

**6.09 INACTIVATED QUADRIVALENT INFLUENZA VACCINE
(SPLIT VIRION),
Injection 0.5 mL,
Fluarix® Tetra,
GlaxoSmithKline Australia Pty Ltd**

1 Purpose of Application

- 1.1 The minor submission requested an extension to the current listing of inactivated quadrivalent influenza vaccine (QIV), Fluarix Tetra, on Schedule 1 (Designated vaccines and circumstances in which vaccines may be provided) of the *National Health (Immunisation Program – Designated Vaccines) Determination 2014 (No.1)* (the Determination). The submission requested extending the existing Determination to include vaccination of healthy children aged 6 months to <5 years eligible for free vaccination under the National Immunisation Program (NIP). This would align with the current NIP listings for Vaxigrip Tetra™ and FluQuadri™ QIVs in this population.

2 Background

Registration status

- 2.1 Fluarix Tetra was TGA registered on 28 August 2013 for active immunisation of adults and children from 3 years of age for the prevention of seasonal influenza disease caused by the influenza virus types A and B contained in the vaccine. In May 2018, the TGA approved Fluarix Tetra for use in infants and young children 6 to 35 months of age. This extension of the age indication enables Fluarix Tetra to be administered to adults and children from the age of 6 months.

Previous PBAC consideration

- 2.2 A summary of relevant prior PBAC considerations is provided below.

Public Summary Document – July 2020 PBAC Meeting

Table 1: Previous relevant PBAC considerations

Meeting date	Request	Outcome	Detail
Relevant Fluarix Tetra recommendations			
March 2015	A listing of Fluarix Tetra on the National Immunisation Program (NIP) – Designated Vaccines List for the prevention of seasonal influenza.	Recommended	The PBAC recommended the listing of Fluarix Tetra on the NIP – Designated Vaccines List for the prevention of seasonal influenza based on a cost-minimisation basis with Fluarix trivalent influenza vaccine.
November 2018	A request by the CMO of the Department of Health that eligibility for NIP funded seasonal influenza vaccine for Aboriginal and/or Torres Strait Islander (indigenous) people to be expanded to include children and adolescents aged 5 to <15 years. (free influenza vaccines were then provided for Indigenous people aged 6 months to <5 years and 15 years and over on the NIP)	Recommended	The PBAC recommended a change to the existing Determination to include FluQuadri and Fluarix Tetra for Aboriginal and/or Torres Strait Islander people aged 3 years and older for the prevention of influenza on the NIP.
March 2019	A request for an extension of the existing Determination listing for Fluarix Tetra to include vaccination of infants and young children aged 6 - 35 months of age eligible for free vaccination under the NIP for the prevention of seasonal influenza.	Recommended	The PBAC recommended the extension to the listing of Fluarix Tetra on the Determination to include high risk and Aboriginal and/or Torres Strait Islander infants and children aged 6 to 35 months of age on a cost-minimisation basis to FluQuadri Junior. The PBAC considered the claim of non-inferior comparative effectiveness and safety was reasonable.
Relevant recommendations in healthy children 6 months to < 5 years			
July 2019	A NIP listing of Vaxigrip Tetra for the prevention of seasonal influenza in children aged 6 months to <5 years, who were not eligible, and at-risk individuals who were eligible for vaccination on the NIP at the time of PBAC consideration.	Recommended	The PBAC recommended the listing of Vaxigrip Tetra on the Determination for the prevention of seasonal influenza in children aged 6 months to <5 years and in at-risk individuals who were eligible for vaccination through the NIP, under the same provisions as the other QIVs currently listed on the NIP.
November 2019	An extension to the current listing of FluQuadri for the prevention of influenza on the NIP to include at-risk children aged 6-35 months and healthy children aged 6 months to <5 years.	Recommended	The PBAC recommended extending the current listing of FluQuadri™, on the Determination for the prevention of influenza, to include healthy children aged 6 months to <5 years and at-risk children aged 6-35 months who were eligible for influenza vaccination through the NIP under the same provisions as the other QIVs currently listed on the NIP.

