# 5.12 QUADRIVALENT INFLUENZA VACCINE, 0.25/0.5 ML PRE-FILLED SYRINGE, FLUQUADRI™, SANOFI PASTEUR.

## 1 Purpose of Application

1.1 The submission sought listing of quadrivalent influenza vaccination (FluQuadri) on the Immunisation Program – Designated Vaccines list, and for inclusion on the National Immunisation Program (NIP).

## 2 Requested listing

2.1 The submission sought the following listing

| Name, Restriction, Manner of administration and form | Max. Qty | №.of Rpts | Dispensed Price for Max. Qty | Proprietary Name and Manufacturer |
|---|---|---|---|---|
| FluQuadri (FluQuadri Junior for infants) (quadrivalent influenza vaccine)<br>15 µg HA/strain (4 strains) in 0.25ml suspension of phosphate buffered saline for IM injection in pre-filled syringe.<br>15 µg HA/strain (4 strains) in 0.5ml suspension of phosphate buffered saline for IM injection in pre-filled syringe. | 1 | 1 | $[redacted] | FluQuadri Sanofi-Pasteur |
| 3 to 9 years | 1 | 1 | $[redacted] | |
| >9 years | 1 | | $[redacted] | |

[a] Ex-manufacturer price

Restrictions:
All persons ≥65 years, ATSI individuals aged ≥15 years, pregnant women and high risk individuals aged ≥6months, consistent with the registered TGA indication. If a child 6 months to ≤9 years of age receiving influenza vaccine for the first time inadvertently does not receive the 2nd dose within the same year, he/she should have 2 doses administered the following year.
† Two doses, at least 4 weeks apart, are recommended for children aged ≤9 years who are receiving influenza vaccine for the first time. The same vial should not be re-used for the 2 doses.
‡ Two doses, at least 4 weeks apart, are recommended for immunocompromised persons receiving influenza vaccine for the first time
Source: Australian Immunisation Handbook 10th Edition 2013 (updated January 2014) Table 4.7.1 p. 251

2.2 The listing was requested based on a cost minimisation compared to Fluarix tetra influenza vaccine for individuals over 36 months, and compared to FluQuadri (for FluQuadri Junior) for 6 to < 36 month olds. FluQuadri is not the appropriate comparator for infants (6 to < 36 months) as it is not currently PBS listed. TIVs are the appropriate comparator.

*For more detail on PBAC's view, see section 7 "PBAC outcome"*

## 3 Background

3.1 TGA status: FluQuadri was TGA registered on 3rd October 2014 for prevention active immunization of influenza disease caused by influenza A subtype viruses and influenza B subtype viruses contained in the vaccine.

3.2 FluQuadri has not been considered by PBAC previously.

3.3 Fluarix Tetra, a QIV, was recommended at the PBAC March, 2015 meeting.

## 4 Clinical place for the proposed therapy

4.1 The submission stated FluQuadri will be used for active immunisation against four influenza strains (two influenza A strains and two influenza B strains) in all individuals listed on the NIP.

4.2 Flu Quadri includes immunisation against two influenza A strains and two influenza B strains similar to Fluarix Tetra, another quadrivalent vaccine which includes two influenza A strains and two influenza B strains for individuals 3 years and above.

4.3 Flu Quadri includes immunisation against two influenza A strains and two influenza B strains compared to the normal trivalent influenza vaccines for infants aged 6 to <36 months, which include immunisation against two influenza A strains and only one influenza B strain under guidelines from the World Health Organization.

## 5 Comparator

5.1 Fluarix Tetra influenza vaccine was listed as the main comparator for children 3 years and older. With the recommendation of Fluarix Tetra at the March 2015 meeting, this was the appropriate comparator as they are both quadrivalent vaccines.

