



Public Health  
England

Protecting and improving the nation's health

# **The national influenza immunisation programme 2018/19**

## **Inactivated influenza vaccine information for health care practitioners**

## About Public Health England

Public Health England exists to protect and improve the nation's health and wellbeing, and reduce health inequalities. We do this through world-leading science, knowledge and intelligence, advocacy, partnerships and the delivery of specialist public health services. We are an executive agency of the Department of Health and Social Care, and a distinct delivery organisation with operational autonomy. We provide government, local government, the NHS, Parliament, industry and the public with evidence-based professional, scientific and delivery expertise and support.

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## Background

The seasonal influenza vaccination programme was introduced in England during the late 1960s to protect those in clinical risk groups. These groups were found to be at higher risk of influenza associated morbidity and mortality. Since then, the programme has been extended to include all those aged over 65 years (2000) and pregnant women (2010).

During 2013, a phased programme commenced to offer influenza vaccine to all children from 2 years of age<sup>1</sup>. During the 2018/19 flu season, this programme will be extended. Influenza vaccine will continue to be offered to children in at risk groups but the upper age for the routine childhood programme will be extended so that flu vaccine will also be offered to all children who are aged two to nine years of age (but not ten years or older) on 31 August 2018. These children will be offered Live Attenuated Influenza Vaccine (LAIV) unless contraindicated.

Further details of the influenza vaccination programme for children can be found at <https://www.gov.uk/government/collections/annual-flu-programme#2018-to-2019-flu-season>.

The requirements of the influenza vaccination programme are set out in the following key documents:

1. the [Enhanced service specification for the influenza and pneumococcal vaccination programmes 2018/19](#)<sup>1</sup> describes the services to be provided by GP practices delivering the programme in England.
2. the [Annual flu letter 2018 / 19](#)<sup>2</sup> provides detailed information to support the successful implementation of the programme
3. the Green Book [Influenza chapter](#)<sup>3</sup> provides information on influenza disease, epidemiology, the vaccines and the vaccination programme

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<sup>1</sup> NHS England. Directed Enhanced Service Specification - Seasonal influenza and pneumococcal polysaccharide vaccination programme 2018/19. Available at: <http://www.nhsemployers.org/your-workforce/primary-care-contacts/general-medical-services/vaccination-and-immunisation/2018-19-vaccination-and-immunisations>

<sup>2</sup> Department of Health, Public Health England, NHS England The national flu immunisation programme 2018/19. 26 March 2018. Available at: <https://www.gov.uk/government/publications/national-flu-immunisation-programme-plan>

<sup>3</sup> Public Health England. Immunisation against infectious disease. Influenza chapter 19. Available at: <https://www.gov.uk/government/publications/influenza-the-green-book-chapter-19>

The national influenza immunisation programme:  
inactivated influenza vaccine - Information for healthcare practitioners

Additional resources to support the implementation of the programme include template letters, leaflets, posters, a training slide set and an e-learning programme, all of which can be found on the [Annual flu programme](#) page of the GOV.UK website.

Any updates to the flu programme are also published in the monthly PHE publication [Vaccine Update](#).

The information in this document focuses on the inactivated influenza vaccine. A separate document containing information for healthcare practitioners on the [national childhood flu immunisation programme \(LAIV\)](#) is also available.

## Influenza

Influenza is a highly infectious, acute viral respiratory tract infection which has a usual incubation period of one to three days. Patients can experience sudden onset of symptoms such as dry cough, headache, fever and extreme fatigue.

There are three types of influenza virus which affect humans: types A, B and C. Types A and B are responsible for most disease. Influenza is spread by droplets, aerosol or through direct contact with the respiratory secretions of someone with the infection. For otherwise healthy individuals, it is usually a mild self-limiting disease with recovery occurring within two to seven days.

Further information on influenza infection is included in the Green Book [Influenza chapter](#) and on [NHS Choices](#).

## Influenza vaccination programme

The purpose of the influenza vaccination programme is to protect those most at risk of developing severe disease or complications or from dying if they develop the infection.

Individuals not eligible for vaccination, for example, infants under the age of six months, will benefit from passive protection if their mother received the vaccine during pregnancy.

Vaccination of eligible individuals should commence as soon as stock of the recommended vaccine is available and ideally be completed by the end of November. However, eligible patients can be offered influenza vaccine at any point in the flu season and the [enhanced service specification for flu](#) includes payment for vaccines given up until 31 March 2019.

## Risk groups and influenza vaccine eligibility

Influenza can affect anyone although those aged over 65 years, those with underlying health conditions, pregnant women and children under six months of age have a higher risk of developing severe disease or complications such as bronchitis or secondary bacterial pneumonia, or otitis media in children.

During 2018/19, patients aged six months to less than 65 years of age with the following underlying health conditions are eligible to receive influenza vaccine:

- chronic (long-term) respiratory disease, such as severe asthma, chronic obstructive pulmonary disease (COPD) or bronchitis
- chronic heart disease, such as heart failure
- chronic kidney disease at stage three, four or five
- chronic liver disease
- chronic neurological disease, such as Parkinson's disease or motor neurone disease, or learning disability
- diabetes
- splenic dysfunction or asplenia
- a weakened immune system due to disease (such as HIV/AIDS) or treatment (such as cancer treatment)
- morbidly obese (defined as BMI of 40 and above)

All pregnant women, including those who become pregnant during the delivery of the influenza programme, are eligible to receive influenza vaccine at any stage of pregnancy. Influenza infection during pregnancy may be associated with perinatal mortality, prematurity, lower birth weight and smaller neonatal size.