Abbreviation: CMO: Chief Medical Officer, the Determination: the National Health (Immunisation Program – Designated Vaccines) Determination 2014 (No.1)

Note: high-risk (or at risk) populations as defined by the Determination are consistent with high-risk populations defined by the NIP.

- 2.3 At its March 2019 meeting, the PBAC recommended extending the existing Determination of Fluarix Tetra (0.5 mL dose) for the prevention of seasonal influenza to include high risk and Aboriginal and/or Torres Strait Islander children aged 6 to 35 months of age on a cost-minimisation basis to FluQuadri Junior (0.25 mL dose) (paragraph 6.1, Fluarix Tetra Public Summary Document (PSD), March 2019).
- 2.4 The submission noted that all children aged 6 months to <5 years are currently eligible for NIP funded influenza vaccination (Vaxigrip Tetra and FluQuadri), based on the recommendation from the Australian Technical Advisory Group on Immunisation (ATAGI) that all infants and children aged <5 years have a higher risk of hospitalisation and increased morbidity after influenza¹. In its July 2019 consideration of Vaxigrip Tetra, the PBAC considered that listing a QIV on the NIP for all children aged 6 months to <5 years was warranted from a public health perspective as an additional measure to directly target this group which has a relatively high burden of disease (paragraph 7.2, Vaxigrip Tetra PSD, July 2019).

For more detail on PBAC's view, see section 6 PBAC outcome.

3 Requested listing

- 3.1 The submission requested the additions indicated below (in italics) to the exiting Determination:

¹ <https://immunisationhandbook.health.gov.au/vaccine-preventable-diseases/influenza-flu>

Public Summary Document – July 2020 PBAC Meeting

Name, Restriction, Manner of administration and form	Nationally Negotiated Price	Proprietary Name and Manufacturer
Inactivated Quadrivalent Influenza Vaccine (split virion) Injection 0.5 mL	\$ [REDACTED]	Fluarix® Tetra GlaxoSmithKline Australia Pty Ltd
Category/Program	NIP	
Subsection 7 (7A) For items 207A of Schedule 1, a designated vaccine mentioned in this item may be provided to:		
Groups eligible for the requested NIP listing of Fluarix® Tetra, including	a person who is at least 65 years; or an Aboriginal or Torres Strait Islander person who is at least 6 months; or a child who is at least 6 months old but less than 5 years old; a person who is at least 6 months who: <ul style="list-style-type: none"> (i) has cardiac disease including cyanotic congenital heart disease, coronary artery disease and congestive heart failure; or (ii) has a chronic respiratory condition including suppurative lung disease, bronchiectasis, cystic fibrosis, chronic obstructive pulmonary disease, chronic emphysema and severe asthma; or (iii) has another chronic illness requiring regular medical follow-up or hospitalisation in the preceding year, including diabetes mellitus, chronic metabolic diseases, chronic renal failure, haemoglobinopathies and impaired immunity (including drug-induced immune impairment); or (iv) has a chronic neurological condition, including multiple sclerosis, spinal cord injuries, seizure disorders or other neuromuscular disorders; or (v) has impaired immunity, including HIV infection; or (vi) is less than 11 years and is receiving long term aspirin therapy; or a woman who is pregnant.	
Number and timing of doses	Should be administered in accordance with the national recommendation as per the current Immunisation Handbook: Children ≥6 months to <9 years of age: <ul style="list-style-type: none"> • If the child has not previously been vaccinated: two 0.5 ml injections at least one month apart. • If the child has been previously vaccinated: a single 0.5 ml injection. 	

For more detail on PBAC's view, see section 6 PBAC outcome.

4 Comparator

- 4.1 The minor submission nominated Vaxigrip Tetra as the main comparator given that this was the first QIV recommended for use in healthy children aged 6 months to <5 years at the July 2019 PBAC meeting. The submission also nominated FluQuadri as an alternative comparator. The PBAC noted it had previously accepted the claim of non-inferiority of FluQuadri compared with Vaxigrip Tetra in terms of comparative effectiveness and safety in this population (paragraph 7.1, FluQuadri PSD, November 2019).