5.2 FluQuadri (≥ 3yrs) influenza vaccine, itself, was presented as the main comparator for infants 6 months to <36 months. This is not the appropriate comparator as FluQuadri (≥ 3yrs) is not currently NIP listed. The appropriate comparator was the NIP listed trivalent vaccines. Fluarix Tetra was not the appropriate comparator for this group as it is registered for active immunisation of children aged 3 years and older and adults. The ATAGI advice states 'ATAGI also advises that comparative immunogenicity data between the candidate QIV and the comparator TIV should be assessed by clinically relevant age groups'.(page 3, post-submission advice)

*For more detail on PBAC's view, see section 7 "PBAC outcome"*

## 6 Consideration of the evidence

### *Sponsor hearing*

6.1 There was no hearing for this item.

### *Consumer comments*

6.2 The PBAC noted that no consumer comments were received for this item.

### *Clinical trials*

6.3 The submission is based on an indirect comparison of 3 FluQuadri trials and 5 Fluarix Tetra trials.

6.4 Details of the trials presented in the submission are provided in the table below. Trial QIV-04 was used for the FluQuadri vs. TIVs comparison for infants 6 months to <36 months.

**Table 1: Trials and associated reports presented in the submission**

| Trial ID/First Author | Protocol title/ Publication title | Publication citation |
|---|---|---|
| **Direct randomised trials- FluQuadri** | | |
| QIV03<br>Pépin, et al. 2013 | Phase III, randomised, four-arm, trivalent-controlled, multi-centre, immunogenicity trial of 739 subjects primarily aged ≥ 65 years. CSR 'Safety and Immunogenicity Among Adults Administered Quadrivalent Influenza Vaccine' Sanofi Pasteur. | Final report version 2.0 dated 20 February 2012.<br>Vaccine, 2013 : 31; 5572-5578 |
| GRC43<br>(Greenberg, Robertson, Noss, Blatter, Biedenbender, & Decker, 2013) | Phase II, open-label, controlled, three-arm, multi-centre trial designed to assess the QIV in adults compared to two licenced TIVs. CSR 'Immunogenicity and Safety Among Children and Adults of the 2009-2010 Trivalent Influenza Vaccine, 2008-2009 Trivalent Influenza Vaccine, and Quadrivalent Influenza Vaccine (Intramuscular Route).' Sanofi Pasteur. | Final report version 2.0 dated 01 June 2012.<br>Vaccine, 2013: 31; 770-776 |
| QIV04<br>(Greenberg, Robertson, Landolfi, Bhaumik, Senders, & Decker, 2014) | Phase III, randomised, observer-blinded, active-controlled, 3-arm trial, in subjects from two age strata: 6 months to < 36 months and 3 years to < 9 years of age. CSR 'Safety and Immunogenicity Among Children Administered Quadrivalent Influenza Vaccine' Sanofi Pasteur. | Final Report Version 1.0 dated 23 April 2012.<br>Pediatr Infect Dis J, 2014: 33:630–636. |
| **Direct randomised trials- Fluarix Tetra** | | |
| D-QIV-001<br>(Beran, Peeters, Dewé, Raupachová, Hobzová, & Devaster, 2013) | Phase I/II, single-centre, single-blind, controlled study conducted in the Czech Republic designed to assess the immunogenicity of two candidate QIVs in adults aged 18-60 years. Immunogenicity and safety of quadrivalent versus trivalent inactivated influenza vaccine: a randomized, controlled trial in adults. | BMC Infectious Diseases, 2013: 13:224. |
| D-QIV-008<br>(Kieninger, Sheldon, Lin, Yu, & Bayas, 2013) | Phase III, randomised, partially-blind, multinational study evaluating lot-to-lot consistency and immunogenicity, reactogenicity and safety of Fluarix tetra to the TIV Fluarix in adults aged ≥18 years. Immunogenicity, reactogenicity and safety of an inactivated quadrivalent influenza vaccine candidate versus inactivated trivalent influenza vaccine: a phase III, randomized trial in adults aged ≥18 years. | Date<br>22 November 2011<br><br>BMC Infectious Diseases (2013) 13: 343.<br>Date: 24 Jul 2013 |
| Tinoco 2014<br>(Tinoco, Pavia-Ruz, Cruz-Valdez, Aranza Doniz, & Chandrasekaran, 2014) | Phase III, randomised, lot-to-lot consistency study of QIV vs TIV in healthy adults aged ≥18 yrs. Immunogenicity, reactogenicity, and safety of inactivated quadrivalent influenza vaccine candidate versus inactivated trivalent influenza vaccine in healthy adults aged >18 years: A phase III, randomized trial. | Vaccine, 2014: 32(13):1480-7 |
| D-QIV-003<br>(Domachowske, et al., 2013) | Phase III, double-blind, randomised, multicentre study conducted to assess immunogenicity, reactogenicity, and safety of QIV vs TIV in children aged 3–17 years, and QIV in | Date<br>02 December 2011<br>Journal of Infectious |