Further details of those eligible to receive the vaccine can be found in [Chapter 19 of the Green Book](#)<sup>3</sup> and in the [Annual flu letter for 2018/19](#)<sup>2</sup>.

# Inactivated influenza vaccines recommendations

In previous years, the majority of the inactivated vaccines available in the UK have been trivalent vaccines, containing two subtypes of Influenza A virus strains and one Influenza B virus strain.

In 2017, the Joint Committee on Vaccination and Immunisation (JCVI) considered both vaccine efficacy and cost effectiveness of influenza vaccines<sup>4</sup> and recommended:

- the optimal choice of vaccine for those aged 65 years and over would be the adjuvanted trivalent influenza vaccine (aTIV)
- a quadrivalent influenza vaccine (QIV) would offer a public health benefit and potential reduction in terms of influenza-related GP consultations and hospitalisations for those aged 18 to under 65 years and in an at risk group

Children aged from 2 years to less than 18 years are recommended to have a live attenuated quadrivalent influenza vaccine (LAIV) unless contraindicated. Further information on this programme can be found on the [PHE national flu immunisation programme page](#).

As LAIV is not licenced for use in those aged 6 months to two years, eligible at risk children are recommended to receive an age appropriate inactivated quadrivalent influenza vaccine (injected).

## Quadrivalent influenza vaccines

Quadrivalent influenza vaccines (QIV) contain two influenza A strains and the two main influenza B strains. By including both B strains, they should provide better protection in seasons when the circulating influenza B strain is not well matched to the single B strain contained in the previously used trivalent vaccines (TIV).

As influenza B is relatively more common in children than older age groups, the main clinical advantage of quadrivalent vaccines is in childhood. The use of the quadrivalent LAIV in children should not only protect the age group where flu infection is most common but also by preventing transmission from children to others, it also reduces circulation of influenza B across the whole population and thus indirectly protect them.

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<sup>4</sup> Joint Committee on Vaccination and Immunisation. Minutes from meeting 4 October 2017. Available at: <https://app.box.com/s/iddfb4ppwkmjtjusir2tc/file/247634612957>

However, modelling suggests that, even once the programme in children of primary school age is fully established, there is still benefit from using QIV in at risk adults under 65 years of age, including pregnant women. Healthcare workers are also likely to benefit from protection against the additional B strain.

## Adjuvanted influenza vaccines

In response to increasing evidence of the limited effectiveness of non-adjuvanted, standard-dose egg-based influenza vaccines in older people, some pharmaceutical companies have developed vaccines that lead to a better immune response in this group. An adjuvanted trivalent inactivated influenza vaccine (aTIV), Fludac<sup>®</sup>, is now licensed (2017) for use in those aged 65 years and older in the UK. The aTIV has been licensed in some countries in Europe since 1997 and in the USA since 2015. It has been used for 20 years, is now used in over 20 countries and over 93 million doses have been distributed. Published data indicates that the adjuvanted vaccine has higher immunogenicity and effectiveness than non-adjuvanted vaccines in the elderly. Modelling indicates that the adjuvanted vaccine would be highly cost-effective in both the 65-74 and 75 year and over age groups with large reductions in GP consultations and hospitalisations.

Adjuvanted vaccines are vaccines which have had a very small amount of a substance (for example, an aluminium salt) added to them to help create a stronger immune response to that vaccine. See section on 'Influenza vaccine components' below for more information.

## Adjuvanted influenza vaccines recommended for elderly patients, rather than quadrivalent unadjuvanted standard dose vaccines

At the present time, there are no adjuvanted quadrivalent vaccines licensed in the UK. Based on the existing evidence, JCVI have said that the best vaccine currently available for the over 65s is the recently licensed adjuvanted vaccine, even though it is trivalent. Although quadrivalent vaccine offers the potential to provide broader direct protection against influenza B, this strain is relatively less common in the elderly than in children and young adults. The successful childhood programme which uses quadrivalent LAIV is likely to offer indirect protection by reducing transmission of the additional B strain contained in the quadrivalent vaccine.



More information about recommendations for quadrivalent and adjuvanted trivalent vaccines is available on the PHE webpage [Summary of data to support the choice of influenza vaccination for adults in primary care](#)<sup>5</sup>.

## Exceptional use of QIV and non-adjuvanted TIV outside of national recommendations for the 2018/19 influenza season

The recommended vaccine in those aged 65 years and over is aTIV. QIV should not be offered to those aged 65 years and over, other than in exceptional circumstances. In the event that aTIV is not available, and is highly unlikely to become available, QIV may be offered as a second line option. Before offering the second line option, however, individuals should be sign-posted to other providers to access the recommended vaccine, as appropriate.

Non-adjuvanted trivalent influenza vaccine (TIV) is not one of the recommended vaccines for 2018/19. For those aged under 65 years, if QIV is not available, and is highly unlikely to become available, TIV may be offered as a second line option. For those aged 65 years and over, if neither QIV nor aTIV are available, and are highly unlikely to become available, TIV may administered in exceptional circumstances. In both situations, individuals should be sign-posted to other providers to access the recommended vaccine, as appropriate.