For more detail on PBAC's view, see section 6 PBAC outcome.

5 Consideration of the evidence

Sponsor hearing

5.1 There was no hearing for this item as it was a minor submission.

Consumer comments

5.2 The PBAC noted and welcomed the input from one organisation via the Consumer Comments facility on the PBS website. Lung Foundation Australia was supportive of the requested extension to the existing listing of Fluarix Tetra, and noted that an additional QIV available for NIP-funded vaccination in healthy children aged 6 months to <5 years would provide a range of benefits by ensuring continued access to required vaccines at the right times. The comments emphasized that vaccination for the prevention of seasonal influenza in this population would reduce costs to health systems, the risk of disease, disability and death associated with influenza outbreaks, the economic and social burden experienced by parents required to care for ill children, and strengthening the respiratory health of the Australian community.

Clinical trials

5.3 The minor submission was based on a naïve indirect comparison of two studies (Study D-QIV-004 and GQM05) in the absence of a head-to-head trial comparing Fluarix Tetra to Vaxigrip Tetra in children aged 6 to 35 months. No evidence was provided in the submission for children aged 36 months to < 5 years; however, ATAGI considered it was reasonable to assume the efficacy of Fluarix Tetra is similar in children aged 3 to 4 years as in children aged 6 to 35 months (ATAGI March 2020 pre-submission advice).

5.4 The clinical evidence presented in the submission relevant to an assessment of the efficacy and safety of Fluarix Tetra in children aged 6 to 35 months included one pivotal study for Fluarix Tetra's vaccine efficacy (VE) and safety in children aged 6 to 35 months (D-QIV-004), two supportive immunogenicity and safety studies for Fluarix Tetra in approximately 1,300 children aged 6 to 35 months (D-QIV-009 and D-QIV-015), and a comparative immunogenicity and safety study for FluLaval Tetra (which has the same antigen content as Fluarix Tetra) and the former paediatric dose (0.25 mL) of Fluzone QIV (which has the same antigen content as FluQuadri Junior) in approximately 2,300 children (Q-QIV-022). The Secretariat noted that trial data for the 6 to 35 month age cohort from these studies were considered by the PBAC to recommend an extension to the Determination for Fluarix Tetra for the prevention of seasonal influenza to include high risk and Aboriginal and/or Torres Strait Islander infants and children aged 6 to 35 months of age in March 2019 (see Table 3, Fluarix Tetra PSD, March 2019).

5.5 Details of the trial presented in the submission are provided in Table 2.

Public Summary Document – July 2020 PBAC Meeting

Table 2: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
FLU D-QIV-004	An efficacy study of GSK Biologicals' quadrivalent influenza vaccine GSK2321138A (FLU D-QIV) when administered in children.	<i>Lancet Child Adolescent Health</i> ;2: 338-49
FLU D-QIV-009	Immunogenicity, safety and reactogenicity study of GSK Biologicals' quadrivalent seasonal influenza candidate vaccine GSK2321138A, administered to children who previously participated in study 115345. An extension of D-QIV-004, was designed to evaluate the adequacy of the immunological priming of children 6-35 months of age.	<i>Unpublished</i>
FLU D-QIV-015	Safety and immunogenicity study of GSK Biologicals' Quadrivalent Influenza Vaccine (GSK2321138A) manufactured with a new process in adults and children.	<i>BMC Infectious Diseases</i> , vol:18 iss:1, 1471-2334
FLU Q-QIV-022	Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone® Quadrivalent in children 6 to 35 months of age.	<i>Journal of the Pediatric Infectious Diseases Society</i> , 6 (March): 9 -19

Source: Table 3, p13 of the submission

- 5.6 The evaluation of non-inferiority for Fluarix Tetra VE and safety compared with Vaxigrip was primarily based on the data from Study D-QIV-004 in both previously vaccinated and influenza vaccine-naïve children aged 6 to 35 months.
- 5.7 The submission identified one relevant comparator trial (GQM05, Pepin et al., 2019) which was considered by the PBAC in July 2019 as part of the evaluation for Vaxigrip Tetra compared to placebo (no vaccine) in children aged 6 to 35 months who were healthy and influenza vaccine-naive.
- 5.8 Key features of the trials for an indirect comparison are provided in the table below.