| | | |
|---|---|---|
| | children aged 6–35 months. A Randomized Trial of Candidate Inactivated Quadrivalent Influenza Vaccine versus Trivalent Influenza Vaccines in Children Aged 3–17 Years | Diseases (2013) 207:12 (1878-1887). Date: 15 Jun 2013 |
| Langley 2013 (Langley, Martinez, Chatterjee, Halperin, & McNeil, 2013) | Phase III randomised study of QIV vs TIV-VIC and TIV-Yam in children and adolescents 3 through 17 years of age, with an open label assessment of QIV in children 6–35 months of age. Immunogenicity and reactogenicity of an inactivated quadrivalent influenza vaccine administered intramuscularly to children 6 to 35 months of age in 2012-2013 | J Pediatr Infect Dis Soc, 2014: 1-10 |

Source: Table B.4.1, Section B, p 22 of the submission.

6.5 The key features of the trials used in the indirect comparison are summarised in the Table 2 below. The common comparator is trivalent vaccines (TIVs).

**Table 2: Key features of the included evidence – indirect comparison**

| Trial ID | Design | Compared interventions | Risk of bias | Population | Main outcomes | Used in Indirect Comparison |
|---|---|---|---|---|---|---|
| FluQuadri | | | | | | |
| QIV03 | Ph III, R, DB | QIV; N=225<br>TIV licensed; N=225<br>TIV investigational; N=225<br>TIV investigational; N=64 | Low | Adults<br>18-64 or ≥65 years | Primary: NI GMTs<br>Secondary: NI SCRs S GMTs and SCRs (B)<br>Other: immunogenicity, safety | Yes NI SCRs children >3yrs and adults |
| GRC43 | Ph II, R, OL | QIV; N=190<br>TIV licensed; N=190<br>TIV investigational N=190 | Low | Adults aged 18-60 or ≥61 years<br>A subgroup of children received investigational TIV | Primary: NI GMTs<br>Other: immunogenicity , safety | Yes descriptive SCRs children >3yrs and adults |
| QIV04 | Ph III, R, DB | QIV; N=2902<br>TIV licensed; N=736<br>TIV investigational N=725 | Low | Children<br>6- < 36 months or<br>3 - < 8 years | Primary: NI GMTs and SCRs<br>Secondary: S GMTs and SCRs (B)<br>Other: immunogenicity, safety | Yes NI SCRs infants 6-36months |

| **Fluarix Tetra** | | | | | | |
|---|---|---|---|---|---|---|
| D-QIV-001 | Ph I, R, SB | QIV; N=105<br>TIV; N=105<br>Adjuvant QIV; N=105<br>Adjuvant TIV; N=105 | Low | Adults<br>19-59 years | Primary: NI GMTs S GMTs<br>Secondary: , Other: immunogenicity, safety | Yes descriptive SCRs Adults |
| D-QIV-008 | Ph III, R, PB | 3 lots QIV; N=1012 per group<br>Fluarix; N=110<br>Investigational TIV; N=610 | Low | Adults ≥18 years | Primary: NI GMTs and SCRs; S GMTs and SCRs;<br>Other: immunogenicity, safety | Yes NI SCRs Adults |
| Tinoco 2014 | Ph III R, DB | QIV (lot 1, 2, or 3); or,<br>One of two TIVs;<br>N=1707 total | Low | Adults ≥18 years | Primary: NI GMTs<br>Secondary: S; GMT<br>Other: immunogenicity, safety | Yes descriptive SCRs Adults |
| D-QIV-003 | Ph III, R, DB | QIV;<br>Fluarix;<br>Investigational TIV;<br>N=2741 total | Low | Children 3-17 years<br>Infants aged 6-35 months who received QIV only | Primary: NI GMTs and SCRs<br>Secondary: S GMTs and SCRs; Other: immunogenicity, safety | Yes NI SCRs Children >3yrs |
| Langley 2013 | Ph III, R, DB | QIV<br>TIV-Vic or TIV-Yam;<br>N=3094 total | Low | Children 3-17 years<br>Infants aged 6-35 months who received QIV only | Primary: NI GMT and SCR<br>Secondary: S GMT and SCR, immunogenicity, safety | Yes NI SCRs Children >3yrs |