**If offering QIV to individuals not recommended to have it, or if offering non-adjuvanted TIV to any individual, when gaining consent for immunisation, practitioners should ensure they inform the individual the vaccine is not one nationally recommended for them. Healthcare practitioners should ensure they explain to the individual the possible lower efficacy of the vaccine being offered to them, why it is being offered instead of the recommended vaccine and why it may still offer protection against seasonal flu, or attenuate the progression of the infection should they get it. The discussion should be documented in the individuals records.**

Further information on consent to immunisation is available here:

<https://www.gov.uk/government/publications/consent-the-green-book-chapter-2>

## Flu vaccination for healthcare workers aged 65 years old and over

In the health care setting, where it is easier to procure only one vaccine and where most recipients are aged under 65 years, it is acceptable to offer QIV to the small number of staff aged over 65 years, to ensure high coverage and to offer protection against a

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<sup>5</sup> Public Health England. Summary of data to support the choice of influenza vaccination for adults in primary care. 29 January 2018. Available at: <https://www.gov.uk/government/publications/flu-vaccination-supporting-data-for-adult-vaccines/summary-of-data-to-support-the-choice-of-influenza-vaccination-for-adults-in-primary-care#adjuvanted-influenza-vaccines>

broader range of strains. The rationale is that most health care workers are likely to be under 75 years of age and relatively healthy, and therefore will probably also derive individual benefit from the QIV. Given the nature of the setting in which vaccines are being delivered, this decision would not need individual consent to offer the QIV instead of the adjuvanted trivalent vaccine (aTIV) but could be handled by general literature (posters/ leaflets/ website) available in the trust/practice. As this would then form part of a QIV programme, giving QIV to a small number of HCWs aged 65 years and over would also not constitute a medication error. Any general literature should also make clear that staff aged 65 years and over can get aTIV from their GP or a pharmacy and those with underlying medical conditions that make them less likely to respond to standard vaccines should be encouraged to go to their GP or pharmacy to get the aTIV instead.

### Flu vaccination for healthcare workers aged under 18 years old

In the health care setting, where it is easier to procure only one vaccine and where most recipients are aged 18 years and over, it is acceptable to offer QIV to the small number of staff under 18 years of age to ensure high coverage. Staff under 18 years of age in a clinical risk group, who are not contraindicated to receive the live attenuated influenza vaccine (LAIV), will need to be immunised in their GP surgery, otherwise they can be vaccinated with QIV in the hospital (or wherever the OH service is being offered). The effectiveness of LAIV and QIV for young people in this age group (i.e. 16 and 17 year olds) is likely to be equivalent. Given the nature of the setting in which vaccines are being delivered, this decision would not need individual consent to offer the QIV instead of LAIV but could be handled by general literature (posters/ leaflets/ website) available in the trust/practice. As this would then form part of a QIV programme, giving QIV to a small number of HCWs aged under 18 would also not constitute a medication error. Any general literature should also make clear that staff under 18 years with underlying medical conditions can get LAIV from their GP (provided they are not contraindicated to LAIV). TIV from Pfizer (Influenza Vaccine (split virion, inactivated))

Due to the risk of febrile convulsions, the indication for TIV from Pfizer (Influenza Vaccine (split virion, inactivated)) is restricted to use in adults and children aged five years and older. The SPC for TIV from Pfizer indicates that a high rate of fever was reported in the age group aged five to under nine years. This vaccine will not be part of the central supply for use in children in the 2018/19 season, but may be available for purchase. If no suitable alternative vaccines are available, clinicians should ensure parents are aware of the risk and give advice on the management of vaccine-induced fever.

## Vaccine ordering and supply

Given that some influenza vaccines are restricted for use in particular age groups, the Summary of Product Characteristics (SPCs) for individual products should always be referred to when ordering vaccines to ensure that they can be given appropriately to particular patients or patient age groups.

General Practices are responsible for ordering sufficient inactivated influenza vaccine for all eligible patients aged 18 years and over directly from the manufacturer. A list of vaccines available for the 2018/19 flu programme is contained in [2018/19 annual flu programme letter](#)<sup>2</sup>. More information about vaccine ordering is given in the [LMC Federation Update: Seasonal flu vaccines for 2018-19](#)<sup>6</sup> and the NHS England letter [Vaccine ordering for 2018-19 influenza season](#)<sup>7</sup>.

During the 2018/19 season, aTIV will be delivered to providers using a phased delivery system with orders expected to be delivered in a 40:20:40 ratio (Sept/Oct/Nov). Manufacturers will inform providers of their confirmed delivery allocation and dates in August 2018.

All influenza vaccines for children aged 6 months to less than 18 years are purchased centrally by Public Health England and should be ordered via [ImmForm](#). This includes LAIV and inactivated vaccines for children for whom the LAIV is medically contraindicated or otherwise unsuitable.

With the exception of flu vaccines for the children's programme which are centrally procured, the supply of influenza vaccine to community pharmacies and general practices is a private transaction between the individual provider and their vaccine supplier.

## Accessing additional stock

Additional vaccines should be ordered directly from any of the vaccine manufacturers. There will be no national reserve of vaccines to order from. Practices are advised to review their current orders with their suppliers and ensure they have ordered sufficient stock to vaccinate their eligible patient population.

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<sup>6</sup> LMC Buying Groups Federation. Update: Seasonal flu vaccines for 2018-19. Available at: <https://lmcbuyinggroups.co.uk/admin/resources/update-seasonal-flu-vaccines-2018-19.pdf>

<sup>7</sup> NHS England. Vaccine ordering for 2018-19 influenza season. 5 February 2018. Available at: <https://lmcbuyinggroups.co.uk/admin/resources/nhse-name-2.pdf>

## Prioritisation of vaccine stock

If limited aTIV stock is available (for example at the beginning of the flu vaccination season), those aged 75 years and over and those aged 65-74 years with an underlying clinical risk factor should be prioritised for vaccination. Once these groups have been covered, all other 65-74 year olds should then be targeted as further deliveries of aTIV vaccine are made.