Table 3: Key features of the included evidence for a naïve comparison

	Fluarix Tetra	Vaxigrip Tetra
Trial ID	Study D-QIV-004	Study GQM05
First Author	Claeys et al., 2018	Pepin et al., 2019
Publication citation	<i>Lancet Child Adolescent Health</i> ;2: 338-49	<i>Vaccine</i> , 37 (2019): 1876-1884, 1885-1888
Study design	Phase 3, observer-blind, multinational RCT with children aged 6–35 months across five influenza seasons in 13 temperate and subtropical countries in Europe, Central America, and Asia between Oct 1, 2011, and Dec 31, 2014.	Phase 3, RCT with children aged 6–35 months at 49 centres in Asia, Latin America, Europe and Africa between March 2014 and July 2016. Observer blinded for QIV and placebo groups and open label for trivalent influenza vaccine (TIV) groups.
Population	Healthy children, as determined by clinical examination and medical history, were eligible irrespective of influenza vaccination in previous seasons, aged 6 – 35 months.	Healthy children aged 6 to 35 months who had not been previously vaccinated for or infected with influenza.
Number of subjects	Fluarix Tetra (QIV): N = 6,006 Control vaccines (comparators; Havrix, Varivax, Varilrix, Prevenar): N=6,012.	Vaxigrip Tetra (QIV) N=2,559 Placebo N=2,570
Intervention	Fluarix Tetra, QIV contained 15 mcg haemagglutinin antigen per strain per 0.5 mL dose; strain composition followed WHO recommendations. The vaccine was administered intramuscularly.	Vaxigrip Tetra, QIV, split-virion, 15 mcg haemagglutinin antigen per strain per 0.5 mL dose. Participants were randomised to receive two 0.5-ml doses 28 days apart Vaxigrip Tetra or a licensed TIV or placebo (saline).

Public Summary Document – July 2020 PBAC Meeting

	Fluarix Tetra	Vaxigrip Tetra
	Vaccine-primed children received a single 0.5 mL dose on day 0; vaccine-unprimed children received two doses (0.5 mL each on days 0 and 28).	
Comparator	Pneumococcal conjugate vaccine (PCV), hepatitis A vaccine, or varicella vaccine. Control vaccine allocation was based on age and influenza vaccine priming status.	TIV, 2 different vaccines (one containing WHO recommended B strain (TIV-2) and the other with non-WHO recommended B strain (TIV-1)) and placebo vaccine (saline).
Outcomes	<p>The two primary endpoints, VE in preventing:</p> <ul style="list-style-type: none"> ○ RT-PCR-confirmed, moderate-to-severe influenza A and/or B disease due to any seasonal influenza strain ○ all influenza (irrespective of disease severity) associated with any seasonal influenza strain. <p>Secondary endpoints:</p> <ul style="list-style-type: none"> ● lower respiratory infection with RT-PCR-confirmed influenza ● culture-confirmed influenza associated with antigenically matching strains ● culture-confirmed influenza associated with any seasonal strain ● acute otitis media with RT-PCR-confirmed influenza ● RT-PCR-confirmed severe influenza <p>Immunogenicity</p> <p>Reactogenicity and Safety</p>	<p>The two primary endpoints, VE in (assessed in QIV and placebo groups) preventing:</p> <ul style="list-style-type: none"> ○ Laboratory-confirmed influenza caused by any A or B strain ○ Laboratory – confirmed influenza associated with any seasonal influenza strain. <p>Secondary endpoints:</p> <ul style="list-style-type: none"> ● RT-PCR-confirmed influenza illness caused by any influenza A or B type <p>Safety</p>
Definitions	Moderate-to-severe influenza was defined as RT-PCR confirmed influenza with any of the following: high fever (body temperature above 39°C); doctor-diagnosed acute otitis media; doctor-diagnosed lower respiratory infection; doctor-diagnosed serious extra-pulmonary complication (e.g., myositis, encephalitis, seizure, myocarditis or pericarditis, or other serious medical condition); hospital admission in the intensive care unit; or supplemental oxygen for more than 8 h. Any of the latter three criteria defined severe influenza.	Participants were considered to have influenza-like illness if they had a fever $\geq 38^{\circ}\text{C}$ lasting ≥ 24 h concurrently with cough, nasal congestion, rhinorrhoea, pharyngitis, otitis, vomiting, or diarrhoea. For participants diagnosed with influenza-like illness, a nasopharyngeal swab was taken for laboratory confirmation of influenza within 10 days after onset.