Abbreviations: DB = double-blind; SB = single blind; PB = partially blind; OL = open label; R = randomised; NI = Non-inferiority; S = superiority; GMT = Geometric Mean Titres; SCR = Seroconversion rate; LTLC = lot to lot consistency.
Source: compiled during the evaluation

### *Comparative effectiveness*

6.6 The claim in the submission was based on seroconversion rates (SCRs). Haemagglutination antibody geometric titres (GMTs) were not presented in the meta-analysis used as the basis for the indirect comparison of the submission. GMTs are presented in Section B6.1 of the submission. The submission states that this outcome was used as they were assessed similarly, reported reasonably consistently and defined identically across the two trial sets. These surrogate outcomes have been used previously for PBAC decision making. The results of meta-analysis and indirect comparison are indicated in Table 3 and Table 4 below.

**Table 3: Results of meta-analysis of SCRs across the direct randomised trials**

| Study ID | Strain | OR QIV vs. TIV | | | Heterogeneity | |
|---|---|---|---|---|---|---|
| Age group | | OR | 95% CI | p-value | Chi2; I2 | NNT |
| FluQuadri Trials | | | | | | |
| QIV-03/GRC43 Adults ≥ 18 years | A/H1/N1 | 1.02 | 0.69; 1.50 | 0.93 | 2.44; 59% | 1 |
| | A/H3N2 | 1.13 | 0.61; 2.07 | 0.7 | 5.89; 83% | 1 |
| | B1 (Brisbane) | 1.24 | 0.65; 2.38 | 0.52 | 4.66; 79% | 1 |
| | B2 (Florida) | 1.37 | 0.88; 2.14 | 0.17 | 2.43; 59% | 1 |
| QIV-04 Children 3-< 9 years | A/H1/N1 | 1.09 | 0.76; 1.55 | 0.63 | NA | 1 |
| | A/H3N2 | 1.31 | 1.05; 1.65 | 0.02 | | 1 |
| | B1 (Brisbane) | 1.78 | 1.40; 2.26 | <0.01 | | 1 |
| | B2 (Florida) | 1.03 | 0.79; 1.33 | 0.84 | | 1 |
| QIV-04 Infants 6 to < 36 months | A/H1/N1 | 1.19 | 0.83; 1.73 | 0.34 | NA | 1 |
| | A/H3N2 | 1.69 | 1.07; 2.69 | 0.02 | | 1 |
| | B1 (Brisbane) | 1.39 | 1.02; 1.89 | 0.04 | | 1 |
| | B2 (Florida) | 1.18 | 0.89; 1.56 | 0.26 | | 1 |
| Fluarix Tetra trials | | | | | | |
| 001/008/Tinoco Adults ≥ 18 years | A/H1/N1 | 0.96 | 0.82; 1.13 | 0.64 | 1.44; 0% | 1 |
| | A/H3N2 | 1.05 | 0.79; 1.41 | 0.74 | 3.29; 39% | 1 |
| | B1 (Malaysia-VIC;Brisbane VIC;Brisbane VIC respectively) | 1.12 | 0.95; 1.33 | 0.18 | 1.53; 0% | 1 |
| | B2* (Brisbane-VIC;Florida-Yam respectively) | 1.12 | 0.93; 1.36 | 0.22 | 0.06; 0% | 1 |
| 003/Langley Children 3-17 years | A/H1/N1 | 0.95 | 0.77; 1.18 | 0.63 | 1.36; 26% | 1 |
| | A/H3N2 | 1.02 | 0.98; 1.06 | 0.38 | 0.02; 0% | 1 |
| | B1(Brisbane-VIC) | 1.12 | 0.96; 1.30 | 0.14 | 0.29; 0% | 1 |
| | B2 Brisbane-YAM) | 1.10 | 0.94; 1.28 | 0.24 | 0.00; 0% | 1 |