# Vaccine storage and handling

## Storage of inactivated influenza vaccine

Inactivated influenza vaccines should be stored between 2°C and 8°C and should be stored in the original packaging to protect the vaccine from light. Vaccine should not be removed from the fridge until it is required for use.

## Vaccine storage incidents including cold chain issues

Should vaccines be inadvertently stored outside the recommended temperature range of 2°C to 8°C, the vaccine should be quarantined and risk assessed for suitability of continued off-label use or appropriate disposal. Refer to the [Vaccine incident guidance document](#)<sup>8</sup>. Further advice on vaccine stability or cold chain storage incidents should be obtained from your local screening and immunisation team (<https://www.england.nhs.uk/about/regional-area-teams/>).

# Influenza vaccine components

## Vaccine antigens

Each year, the World Health Organisation (WHO) monitors the epidemiology of influenza across the world and makes recommendations to vaccine manufacturers regarding the strains of influenza to include in the vaccine. For the 2018 /19 flu season (northern hemisphere winter), it is recommended that quadrivalent vaccines contain the following:

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<sup>8</sup> Health Protection Agency. Vaccine incident guidance. Responding to vaccine errors. March 2012. Available at: <https://www.gov.uk/government/publications/vaccine-incident-guidance-responding-to-vaccine-errors>

- an A/Michigan/45/2015 (H1N1)pdm09-like virus;
- an A/Singapore/INFIMH-16-0019/2016 (H3N2)-like virus;
- a B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage); and
- a B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage).

This vaccine composition differs from the 2017/18 vaccine composition as there has been a replacement of one of the influenza A strains and one of the influenza B strains. The influenza B component of the trivalent vaccines for use in the 2018/19 northern hemisphere influenza season will be a B/Colorado/06/2017-like virus of the B/Victoria/2/87-lineage<sup>9</sup>.

### Egg (ovalbumin) content

There is no ovalbumin-free vaccine available for the 2018/19 flu season. Inactivated influenza vaccines may contain traces of egg such as ovalbumin. A table stating the **ovalbumin content of the flu vaccines for the 2018/19 season** is available on the **PHE Annual flu programme** webpage.

With the exception of those individuals with a severe anaphylaxis to egg which has previously required intensive care, patients with less severe egg allergy can be immunised in any setting using an inactivated influenza vaccine with an ovalbumin content less than 0.12 micrograms/ml (equivalent to 0.06 micrograms in a 0.5 ml dose).

The aTIV vaccine, Fludax<sup>®</sup>, contains more than the recommended ovalbumin content for patients with egg allergy (each 0.5ml dose contains less than or equal to 0.2µg ovalbumin). Patients aged 65 years and over with an egg allergy should therefore be given a quadrivalent vaccine with an ovalbumin content less than 0.12 micrograms/ml (0.06 micrograms in a 0.5 ml dose).

### Patients with a previous anaphylactic reaction to egg

Patients with severe anaphylaxis to egg who have previously required intensive care should be referred to specialists for immunisation in hospital. If there is any uncertainty about the cause of an anaphylactic reaction, the patient should be advised to consult with an immunologist.

Further information about egg allergy and influenza vaccine can be found in the **Influenza chapter 19 of the Green Book**<sup>3</sup>.

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<sup>9</sup> World Health Organization. Recommended composition of influenza virus vaccines for use in the 2018-2019 northern hemisphere influenza season. 22 February 2018. Available at: [http://www.who.int/influenza/vaccines/virus/recommendations/2018\\_19\\_north/en/](http://www.who.int/influenza/vaccines/virus/recommendations/2018_19_north/en/)

## Vaccine adjuvant in aTIV

Vaccine adjuvants can reduce the amount of virus required for the production of a vaccine but they are primarily added to vaccines to enhance and lengthen the duration of the immune response.

This is particularly important for those aged 65 years and older as the aging immune system may result in a sub optimal response to influenza vaccine and there is evidence of limited effectiveness of standard trivalent vaccines in those aged 65 years and over<sup>5</sup>.

The aTIV vaccine (Fluad<sup>®</sup>) contains an adjuvant called MF59 which improves the immune system's response to vaccination and helps it to produce more antibodies against the influenza virus strains in the vaccine. MF59 is an oil-in-water emulsion of squalene oil, polysorbate 80, sorbitan trioleate, sodium citrate, citric acid and water for injections. Squalene is a naturally occurring substance that is found in humans, animals and plants<sup>10</sup>. In humans, it is made in the liver and circulates in the bloodstream<sup>11</sup>. Squalene is also found in a variety of foods, cosmetics, over-the-counter medications and health supplements. The squalene used in pharmaceutical products and vaccines is commercially extracted from fish oil and is then highly purified during the manufacturing process.

A single dose of Fluad<sup>®</sup> contains less than 10mg of squalene. To put this in context, over 1000mg of squalene is made in the liver every day, and humans ingest around 50mg to 200mg of squalene every day in a normal diet<sup>12</sup>.

Polysorbate 80, sorbitan trioleate and sodium citrate are emulsifiers which stop the squalene oil from separating out of the water in the vaccine. These, along with citric acid (also contained in the adjuvant) are all commonly used in foods and drinks.

## Latex

Fluad<sup>®</sup> will be supplied to the UK market predominantly as a pre-filled syringe with a syringe tip cap. The manufacturer's SPC states that no natural rubber latex is detected in the syringe tip cap. The unattached needles supplied along with the pre-filled syringes do not contain latex: the needle hub and needle sheath are both polypropylene.

