High-dose quadrivalent influenza vaccine for older populations

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A high-dose quadrivalent influenza vaccine (Fluzone High-Dose Quadrivalent) is available on the private market in Australia in 2022 for adults aged 60 years and older. It contains four times the antigen content of standard influenza vaccines and has higher effectiveness in people aged 65 years and older while maintaining an acceptable safety profile. It also has comparable effectiveness and safety to the adjuvanted influenza vaccine in this age group.

Influenza is a seasonal infectious disease that usually circulates in the colder months, between April and October in Australia. Most people recover from influenza without serious illness; however, older adults, young children, pregnant women and people with certain chronic medical conditions are at higher risk of developing serious complications.[1] Influenza-associated mortality rates are highest among adults aged 65 years and older.[1,2]

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In Australia, annual influenza vaccination is recommended and funded under the National Immunisation Program (NIP) for all people aged 65 years and older and other susceptible groups. The protection provided by influenza vaccines is lower in older compared with younger adults.[3,4] A possible approach to improve the level of protection is to increase the amount of antigen in the vaccine.

Currently in Australia, adults aged 65 years and older can receive a standard quadrivalent influenza vaccine or an adjuvanted quadrivalent influenza vaccine. The adjuvanted influenza vaccine is NIP-funded for adults aged 65 years and older and is recommended in preference to standard influenza vaccines because of evidence of its greater effectiveness against severe disease in this population.[3-5]

The newly available high-dose quadrivalent influenza vaccine contains more antigen than standard-dose influenza vaccines, to provide greater protection for older adults. It has been approved by the TGA and is available in Australia for the 2022 influenza season. A trivalent version of the high-dose vaccine was available in Australia for the 2018 influenza season. This article discusses the new high-dose quadrivalent vaccine.

What is the high-dose influenza vaccine?

The newly registered high-dose influenza vaccine (Fluzone High-Dose Quadrivalent) is an inactivated split-virus quadrivalent influenza vaccine. It contains 240 micrograms of influenza virus haemagglutinin (60 mcg for each strain), four times as much as standard influenza vaccines. It is prepared using the traditional egg-based method.

The high-dose quadrivalent vaccine contains components of four influenza viruses: two influenza virus A strains (subtypes H1N1 and H3N2) and two influenza virus B strains (one from each of the Victoria and Yamagata lineages). The specific strains

1. PRECAUTIONS AND CAVEATS WHEN ADMINISTERING INFLUENZA VACCINE

- Appropriate medical treatment and supervision should always be readily available in case of the rare event of anaphylaxis following vaccine administration
- If Guillain-Barré syndrome has occurred within six weeks of previous influenza vaccination, the potential benefits and risks should be considered before vaccine administration
- In immunocompromised patients, vaccine immunogenicity may be lower
- A protective immune response may not be elicited in all vaccine recipients
- In patients with any bleeding disorder, the potential risks and benefits should be considered because of the risk of injection-site haematoma
- Vaccination should be postponed in patients with febrile illness or acute infection

2. KEY PRACTICE POINTS ON THE NEW HIGH-DOSE INFLUENZA VACCINE

- A new high-dose quadrivalent influenza vaccine is available in Australia in 2022
- The vaccine is registered for use in adults aged 60 years and older and will be available on the private market only
- The new vaccine contains four times the antigen dose of standard-dose influenza vaccines
- It has higher effectiveness and an acceptable safety profile compared with standard-dose vaccines and comparable effectiveness and safety to adjuvanted influenza vaccines

included comply with the seasonal recommendation of the Australian Influenza Vaccine Committee, which is based on the WHO recommendation for each annual influenza season.

When and how is the vaccine used?

The high-dose quadrivalent influenza vaccine was registered in Australia in 2021 for use in adults aged 60 years and older to prevent influenza disease.[6] It is not recommended or registered for people aged less than 60 years. The vaccine has also been approved for use in the USA, UK and Canada for use in adults aged 65 years and older.