*Analysis includes only D-QIV-008 and Tinoco, as only one TIV, containing the B1 strain, was included in D-QIV-001.
Source: Table B.5.8, Section B, p62 of the submission. NNT added as part of the evaluation. OR=Odds Ratio B1=primary strain; B2= alternate strain, VIC = Victroria, YAM = Yamagata.

**Table 4: Results of indirect comparison of SCRs (against Fluarix Tetra) and direct comparison (v TIVs, Infants)**

| | OR | 95% CI | OR | 95% CI | OR | 95% CI |
|---|---|---|---|---|---|---|
| Adults | FluQuadri | | Fluarix Tetra | | FluQuadri vs. Fluarix Tetra | |
| A/H1N1 | 1.02 | 0.69; 1.50 | 0.96 | 0.82; 1.13 | 1.063 | 0.698; 1.617 |
| A/H3N2 | 1.13 | 0.61; 2.07 | 1.05 | 0.79; 1.41 | 1.076 | 0.547; 2.116 |
| B1 | 1.24 | 0.65; 2.38 | 1.12 | 0.95; 1.33 | 1.107 | 0.566; 2.164 |
| B2 | 1.37 | 0.88; 2.14 | 1.12 | 0.93; 1.36 | 1.223 | 0.754; 1.983 |
| Children≥3yrs | FluQuadri | | Fluarix Tetra | | FluQuadri vs. Fluarix Tetra | |
| A/H1N1 | 1.09 | 0.76; 1.55 | 0.95 | 0.77; 1.18 | 1.147 | 0.757; 1.738 |
| A/H3N2 | 1.31 | 1.05; 1.65 | 1.02 | 0.98; 1.06 | 1.284 | 1.021; 1.615 |
| B1 | 1.78 | 1.40; 2.26 | 1.12 | 0.96; 1.30 | 1.589 | 1.197; 2.110 |
| B2 | 1.03 | 0.79; 1.33 | 1.10 | 0.94; 1.28 | 0.936 | 0.692; 1.267 |
| Infants 6-< 36 months | | | | | FluQuadri Junior vs. TIVs[1] | |
| A/H1N1 | | | | | 1.19 | 0.83; 1.73 |
| A/H3N2 | | | | | 1.69 | 1.07; 2.69 |
| B1 | | | | | 1.39 | 1.02; 1.89 |
| B2 | | | | | 1.18 | 0.89; 1.56 |

[1]As part of the evaluation FluQuadri was compared to TIVs for infants aged 6-36 months using the QIV-04 trial as this was the appropriate comparator. Source: Table B.59, Section B, p63 of the submission.

6.7 FluQuadri demonstrated no significant difference in SCR compared to Fluarix Tetra vaccines for all strains in adults. FluQuadri demonstrated no significant differences in SCR compared to Fluarix Tetra vaccines for Strain A/H1N1 and Strain B2 and significant difference for Strain A/H3N2 and Strain B1 in children aged 3 to < 18 years. FluQuadri demonstrated no significant differences in SCR compared to TIV vaccines for Strain A/H1N1 and Strain B2 and significant difference for Strain A/H3N2 and Strain B1 in children aged 6 to < 36 months. For the two A strains, the analyses use pooled SCRs for both TIV products included in each trial, while for the B strains the submission uses results only for the TIV containing the relevant virus strain; i.e. they rely on the non-inferiority analyses as opposed to the superiority analyses from the trials

### *Comparative harms*

6.8 The submission presents descriptive results of the comparative harms of the 8 trials. The PBAC has previously accepted that Fluarix is non-inferior to TIVs in the listing of FluarixTetra on the PBS (March 2015). The incidence of AE was higher in children, but this was consistent across all trials. The incidence of solicited injection site reactions was more frequent in children aged 6 to < 36 months. (Product Information, p17)

### *Clinical claim*

6.9 The submission described FluQuadri as non-inferior in terms of comparative effectiveness and non-inferior in terms of comparative safety over Fluarix Tetra for children and adults. This claim was adequately supported by the serology data.