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<sup>10</sup> Centers for Disease Control and Prevention. FLUAD™ Flu Vaccine With Adjuvant. Available at: <https://www.cdc.gov/flu/protect/vaccine/adjuvant.htm>

<sup>11</sup> World Health Organization. Squalene-based adjuvants in vaccines. Available at: [http://www.who.int/vaccine\\_safety/committee/topics/adjuvants/squalene/questions\\_and\\_answers/en/](http://www.who.int/vaccine_safety/committee/topics/adjuvants/squalene/questions_and_answers/en/)

<sup>12</sup> Personal communication from Seqirus. 8 June 2018

However, a small proportion of Flud<sup>®</sup> supplied in the UK will be presented with an attached needle. In this presentation alone, the needle sheath contains natural rubber latex. In theory, latex could be transferred from the needle sheath to the needle and then to the patient. However, as the latex-containing component (the needle sheath) is not in contact with the injection solution/suspension, the latex will not be leached from it. Furthermore, the needle sheath is made of Dry Natural Rubber (DNR) and there is considerable processing which removes latex during its manufacture. Contamination with latex proteins from this source are therefore deemed negligible by experts in the field.

As a precaution, the Flud<sup>®</sup> **pre-filled syringe with attached needle presentation** should not be used if an individual has a history of severe (i.e. anaphylactic) reaction to latex. However, Flud<sup>®</sup> presented as a **pre-filled syringe presentation with unattached needle(s)** is latex free and may be used for individuals with a latex allergy.

In accordance with **Chapter 6** of the Green Book, for latex allergies other than anaphylactic reactions (e.g. a history of contact allergy to latex gloves), vaccines supplied in vials or syringes that contain latex can be administered (i.e. either Flud<sup>®</sup> presentation may be used).

## Antibiotics

Inactivated flu vaccines may contain residues of antibiotics which are used during the vaccine manufacturing process. For example, Flud<sup>®</sup> may contain residues of the antibiotics kanamycin and neomycin sulphate so patients with a severe / anaphylactic kanamycin or neomycin sulphate allergy should be offered an alternative vaccine if available.

## Other additives

The inactivated flu vaccines do not contain thiomersal or gelatine.

There is a lot of useful information about what is in the inactivated flu vaccines and why available on the Vaccine Knowledge Project Inactivated Flu Vaccine webpage at:  
<http://vk.ovg.ox.ac.uk/inactivated-flu-vaccine>

## Vaccine dose

Inactivated influenza vaccines contain 0.5ml of vaccine. JCVI has previously advised that where alternative doses are given in the manufacturer's Summary of Product Characteristics (SPC), the 0.5ml dose of intramuscular inactivated influenza vaccine should be given to infants and young children aged six months and older.

Children under nine years of age who are in a clinical risk group and require inactivated influenza vaccine (due to the LAIV being contraindicated or unsuitable) but have never previously received influenza vaccine should be offered two doses of the vaccine with a four week interval between them.

Children who are in a clinical risk group and require inactivated influenza vaccine (due to the LAIV being contraindicated or unsuitable) but have received one or more doses of influenza vaccine in previous flu seasons should be considered as previously vaccinated and only require a single dose of vaccine.

All others eligible to receive the inactivated flu vaccine, including pregnant women and those aged 65 years and over should receive a single 0.5ml dose.

## Contraindications and precautions

The inactivated influenza vaccine is contraindicated for all patients who have had:

- an anaphylactic reaction to a previous dose of the vaccine
- an anaphylactic reaction to any of the vaccine components (other than ovalbumin – see section on egg allergy above)

For a full list of influenza vaccine components, please see the manufacturer's Summary of Product Characteristics (SPC) available on the [Electronic Medicines Compendium](#) website.

In addition, the SPC for individual products should be referred to when assessing the suitability of the vaccine for the patient (for example if they have egg or antibiotic allergy).



## Preparing the vaccine

Vaccines in prefilled syringes may contain an air bubble. This should not be expelled unless it is specifically stated to do so in the vaccine SPC. To try to expel it risks accidentally expelling some of the vaccine and therefore not giving the patient the full dose. Once injected, the air bubble forms an airlock preventing the vaccine seeping out along the needle track into subcutaneous tissue and onto the skin. The small bolus of air injected following administration of the vaccine clears the needle and prevents a localised reaction to the vaccination.

## Vaccine administration

Influenza vaccine should ideally be offered before influenza viruses start to circulate so the ideal time for immunisation is between September and end of November. However, as peak influenza activity generally occurs in January or February or sometimes later, providers should continue vaccinating patients throughout the influenza season, as long as they have unexpired vaccine in stock and unvaccinated patients in their practice. Providers should apply clinical judgement, taking into account the level of flu-like illness in their community and the fact that the immune response following flu vaccination takes about two weeks to develop fully.

The inactivated influenza vaccine should be administered as an intramuscular injection. For infants aged six months to one year, the anterolateral aspect of the thigh should be used. For those aged one year and over, the deltoid muscle in the upper arm is the preferred muscle.

Due to the presence of the adjuvant (MF59), Flud@ **should be administered intramuscularly using a 25mm needle** to enable the vaccine to be delivered into the muscle. Flud@ is being supplied with an orange hub 25mm needle. Immunisers should not confuse this needle with the shorter orange (16mm) needle used to give subcutaneous injections.

### Vaccination of patients taking anticoagulants or with a bleeding disorder

There is a lack of evidence that the subcutaneous route of vaccination is any safer than the intramuscular route in people taking anticoagulants. The subcutaneous route can itself be associated with an increase in localised reactions.