The high-dose vaccine is available on the private Australian market in the 2022 influenza season but is not currently funded under the NIP. It is administered by intramuscular injection in a single 0.7 mL dose.

Common side effects

Side effects may occur after vaccination as with any influenza vaccine. Some of these expected adverse events mimic the symptoms of influenza (e.g. fever and myalgia). The high-dose influenza vaccine does not contain live influenza virus and thus cannot cause influenza. Common, usually mild and temporary adverse events after vaccination with the high-dose vaccine may include:

- pain, redness, swelling or bruising at the injection site
- muscle aches or myalgia
- malaise
- headache.

Fever has also been reported in 2 to 3% of recipients of the high-dose vaccine.[7] Adverse events after vaccination were slightly more common with the high-dose vaccine than with standard influenza vaccines but were mostly mild and temporary, resolving within three days.[7] Reported adverse events after vaccination with the high-dose vaccine are similar to those with adjuvanted influenza vaccines.[8-10]

Use in pregnancy and breastfeeding

Pregnant women are strongly recommended to receive influenza vaccine during each pregnancy because of a higher risk of morbidity, mortality and adverse birth outcomes if infected.[11-13] However, the high-dose influenza vaccine is not registered for use in people under the age of 60 years. It is currently classified as pregnancy category B2, as data are lacking on use of this vaccine in pregnant women.

Important precautions and interactions

Precautions to be taken when administering high-dose influenza vaccines are similar to those for standard and adjuvanted influenza vaccines (Box 1). The high-dose influenza vaccine is contraindicated in individuals with a history of severe allergic reaction after previous administration of any influenza vaccine and to any component of the vaccine. Although the high-dose vaccine is egg-based, it can be administered to people with a history of anaphylaxis to egg.[14]

There are currently no data on the coadministration of the high-dose influenza vaccine with other vaccines. However, the Australian Technical Advisory Group on Immunisation (ATAGI) recommends that people can receive the high-dose influenza vaccine with most other vaccines, including COVID-19 vaccines.[6,15]

Effectiveness of the high-dose influenza vaccine

Much of the current evidence on relative effectiveness of high-dose compared with standard and adjuvanted influenza vaccines comes from observational studies. These studies indicate that, compared with standard influenza vaccines, high-dose vaccine may slightly reduce influenza- or pneumonia-associated mortality and hospitalisation from influenza or pneumonia in

people aged 65 years and older.[16-25] Compared with adjuvanted influenza vaccines, studies in people aged 65 years and older also suggest that the rates of influenza-related hospitalisations are similar.[18-20,26-28]

Based on this evidence, high-dose influenza vaccine can be considered a preferred alternative to standard influenza vaccines and an equivalent alternative to adjuvanted influenza vaccines in older people. Although the adjuvanted influenza vaccine is available under the NIP at no patient cost for people aged 65 years and older, it is not registered for use in people aged 60 to 64 years.

ATAGI recommends that people aged 65 years and older should receive an adjuvanted or high-dose influenza vaccine but may receive standard influenza vaccine if the adjuvanted or high-dose vaccine is unavailable.[5] The high-dose influenza vaccine is currently not NIP-funded, whereas the adjuvanted influenza vaccine is funded for use in people aged 65 years and older.

Conclusion

After two years of limited circulation of influenza viruses in Australia during the coronavirus disease 2019 pandemic, as international borders begin to open, seasonal influenza is likely to re-emerge. The newly registered high-dose quadrivalent influenza vaccine offers an alternative vaccine to protect older people against influenza. Key practice points about the vaccine are summarised in Box 2.

The new high-dose vaccine is more effective than standard-dose influenza vaccines for older people and is comparable to adjuvanted influenza vaccine. Adverse events may be slightly more common after vaccination with the high-dose vaccine compared with standard vaccines. However, overall, it has an acceptable safety profile compared with both standard and adjuvanted vaccines. Unlike the adjuvanted vaccine, which is NIP-funded for people aged 65 years and older, the high-dose vaccine is currently available only on the private market. MT

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A list of references is included in the online version of this article (www.medicinetoday.com.au).

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