6.10 The submission described FluQuadri Junior as non-inferior in terms of comparative effectiveness and non-inferior in terms of comparative safety over FluQuadri for infants (6 to < 36 months). This claim was supported however FluQuadri is not the appropriate comparator. FluQuadri demonstrated no significant differences in SCR compared to TIV vaccines for Strain A/H1N1 and Strain B2 and significant difference for Strain A/H3N2 and Strain B1 in children aged 6 to < 36 months It is unknown if difference in immunogenicity would equate to differences in protection to matched influenza strains. Flu-Quadri was non-inferior in terms of comparative safety over TIVs, the correct comparator for this sub-group.

### *Economic analysis*

6.11 The equi-effective doses of FluQuadri and Fluarix tetra, in the proposed treatment setting are:

- Adults (≥18 years): FluQuadri (0.5 mL) = Fluarix Tetra (0.5 mL);
- Children (≥3 years): FluQuadri (0.5 mL) = Fluarix Tetra (0.5 mL);
- Infants (6-35 months): FluQuadri Junior (0.25 mL) = FluQuadri (0.5 mL) in older children (≥3 years);

6.12 The submission assumes that the price of Fluarix Tetra is the NIP ceiling price for the existing TIVs ($[redacted]). There was no impact of any additional costs or offsets for administration or adverse events. The evaluation concluded that this was reasonable methodology.

### *Drug cost/course*

6.13 The estimated drug cost per person per year was $[redacted] (ex-manufacturer price).

### *Estimated PBS usage & financial implications*

6.14 This submission was not considered by DUSC. The submission uses an epidemiological/market share approach to forecast the uptake and cost of FluQuadri over a five year period. The submission predicts the current uptake of influenza vaccination using estimates from the literature for the current population (ABS population), prevalence of risk factors (Newell, Wood and McIntyre, 2008), vaccine uptake (Australian Vaccination Survey, 2011) and market share (submission estimates) to determine the eligible population. The price of FluQuadri is assumed to be the current ceiling price of the NIP. The final price will be based on procurement arrangements pertaining to NIP.

6.15 The analysis considers only the costs associated with the vaccine. The submission does not claim any additional health benefits (in terms of morbidity or mortality) in listing FluQuadri. As such, the analysis predicts that including FluQuadri on the NIP as proposed will be cost neutral to both the program and Australian government health budgets (see redacted Table 5).

**Table 5: Estimated use and financial implications**

| | Year 1 | Year 2 | Year 3 | Year 4 | Year 5 |
|---|---|---|---|---|---|
| Eligible population | | | | | |
| Adults ≥65 years | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| ATSI 15-64 years | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| Pregnant women | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| Adults 18-64 years | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| Children 3-17 years | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| Children 6-36 months | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| Uptake | | | | | |
| Adults ≥65 years | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| ATSI 15-64 years | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| Pregnant women | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| Adults 18-64 years | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| Children 3-17 years | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| Children 6-36 months | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| Utilisation | | | | | |
| FluQuadri Adults | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| FluQuadri Children | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| FluQuadri Junior | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| Total | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| Cost | | | | | |
| FluQuadri | $[redacted] | $[redacted] | $[redacted] | $[redacted] | $[redacted] |
| FluQuadri Junior | $[redacted] | $[redacted] | $[redacted] | $[redacted] | $[redacted] |
| Total | $[redacted] | $[redacted] | $[redacted] | $[redacted] | $[redacted] |
| Change in cost of other vaccines | -$[redacted] | -$[redacted] | -$[redacted] | -$[redacted] | -$[redacted] |
| **Net cost to NIP** | **$0** | **$0** | **$0** | **$0** | **$0** |

Source: Table E.4 Section E, p 93 of the submission.