Individuals on stable anticoagulation therapy, including individuals on warfarin who are up-to-date with their scheduled INR testing and whose latest INR was below the upper

threshold of their therapeutic range, can receive intramuscular vaccination. A fine needle (equal to 23 gauge or finer calibre) should be used for the vaccination, followed by firm pressure applied to the site (without rubbing) for at least 2 minutes. If in any doubt, consult with the clinician responsible for prescribing or monitoring the individual's anticoagulant therapy.

Individuals with bleeding disorders may be vaccinated intramuscularly if, in the opinion of a doctor familiar with the individual's bleeding risk, vaccines or similar small volume intramuscular injections can be administered with reasonable safety by this route. If the individual receives medication/treatment to reduce bleeding, for example treatment for haemophilia, intramuscular vaccination can be scheduled shortly after such medication/treatment is administered. A fine needle (equal to 23 gauge or finer calibre) should be used for the vaccination, followed by firm pressure applied to the site (without rubbing) for at least 2 minutes<sup>13</sup>. The individual/parent/carer should be informed about the risk of haematoma from the injection.

The needle provided with the aTIV Fluad<sup>®</sup> vaccine is 25G (gauge) and is therefore suitable for use for patients taking anticoagulants or with a bleeding disorder.

Influenza vaccines licensed for intramuscular or subcutaneous administration may alternatively be administered by the subcutaneous route. **Fluarix<sup>®</sup> Tetra and Fluad<sup>®</sup> are not licensed for subcutaneous administration so should only be administered intramuscularly.** If these vaccines are given subcutaneously in error however, they do not need to be repeated but the vaccinated individual should be warned of the increased risk of local reactions at the injection site.

### Reactions following administration of inactivated flu vaccine

In clinical trials, the incidence of both mild local and systemic reactions following immunisation with aTIV (Fluad<sup>®</sup>) was found to be higher than the incidence of reactions following unadjuvanted TIV vaccines<sup>14</sup>. Commonly reported reactions following administration of inactivated flu vaccine include: malaise, low grade fever, headache, fatigue, myalgia, arthralgia and redness, swelling and pain at the injection site.

The frequency of injection site pain and systemic reactions may be higher in individuals vaccinated concomitantly with inactivated flu vaccine and pneumococcal polysaccharide vaccine (PPV23) compared to vaccination with influenza vaccine alone and similar to

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<sup>13</sup> Centers for Disease Control and Prevention. Vaccine recommendations and guidelines of the ACIP. Vaccinating Persons with Increased Bleeding Risk. Available at: <https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/special-situations.html>

<sup>14</sup> Fluad. Summary of Product Characteristics. Date of last revision of text: 12/2017. Available at: <https://www.medicines.org.uk/emc/product/9223/smpc>

that observed with PPV23 vaccination alone. However, if indicated, flu vaccine and PPV23 can be administered at the same visit in different limbs.

### Reporting of adverse reactions

Healthcare professionals and patients/parents/carers are encouraged to report suspected adverse reactions to the Medicines and Healthcare products Regulatory Agency (MHRA) using the Yellow Card reporting scheme on:

<http://yellowcard.mhra.gov.uk>

The QIVs are black triangle ▼ (including GSK's Fluarix® Tetra and MASTA, Mylan (BGP Products) and Sanofi Pasteur supplied QIV). Therefore, any suspected adverse reactions should be reported via the **Yellow Card Scheme**.

Any adverse reaction to a vaccine should be documented in the individual's record and the individual's GP should be informed.

### Patients who have already received an influenza vaccine during early 2018

If the patient received the vaccine produced for the 2017/18 season then they will still need a dose of the vaccine produced for the 2018/19 season as it contains different viruses to protect against other influenza strains.

In addition, the protection gained from flu vaccine is only thought to last for one season so those eligible to receive the vaccine are recommended to have it every year to ensure on-going protection.

### Individuals who have inadvertently been given a flu vaccine that is not the one recommended for their age group

If an individual has inadvertently received a flu vaccine different to the one recommended for their age group, they should be informed of the error and the potential implications of this error. Although both the QIV and aTIV should provide some protection against flu in all age groups, individuals aged 65 years and over (particularly those more than 75 years of age) may not respond as well to the QIV as they would to the aTIV, and individuals aged under 65 years will not benefit from the opportunity to make protection against an additional flu strain if they have been given aTIV.

If the individual wishes to receive the vaccine that they should have been given, this can be offered following a discussion of the benefits and risks. The clear benefit is the additional protection that may be offered by the correct vaccine but they should be alerted to the potential increased risk of a local or systemic reaction. Although there is

no data available on the safety and effectiveness of administering a second flu vaccine shortly after the first in adults, this advice is based on general principles of vaccination, experience of flu revaccination following cold chain and administration incidents and information about the high dose flu vaccine used in the United States (which contains four times the amount of antigen that is in a single dose of QIV or aTIV).

If a decision is made to offer the vaccine the individual should have received, it is recommended that this is done as soon as possible after the first dose was given and ideally within a week. This will enable protection to be made as soon as possible. It can still be given if more than a week has elapsed however.

This advice also applies to those who have been given unadjuvanted TIV.

### Patients under 65 years of age at time of vaccination but who will be 65 years old by 31<sup>st</sup> March 2019

Although it is stated in the **SPC** that Fluad<sup>®</sup> (aTIV) is indicated for patients aged 65 years and over, patients who will become 65 years of age by 31<sup>st</sup> March 2019 but who are 64 years at the time of vaccination can receive aTIV off-label in accordance with the recommendations for the national influenza immunisation programme for 2018/19<sup>2</sup>. This off label use of aTIV is covered in the **national template PGD for inactivated influenza vaccine**.