Source: Table 3, Table 5, Table 16, Table 18, pp13, 15, 25, 27-28 of the submission; and compiled by the Secretariat
Abbreviation: RCT: Randomised controlled trial; RT-PCR: Reverse transcription polymerase chain reaction; VE: vaccine efficacy; TIV: Trivalent influenza vaccine; QIV: Quadrivalent influenza vaccine

5.9 Overall, the pivotal trials in children aged 6 to 35 months for Fluarix Tetra and Vaxigrip Tetra were relatively similar in design and study outcomes. The key differences of the two trials included:

- Study D-QIV-004 was undertaken over five influenza seasons between October 2011 and December 2014 using four different influenza vaccine compositions while Study GQM05 was conducted over four influenza seasons between March 2014 and July 2016.

- Two doses of Fluarix Tetra were administered at a 28-day interval to unprimed subjects and primed subjects received a single dose to be consistent with the influenza vaccine guidelines, however, fewer than 1% of subjects were classified as primed (i.e. age > 12 months and had previously received at least two doses of influenza vaccine) while Study GQM05 only included healthy vaccine-naïve children who received two doses of Vaxigrip Tetra 28 days apart, excluding a subset of subjects who received Trivalent Influenza Vaccine (TIV).
- Subjects in the control group of Study D-QIV-004 received one or two doses of non-influenza vaccines (Hepatitis A virus vaccine, Havrix; Varicella vaccines, Varilrix or Varivax/ProVarivax; 13-valent pneumococcal conjugate vaccine, Prevenar13) while the control group (placebo) of Study GQM05 received no vaccination (saline).
- The primary endpoints in the Fluarix Tetra trial were VE in preventing:
 - Reverse transcription polymerase chain reaction (RT-PCR)-confirmed, moderate-to-severe influenza; or
 - All influenza (irrespective of disease severity) associated with any seasonal influenza strain.
- The primary endpoints in the Vaxigrip Tetra trial were defined as:
 - Laboratory-confirmed, influenza caused by any A or B strain; or
 - Laboratory-confirmed, influenza associated with any seasonal influenza strain.

Comparative effectiveness

- 5.10 In the previous Fluarix Tetra submission (for high risk and Aboriginal and/or Torres Strait Islander infants and children aged 6 to 35 months), ATAGI (December 2018 pre-submission advice) noted that there were limitations in using immunogenicity data to predict protective immunity, particularly in young children and considered that VE against influenza a more appropriate endpoint for determining protection provided by influenza vaccine than immunogenicity data in children aged 6 to 35 months (paragraph 5.6, Fluarix Tetra PSD, March 2019).
- 5.11 In the context of VE, Fluarix Tetra demonstrated 63.2% (97.5% confidence interval (CI): 52, 72) efficacy in preventing RT-PCR-confirmed moderate to severe influenza disease and 50% (97.5% CI: 42, 57) efficacy against RT PCR-confirmed influenza of any severity (D-QIV-004; Claeys, 2018) whereas Vaxigrip Tetra demonstrated 51.0% (97% CI: 37.4, 61.9) efficacy against laboratory-confirmed influenza illness caused by any influenza A or B type and 68.4% (97% CI: 47.1, 81.9) efficacy against viral strains similar to those contained in the vaccine compared with placebo (GQM05, Pepin, 2019).
- 5.12 The submission presented the results of immunogenicity as a secondary outcome in a subset of subjects (according to protocol (ATP) cohort for immunogenicity, N=1,332), and noted that Fluarix Tetra exhibited a highly immunogenic response against all four

vaccine strains, compared with non-influenza vaccine controls, in children aged 6 to 35 months.

