those required by other regulators, in particular the European Medicines Agency.

Medsafe noted that under Emergency Use Authorisation procedures, product released to the US and UK markets are from smaller batch sizes.

The scale difference of the potential New Zealand batches was a focus of the quality data assessment to ensure vaccine manufactured at commercial scale is comparable to clinical trial batches.

Pfizer has demonstrated that final product specifications are sufficient to ensure that product supplied to New Zealand will be comparable to clinical trial batches. Any gaps in product characterisation would be covered in the conditions of the provisional consent.

The Committee expressed confidence in the Medsafe quality and manufacturing evaluation and were interested in being kept informed of updates in this area.

- **Clinical evaluation report**

The Committee considered the following documentation:

  - Final evaluation report – Clinical

The Committee considered the issue of efficacy data for subpopulations. This subset included Maori, Asian, Pacific peoples, the elderly and groups who are immunocompromised. The Committee commented that the ethnicity subset data submitted was remarkably similar in efficacy and it is not unreasonable to assume there is no genetic reason for different responses in different ethnic groups in New Zealand.

The Committee agreed that it will be important to collect post-market safety data for Maori, Pacific peoples, elderly and immunocompromised subsets as these are the people who are more likely to be at higher risk of complications of COVID-19. However, the clinical picture on efficacy and safety will become clearer over time as more people receive the vaccine.

The Committee discussed the lack of data on the duration of response of the vaccine. Medsafe had asked the sponsor for an early cut-off time for more data, which was not available. The sponsor had confirmed that the next data analysis from the pivotal clinical trial will arrive in April 2021.

Overall, the Committee was satisfied with the clinical report and summary presented. The Committee was satisfied with the efficacy data to date acknowledging that more data will be available over time.

- **RMP evaluation report**

The Committee considered the following documentation:

  - Final evaluation report - RMP

The Committee considered that the latest version of the Risk Management Plan addresses many areas of concern raised by Medsafe. The need for additional safety information regarding the elderly, children, people with comorbidities and immunocompromised people was emphasised.

The Committee noted that patients with autoimmune diseases and patients who are immunosuppressed were not well represented in clinical trials. The planned clinical study in patients with rheumatoid arthritis receiving

immunomodulators was noted. The Committee expressed concern that these individuals might be among those prioritised for vaccination before the results of this study are available. It was noted that this issue is to be managed as part of the Ministry of Health immunisation implementation programme.

The need for more information on potential safety signals such as reactogenicity, anaphylaxis, vaccine-associated enhanced disease and facial paralysis was noted.

The Committee was satisfied with the updated Risk Management Plan, noting that additional clinical studies, pharmacovigilance activities and monthly safety reports are planned to address areas of missing information.

The Committee accepted the Risk Management Plan as written, noting that it is a living document and there is the opportunity to add safety concerns as they emerge.

Discussion with Pfizer

Pfizer representatives joined the meeting to respond to questions from the Committee. The Committee had questions regarding finished product testing, risk of transport to New Zealand, in use data in specific populations, use in severe COVID-19, the emergence of new variants, unforeseen safety signals after the doses given to date, update on duration of protection and the new 6 dose proposal. All questions were suitably addressed by Pfizer.

Discussion to finalise recommendation

Provisional Consent

The Committee unanimously agreed to Medsafe's proposal to grant provisional consent with a nine-month period. This period was proposed to ensure that all post-approval data commitment deadlines were met. The Committee agreed with this rationale.

Indications

The Committee agreed that the proposed indication wording for Comirnaty is revised to the following:

> *Comirnaty has provisional consent (see section 5.1) for the indication below:*
>
> *Active immunisation to prevent coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2, in individuals 16 years of age and older.*
>
> *The use of this vaccine should be in accordance with official recommendations.*

The committee discussed the likely real world use in New Zealand and acknowledged that the vaccine roll-out will be managed by the Ministry of Health.

The Committee suggested that Section 5.1 of the data sheet to be revised to include the following statement:

> *This medicine has been given a provisional consent under Section 23 of the Act. This means that further evidence on this medicine is awaited or that there are specific conditions of use. Refer to the consent notice published in the New Zealand Gazette for the specific conditions.*

Conditions of provisional consent

The Committee reviewed each proposed condition of the provisional consent. The Committee agreed that Medsafe could make technical amendments to the conditions of consent.

The Committee agreed to the addition of the following condition:

> *Provide independent batch certification, such as UK National Institute for Biological Standards and Control (NIBSC) certification, EU Official Control Authority Batch Release (OCABR) certification, Australian TGA batch release assessment, or any other certification agreed with Medsafe, on request for all batches distributed in New Zealand.*

The Committee raised concerns regarding the wording of the following conditions.

> *Provide regular updates on the duration of efficacy and the requirement for booster doses. This should include the six months analysis data from Study C4591001. Interim report due: April 2021.*
>
> *Provide updates on efficacy including regarding asymptomatic infection in the vaccinated group, vaccine failure, immunogenicity, efficacy in population subgroups and results from post-marketing studies, when these become available.*
>
> *Submit the final Clinical Study Reports for Study C4591001 and Study BNT162-01 once they available.*
>
> *Inform Medsafe of all safety reviews they conduct or become aware of and provide the completed review.*

The Committee recommended the following amendments to the conditions to improve clarity of the requirements:

> *Provide regular reports on the duration of efficacy and the requirement for booster doses within five working days of these being produced.*

Provide the six months analysis data from Study C4591001. Report due: April 2021.

Provide any reports on efficacy including regarding asymptomatic infection in the vaccinated group, vaccine failure, immunogenicity, efficacy in population subgroups and results from post-marketing studies, within five working days of these being produced.

Provide the final Clinical Study Reports for Study C4591001 and Study BNT162-01 within five working days of these being produced.

Provide monthly safety reports, as well as all safety reviews they conduct or become aware of.

Recommendation

The Committee recommended that the Minister of Health should grant provisional consent to distribute this medicine under Section 23 of the Medicines Act 1981 and impose the conditions proposed by Medsafe as amended by the Committee. The Committee recommended that the provisional consent should have an effect of nine months.

General Business

The Chair thanks s 9(2)(g)(ii) for his services to the Committee and wishes him well in his future endeavours.

Date of Next Meeting
No date has been set.

There being no further business, the Chair thanked members and guests for their attendance and closed the meeting at 2.14pm.

CHAIR'S SIGNATURE: s 9(2)(g)(ii) [redacted]

DATE: 03/02/2021

This document was prepared and written by
s 9(2)(g)(ii) [redacted]
the Medicines Assessment Advisory Committee Secretary