### Uncertainty regarding previously administered dose of influenza vaccine

If there is no documented evidence of an eligible patient having a flu vaccine during the current flu season then they should be offered a dose. If they have already had one this flu season, an additional dose is unlikely to cause any harm. Any adverse reactions to an extra dose are likely to be similar to those commonly seen after a first dose of flu vaccine such as local redness/pain at the injection site, malaise etc.

### Inadvertent administration of a second dose of influenza vaccine

Any adverse reactions to an extra dose are likely to be similar to those commonly seen after a scheduled first dose of flu vaccine such as local redness/pain at the injection site, malaise etc. The patient should be offered reassurance and local systems reviewed to prevent this happening again. Patients under the age of nine years who have never received influenza vaccine in previous years are specifically recommended to have two doses four weeks apart.

## Incomplete dose of vaccine given

If you do not think the patient received a full dose of vaccine (i.e. because some spilt out whilst administering the vaccine), it is recommended that the dose is repeated. This can be at any interval from the partial dose already given. Giving it the same day or within the next few days will enable protection to be made as soon as possible but the patient should be informed there may be a potential risk of local and systemic reactions from a repeat dose.

## Vaccination of patients recently diagnosed with influenza infection

Individuals eligible to receive the influenza vaccine should have it even if they have recently had confirmed influenza infection. Having the vaccine will help to protect against other circulating strains. Both the inactivated flu vaccine and the LAIV can be given at any time following recovery providing there are no contraindications to vaccination and the patient is not acutely unwell.

## Administering inactivated influenza vaccine at the same time as other vaccines or immunoglobulins

The inactivated influenza vaccine can be given at the same time as, or at any interval before or after, any immunoglobulin or other vaccine (whether live or inactivated). The vaccines should be given at separate sites, preferably in different limbs but if given in the same limb, they should be given at least 2.5cm apart and the site of each should be recorded in the patient's record. Because of the increased risk of local reaction following aTIV, Fluvad<sup>®</sup> should be administered in a separate limb to any other vaccines that need to be given at the same time.

## Inadvertent administration of expired doses of vaccine

As new flu vaccine stock is purchased each year, it is unlikely that a patient will receive a dose that has expired. However in the event that this occurs, an additional dose with a valid expiry date should be offered. Giving an additional dose will ensure that the individual benefits from vaccination. This can be given at any interval from the previous expired dose.

# Pregnancy

All pregnant women should be offered an inactivated quadrivalent influenza vaccine whilst pregnant, regardless of their stage of pregnancy. Studies have demonstrated that pregnant women can safely receive influenza vaccine during pregnancy and that infants

also receive some protection from maternal antibodies as a result of their mother having the vaccination whilst pregnant.

Pregnant women can access influenza vaccine from their GP or pharmacy. Additionally, around 70% of maternity service providers will be offering influenza vaccine to pregnant women during the 2018/19 season.

### Vaccination of women who become pregnant late in the flu season

Women who become pregnant during the flu season should be offered influenza vaccine as soon as possible. The timing of the flu season varies each year but usually commences later in December or in the New Year, followed by two to three months of flu transmission. Although the vaccine takes around two weeks to work, pregnant women and their unborn babies are at higher risk of influenza associated morbidity and mortality and should still benefit from vaccination throughout the season.

### Administering influenza vaccine at the same time as whooping cough (pertussis) containing vaccine and/or anti-D immunoglobulin

The injected flu vaccine and whooping cough (pertussis) containing vaccine are both inactivated vaccines so can be given on the same day or with any interval between them. Pregnant women should be offered the flu vaccine as soon as the vaccine becomes available, regardless of the stage of pregnancy. Influenza vaccine, whooping cough vaccine and anti-D immunoglobulin can all safely be given at the same time or with any interval between them.

### Interval between influenza and pertussis containing vaccines for pregnant women

Influenza vaccine should not be deferred in order to give it at the same appointment as pertussis containing vaccine for pregnant women.

Pertussis containing vaccine is recommended for all pregnant women from 16 weeks of pregnancy but is generally offered at around 20 weeks. It is **not** recommended that pregnant women wait until they reach 20 weeks of pregnancy before having their flu vaccine as this would leave them and their unborn baby at risk of potentially severe illness if they develop influenza. Influenza and pertussis containing vaccines can be administered at the same time or with any interval between them and both should be given at the recommended stage of pregnancy (from 16 weeks for pertussis containing vaccine and at any stage of pregnancy for influenza vaccine).

## Administering influenza vaccine to breastfeeding women

Flu vaccine can be given to breast-feeding women including those who may also be pregnant or in an at risk group. However breast-feeding is not a clinical indication for influenza vaccination.

# Medical conditions

## Immunosuppression

The inactivated influenza vaccine can be safely given to immunosuppressed individuals though they may have a sub optimal response to the vaccine.

Individuals may be immunosuppressed because of a medical condition or because of medical therapy that they are taking. As these patients are at risk of increased morbidity and mortality if they develop influenza, they should be offered the vaccine as soon as stock is available. Immunosuppression may continue for a number of months following completion of treatment. If there is any uncertainty regarding an individual's level of immunosuppression, further advice should be taken from their consultant.

## Patients taking steroid medication

Patients taking steroids can be safely vaccinated with inactivated flu vaccine. As systemic steroids at a dose equivalent to prednisolone 20mg or more per day are considered to be immunosuppressive, patients taking steroids are at risk of serious illness if they develop flu and so should be vaccinated. Patients who are receiving high-dose steroids may be immunosuppressed for at least 3 months after cessation of treatment.