- 5.13 Compared with control vaccines, Fluarix Tetra reduced general medical visits associated with influenza illness by 47% and emergency room visits associated with influenza illness by 79%. Antibiotic use associated with influenza illness was reduced by 50% (Claeys, 2018) while there were 6 events of laboratory-confirmed influenza illness associated with hospitalisation and caused by any influenza A or B types with 3 events for each the Vaxigrip Tetra arm and placebo arm (Pepin, 2019).
- 5.14 The submission considered that an indirect comparison of the VE results between the two studies demonstrated similar VE outcomes, particularly laboratory-confirmed influenza illness caused by any influenza A or B type (51% Fluarix Tetra vs 51% Vaxigrip Tetra) as shown in the table below.

Table 4: Comparison of study outcomes: Fluarix Tetra vs Vaxigrip Tetra

Outcome	VE Fluarix tetra % (2-sided 95% CI)	VE Vaxigrip Tetra % (2-sided 97% CI)
Laboratory-confirmed influenza illness caused by: Any influenza A or B type	51 (44, 58)†	50.98 (37.36, 61.86)
Moderate-to -severe RT-PCR- confirmed influenza of any strain	63.2 (52, 72)	NR
RT-PCR-confirmed influenza illness caused by:		
○ Any influenza A or B type	50 (42, 57)	51.40 (39.20, 61.33)
○ Viral strains similar to those contained in the vaccine	60.1 (49.1, 69.0)	68.40 (49.42, 80.91)
Culture-confirmed influenza illness caused by:		
○ Any influenza A or B type	51.2 (44.1, 57.6)	57.44 (45.36, 67.07)

Source Table 19, p28 of the submission

- 5.15 Despite limitations for the naïve indirect comparison and the key differences between the two studies as outlined in paragraph 5.9, ATAGI considered that the Fluarix Tetra VE of 63.2% (95% CI: 51.8–72.3%) against moderate to severe influenza to be comparable to VE and effectiveness estimates of other QIVs such as Vaxigrip Tetra and FluQuadri. Recognising that influenza VE/effectiveness can vary year to year, and the absence of a direct comparison of the VE/effectiveness of Vaxigrip Tetra or FluQuadri to Fluarix Tetra in 6 to 35 month olds, ATAGI considered the efficacy of Fluarix Tetra to be equivalent to that of Vaxigrip Tetra and FluQuadri in children aged 6–35 months (ATAGI March 2020 pre-submission advice).

Comparative harms

- 5.16 Study D-QIV-004 provided safety data, including solicited, unsolicited, local or general adverse events, on children aged 6 to 35 months who received Fluarix Tetra in comparison to children in the control group who received hepatitis A, varicella or PCV13 vaccines. This study found no clinically meaningful differences between Fluarix Tetra and control vaccine in safety outcomes.
- 5.17 Injection site pain was the most commonly reported solicited local AE during the 7-day post-vaccination period (22.9% of Fluarix Tetra recipients vs 23.3% of control

vaccine recipients). There was no change in the incidence of solicited local AEs from dose 1 to dose 2 in the Fluarix Tetra group. Irritability/fussiness was the most commonly reported solicited general AE during the 7-day post-vaccination period (23.4% vs 24.2%), with fever >39°C being the most commonly reported solicited grade 3 general AE during the 7-day post-vaccination period, occurring among 2.3% of Fluarix Tetra recipients (1.2% overall/dose) and 2.4% of control vaccine recipients (1.3% overall/dose). Lower frequencies of vaccine-related grade 3 fever were reported.