*For more detail on PBAC's view, see section 7 "PBAC outcome"*

## 7 PBAC Outcome

7.1 The PBAC recommended the listing of the quadrivalent influenza vaccine, FluQuadri, on the National Immunisation Program (NIP) – Designated Vaccines List for the prevention of seasonal influenza. This quadrivalent influenza vaccine was recommended to be made available to the same patient population as the trivalent influenza vaccine that is currently included on the National Immunisation Program. The recommendation was based on a cost-minimisation with Fluarix Tetra quadrivalent influenza (for individuals 3 years and above) and with trivalent influenza vaccine (for individuals less than 3 years). One dose of 0.5mL of FluQuadri is equi-effective to one dose of 0.5mL of Fluarix Tetra, and one dose of 0.25mL of FluQuadri Junior is equi-effective to one dose of 0.25mL of junior forms of trivalent influenza vaccine.

7.2 The PBAC noted the general advice on QIV from Australian Technical Advisory Group on Immunisation (ATAGI).

7.3 The PBAC noted that the evidence presented to support non-inferiority in clinical efficacy of FluQuadri Junior over FluQuadri for infants aged 6 to < 36 months was inappropriate as FluQuadri is not recommended for the National Immunisation Program (NIP). The PBAC considered the appropriate comparator was trivalent vaccines (TIVs) in this age group, and Fluarix Tetra in individuals aged 3 years or more.

7.4 The PBAC considered that, based on the clinical evidence presented, it was appropriate to conclude non-inferior efficacy and safety compared to Fluarix Tetra influenza vaccine.

7.5 The PBAC noted in children aged 6 to < 36 months that the seroconversion rates for some antigens was greater following immunization with FluQuadri compared to TIV vaccines, by virtue of the additional fourth viral strain in the QIV. The PBAC noted the ATAGI advice which stated that the QIV formulation offers the potential to be considered superior to TIV due to additional protection gained through the inclusion of the additional influenza B strain of the alternative lineage. However, the magnitude of this incremental benefit is influenced by year-to-year variability and a number of factors for which there are clinical uncertainties, and is difficult to quantify and predict.

7.6 The PBAC considered that on balance the data supported a claim that FluQuadri Junior had non-inferior comparative effectiveness and safety to TIVs in children aged 6 to < 36 months.

7.7 The estimates appear reasonable as FluQuadri is likely to replace other influenza vaccines and the cost to Government is expected to be neutral.

**Outcome:**
Recommended

## 8 Recommended listing

8.1 Add new item to the NIP:

| Name, Restriction, Manner of administration and form | Max. Qty | №.of Rpts | Dispensed Price for Max. Qty | Proprietary Name and Manufacturer |
|---|---|---|---|---|
| FluQuadri (FluQuadri Junior for infants) (quadrivalent influenza vaccine) | | | | FluQuadri Sanofi-Pasteur |
| 15 µg HA/strain (4 strains) in 0.25ml suspension of phosphate buffered saline for IM injection in pre-filled syringe. | 1 | 1 | $[redacted] | |
| 15 µg HA/strain (4 strains) in 0.5ml suspension of phosphate buffered saline for IM injection in pre-filled syringe. | | | | |
| 3 to 9 years | 1 | 1 | $[redacted] | |
| >9 years | 1 | | $[redacted] | |

[a] Ex-manufacturer price

Restrictions:
All persons ≥65 years, ATSI individuals aged ≥15 years, pregnant women and high risk individuals aged ≥6months, consistent with the registered TGA indication. If a child 6 months to ≤9 years of age receiving influenza vaccine for the first time inadvertently does not receive the 2nd dose within the same year, he/she should have 2 doses administered the following year.
† Two doses, at least 4 weeks apart, are recommended for children aged ≤9 years who are receiving influenza vaccine for the first time. The same vial should not be re-used for the 2 doses.
‡ Two doses, at least 4 weeks apart, are recommended for immunocompromised persons receiving influenza vaccine for the first time
Source: Australian Immunisation Handbook 10th Edition 2013 (updated January 2014) Table 4.7.1 p. 251

## 9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

## 10 Sponsor's Comment

The sponsor had no comment.