## Patients having chemotherapy

Patients receiving chemotherapy should receive their flu vaccine at the earliest opportunity. For individuals due to commence immunosuppressive treatments, inactivated vaccines should ideally be administered at least two weeks before commencement. In some cases this will not be possible and therefore vaccination may be carried out at any time.

Further advice regarding vaccination of immunosuppressed individuals can be found in **Chapter 7 of the Green Book**

### Patients previously eligible for influenza vaccine but who are no longer in a risk group

Some patients may have had the vaccine during previous flu seasons whilst in an at risk group but may no longer be in that group. Examples could include women who were pregnant during the last flu season but are not pregnant during this flu season or patients who were taking regular inhaled steroids during last flu season but are no longer taking them.

Providing that these patients are not in any other risk group described in the Green Book or annual flu letter, they would not be eligible for flu vaccination this year. However, the Green Book states that clinicians should exercise professional judgement when assessing a patient and can recommend vaccination for individuals, even if they are not in a listed risk group, if influenza is likely to exacerbate their underlying condition.

### Patients with neurological conditions

The presence of a neurological condition is not a contraindication to immunisation but if there is evidence of current neurological deterioration, deferral of vaccination may be considered to avoid incorrect attribution of any change in the underlying condition. The risk of deferring the vaccine should be balanced against the risk of flu and vaccination should be promptly given once the diagnosis and/or the expected course of the condition becomes clear.

This precaution does not apply to individuals with a chronic neurological condition who should be offered vaccine once vaccine stock becomes available.

### Patients who are generally unwell when presenting for vaccination

Vaccination may be postponed in those who are acutely unwell until they have fully recovered. This is to avoid confusing the differential diagnosis of any acute illness by wrongly attributing any signs or symptoms to the adverse effects of the vaccine.

### Guillain-Barré Syndrome (GBS) and influenza vaccine

Previous GBS is not a contraindication to influenza vaccination. A UK study found that there was no association between GBS and influenza vaccines although there was a



strong association between GBS and influenza-like illness. A causal relationship between immunisation with influenza vaccine and GBS has not been established<sup>15</sup>.

### Patients requesting live intranasal influenza vaccine (LAIV) instead of the inactivated injected one due to needle phobia

Patients for whom the inactivated injected vaccine is recommended should be encouraged, where possible, to have the inactivated injected vaccine.

LAIV is not licensed in adults because there is some evidence of poorer efficacy when compared with the inactivated vaccine.

However, individual medical practitioners may choose to use LAIV 'off-label' for adults, without any other medical contra-indication, who are eligible for influenza vaccination but who cannot be vaccinated with injectable vaccines. This could include patients with learning difficulties who become seriously distressed with needles.

The legislation does allow for such situations and the Medicines and Healthcare products Regulatory Agency state that 'there are clinical situations when the use of medicines outside the terms of the licence (ie, 'off-label') may be judged by the prescriber to be in the best interest of the patient on the basis of available evidence'<sup>16</sup>. The responsibility for such use rests with the health professional. In this situation, a patient specific direction (PSD) will be required. In these exceptional circumstances, where it has not proved possible to administer the inactivated vaccine, PHE has agreed that the national LAIV stock can be used for this purpose.

In previous years, an intradermal inactivated influenza vaccine (Intanza) has been available for those aged 60 years and over. Manufacturers have confirmed that this vaccine will not be available for the current season.

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<sup>15</sup> Stowe J, Andrews N, et al. Investigation of the temporal association of Guillain-Barre syndrome with influenza vaccine and influenza like illness using the United Kingdom General Practice Research Database. Am J Epidemiol. 2009 Feb 1;169(3):382-8. Abstract at: <https://www.ncbi.nlm.nih.gov/pubmed/19033158>

<sup>16</sup> Medicines and Healthcare products Regulatory Agency. Off-label or unlicensed use of medicines: prescribers' responsibilities. Available on Gov.uk website at: <https://www.gov.uk/drug-safety-update/off-label-or-unlicensed-use-of-medicines-prescribers-responsibilities>

## Useful links

### **Letter detailing 2018/19 flu programme**

Department of Health, Public Health England, NHS England. The national flu immunisation programme 2018/19. Published 26 March 2018. Available at:

<https://www.gov.uk/government/publications/national-flu-immunisation-programme-plan>

**Immunisation against infectious disease (the Green Book) Influenza chapter 19.** Available at: <http://www.gov.uk/government/publications/influenza-the-green-book-chapter-19>

**Leaflets, posters, training slides and other resources to support the annual flu programme.** Available at: <https://www.gov.uk/government/collections/annual-flu-programme>

To order hard copies of printed leaflets and posters free of charge, go to

[https://www.orderline.dh.gov.uk/ecom\\_dh/public/contact.jsf](https://www.orderline.dh.gov.uk/ecom_dh/public/contact.jsf)

Telephone number: 0300 123 1003

**Summary of Product Characteristics (SPC) for flu vaccines** are available at

<http://www.medicines.org.uk/emc/>

### **PGD templates for flu vaccines**

<https://www.gov.uk/government/collections/immunisation-patient-group-direction-pgd>

**Links to other key documents relating to the flu vaccine programme** are available on page 5 of the **national flu immunisation programme 2018/19** letter available at

[https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/694779/Annual\\_national\\_flu\\_programme\\_2018-2019.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/694779/Annual_national_flu_programme_2018-2019.pdf)

**Vaccine Knowledge Project. Inactivated Flu Vaccine.** Available at:

<http://vk.ovg.ox.ac.uk/inactivated-flu-vaccine>