- 5.18 The submission noted that a higher proportion of participants reported solicited injection site reactions in the Vaxigrip Tetra group (39.9%; 95% CI: 37.5, 42.4) than in the placebo group (31.9%; 95% CI: 29.6, 34.2) while proportions reporting solicited reactions and AEs were similar for the Vaxigrip Tetra, trivalent influenza vaccine (TIV) and placebo groups. A single vaccine-related serious adverse event (benign febrile seizure) was reported for a participant vaccinated with Vaxigrip Tetra.
- 5.19 The submission did not present an indirect comparison of safety endpoints but concluded that Fluarix Tetra is non-inferior to Vaxigrip Tetra in terms of safety.
- 5.20 The submission noted that ATAGI did not raise any specific concerns regarding the safety of Fluarix Tetra for use in children aged 6 months to <5 years under the NIP; however, considered ongoing surveillance of adverse events following immunisation to be essential. While noting there is no direct evidence comparing the safety profile of Fluarix Tetra with that of Vaxigrip Tetra or FluQuadri, ATAGI considered that the safety profile of Fluarix Tetra is comparable with that of other widely accepted licensed vaccines, with clinical trial evidence showing that Fluarix Tetra is well tolerated in children aged 6–35 months (ATAGI March 2020 pre-submission advice).
- 5.21 As a minor submission, the analyses were not independently evaluated.

Clinical claim

- 5.22 The submission claimed that Fluarix Tetra is non-inferior to Vaxigrip Tetra in terms of effectiveness and safety in the prevention of seasonal influenza disease caused by the influenza virus type A and B contained in the vaccine.
- 5.23 Although based on an indirect comparison, the non-inferiority claim between Fluarix Tetra and other QIVs (Vaxigrip Tetra, FluQuadri) listed on the NIP in the target population was supported by ATAGI (ATAGI March 2020 pre-submission advice).

Economic analysis

- 5.24 The minor submission presented a cost-minimisation analysis of Fluarix Tetra compared with Vaxigrip Tetra. The equi-effective doses were estimated as a single 0.5 mL dose of Fluarix Tetra and a single 0.5 mL dose of Vaxigrip Tetra for children aged 6 months to < 5 years.

- 5.25 Given that the submission assumed no difference in costs of administration, monitoring or management of adverse events, the cost-minimisation analysis was based on equi-effective doses at parity to the nationally negotiated price (\$[REDACTED]).

Estimated PBS usage & financial implications

- 5.26 The submission did not present utilisation or financial estimates associated with the extension of the NIP listing of Fluarix Tetra to include healthy children aged 6 months to <5 years who were eligible for NIP-funded influenza vaccine at the time of the submission.
- 5.27 The submission stated that as the proposed price for Fluarix Tetra is the same as the price for Vaxigrip Tetra and there is no change to the eligible population of children aged 6 months to <5 years, therefore, there is likely to be no financial implications associated with the proposed change to the NIP listing.

For more detail on PBAC's view, see section 6 PBAC outcome.

6 PBAC Outcome

- 6.1 The PBAC recommended an extension to the listing of inactivated quadrivalent influenza vaccine (QIV), Fluarix Tetra, on Schedule 1 (Designated vaccines and circumstances in which vaccines may be provided) of the *National Health (Immunisation Program – Designated Vaccines) Determination 2014 (No.1)* (the Determination), for the prevention of seasonal influenza, to include healthy children aged 6 months to <5 years who are currently eligible for influenza vaccination under the NIP. The PBAC's recommendation for listing was based on, among other matters, its assessment, that the cost-effectiveness of Fluarix Tetra would be acceptable if it were cost-minimised against the nominated comparators (Vaxigrip Tetra and FluQuadri).
- 6.2 The PBAC considered that Vaxigrip Tetra and FluQuadri were appropriate comparators given that these two QIVs are currently listed on the NIP for all children aged 6 months to <5 years and the PBAC has previously accepted that FluQuadri is non-inferior to Vaxigrip Tetra in terms of comparative effectiveness and safety at its November 2019 meeting.
- 6.3 The PBAC noted the minor submission presented an indirect comparison of clinical trials for Fluarix Tetra (Study D-QIV-004) and Vaxigrip Tetra (GQM05) in the 6 to 35 month age subgroup to support the claim that Fluarix Tetra is non-inferior to Vaxigrip Tetra in the prevention of seasonal influenza for healthy children aged 6 months to <5 years. The PBAC noted that, in the absence of direct clinical trial evidence, ATAGI considered the vaccine efficacy (VE) of Fluarix Tetra was comparable to that of Vaxigrip Tetra or FluQuadri in children aged 6 to 35 months (see paragraph 5.15), and ATAGI considered it was reasonable to assume the efficacy of Fluarix Tetra is similar in children aged 3 to 4 years as in children aged 6 to 35 months (see paragraph 5.3). Overall, the PBAC considered it was reasonable to conclude that the effectiveness of

Fluarix Tetra would be similar to that of Vaxigrip Tetra or FluQuadri for the prevention of seasonal influenza in all children aged 6 months to <5 years.

- 6.4 The PBAC noted that the safety outcomes across the clinical trials were provided in the submission without an analysis to demonstrate the comparative safety of Fluarix Tetra to Vaxigrip Tetra or FluQuadri in children aged 6 months to <5 years but the PBAC considered that there are likely no substantive differences in safety between Fluarix Tetra and other NIP listed QIVs in this population.
- 6.5 The PBAC accepted the cost-minimisation analysis based on the equi-effective doses; being a single 0.5 mL dose of Fluarix Tetra, a single 0.5 mL dose of Vaxigrip Tetra, and a single 0.5 mL dose of FluQuadri.
- 6.6 The PBAC considered that Fluarix Tetra is expected to substitute for other QIVs listed on the NIP for this population without altering the market size for influenza vaccines. Therefore, the PBAC considered there would most likely be no financial impact associated with extending the existing NIP listing of Fluarix Tetra to include healthy children aged 6 months to <5 years.
- 6.7 The PBAC noted that this submission is not eligible for an Independent Review because it is only relevant to submissions relating to the PBS.

Outcome:

Recommended

7 Recommended listing

- 7.1 Amend the existing listing on the NIP as follows:

Public Summary Document – July 2020 PBAC Meeting

Name, Restriction, Manner of administration and form	Proprietary Name and Manufacturer
Inactivated Quadrivalent Influenza Vaccine (split virion) Injection 0.5 mL	Fluarix® Tetra GlaxoSmithKline Australia Pty Ltd
Category/Program	NIP
Subsection 7 (7A) For items 207A of Schedule 1, a designated vaccine mentioned in this item may be provided to:	
Groups eligible for the requested NIP listing of Fluarix® Tetra, including	<ul style="list-style-type: none"> (a) a person who is at least 65 years; or (b) an Aboriginal or Torres Strait Islander person who is at least 6 months; or (c) a child who is at least 6 months old but less than 5 years old; (d) a person who is at least 6 months who: <ul style="list-style-type: none"> (i) has cardiac disease including cyanotic congenital heart disease, coronary artery disease and congestive heart failure; or (ii) has a chronic respiratory condition including suppurative lung disease, bronchiectasis, cystic fibrosis, chronic obstructive pulmonary disease, chronic emphysema and severe asthma; or (iii) has another chronic illness requiring regular medical follow-up or hospitalisation in the preceding year, including diabetes mellitus, chronic metabolic diseases, chronic renal failure, haemoglobinopathies and impaired immunity (including drug-induced immune impairment); or (iv) has a chronic neurological condition, including multiple sclerosis, spinal cord injuries, seizure disorders or other neuromuscular disorders; or (v) has impaired immunity, including HIV infection; or (vi) is less than 11 years and is receiving long term aspirin therapy; or (e) a woman who is pregnant.
Number and timing of doses	Should be administered in accordance with the national recommendation as per the current Immunisation Handbook: Children ≥6 months to <9 years of age: <ul style="list-style-type: none"> • If the child has not previously been vaccinated: two 0.5 ml injections at least one month apart. • If the child has been previously vaccinated: a single 0.5 ml injection.

This restriction may be subject to further review. Should there be any changes made to the restriction the Sponsor will be informed.

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor's Comment

GSK welcomes the PBAC's recommendation to list Fluarix Tetra to be included on the NIP to include all children aged 6 months to less than 5 years.