# COVID-19 Vaccine AstraZeneca

INFORMATION FOR HEALTHCARE PROFESSIONALS

Disclaimer: This Product Is Approved Under Malaysia Conditional Registration For Pharmaceutical Products During Disaster Guideline. The Administration Of The Product Is Purely Based On Individual's Preference.

# About this guide

- This guide is for healthcare professionals.
- It covers information about COVID-19 Vaccine AstraZeneca that is most important for you, as defined by qualitative research with doctors, pharmacists and nurses.
- It does not cover other vaccines, COVID-19 treatments or the disease.
- This should be used in conjunction with Malaysian Prescribing Information.
- It does not include national or local guidelines.

There is a separate guide written for doctors and healthcare professionals.

The public guide should be used in conjunction with **Patient Information Leaflet (RiMUP).**

Version 2.0. Updated on 20 January 2021.

## How to use this guide

- Click on the tabs (above) or the links in Contents to navigate to each section of this guide
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# Contents



## How to use this guide

- Click on the **tabs** (above) or the links in **Contents** to navigate to each section of this guide
- Click on **underlined links** to go to content

# Checklist

## Before vaccination

- ☐ Indicated for active immunisation of individuals **18 years or older** for the prevention of COVID-19.
- ☐ **Consult local guidelines** on who is included in local vaccination programs.
- ☐ **Consider the benefits and potential risks** of vaccination for each in dividual, including:
  - ☐ review of Contraindications and Precautions
  - ☐ review of Risks and benefits.

As with all vaccines, ensure appropriate medical treatment and supervision is readily available in case of anaphylaxis following administration of the vaccine.

## At the time of vaccination

- ☐ **Educate the recipient on key points** relevant to vaccination including:
  - ☐ risks and benefits
  - ☐ to expect flu-like symptoms
  - ☐ that the vaccine cannot cause COVID-19
  - ☐ use of paracetamol
- ☐ Inspect the vaccine for particulate matter or discolouration prior to administration.
- ☐ Administer 0.5 ml (1 dose) injection **intramuscularly**, preferably in the deltoid muscle.

## After vaccination

- ☐ Advise the recipient:
  - ☐ to return for their next vaccination in 4 to 12 weeks
  - ☐ that information is available in the Prescribing Information and Patient Information Leaflet (RiMUP)
  - ☐ to contact a healthcare professional if they have any concerns about side effects
  - ☐ to retain a record of vaccine name and batch/lot number.
- ☐ Observe the vaccine recipient for at least 15 minutes for possible anaphylaxis.
- ☐ Retain appropriate vaccination records, including vaccine name and batch/lot number.

# What the vaccine is

## About this vaccine

COVID-19 Vaccine AstraZeneca is a replication-deficient chimpanzee adenovirus-vectored vaccine (**ChAdOx1 - C**himpanzee **Ad**enovirus **Ox**ford **1)** which expresses the gene for the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) spike protein.

This vaccine stimulates neutralizing antibody and cellular immune responses, to protect against COVID-19.

**Is it a live attenuated vaccine?**
This vaccine is not a live attenuated vaccine and does not contain live coronavirus. The replication-deficient adenovirus utilised in this vaccine cannot multiply or spread throughout the body.

## How the vaccine works

After administration, the modified adenovirus (viral vector) binds to the surface of human cells and delivers the genetic code for the coronavirus spike protein, where it is processed to form the spike protein itself.

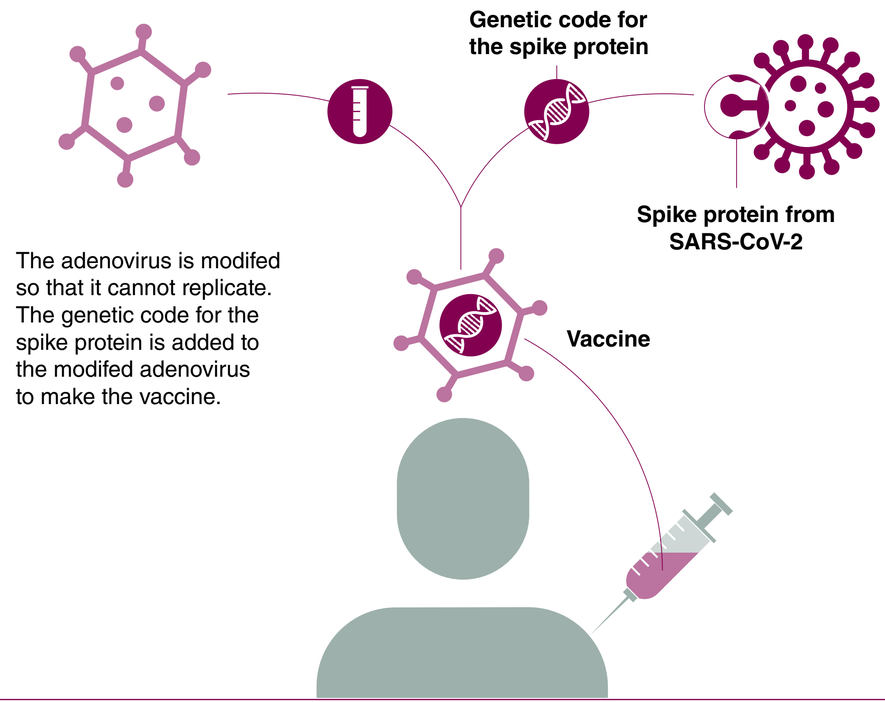
Antibodies and immune cells (T-cells) in the circulation recognise the spike protein which instigates the neutralising antibody and cellular immune responses.

The immune system subsequently forms an immune memory of the coronavirus spike protein, which facilitates quick recognition and rapid immune response in the case of future SARS-CoV-2 coronavirus exposure.

**Click to see more details on:**


- ▸ *Vaccine ingredients*
- ▸ *Genetically modified organisms (GMOs)*
- ▸ *Risks and benefits*


## How the vaccine is made

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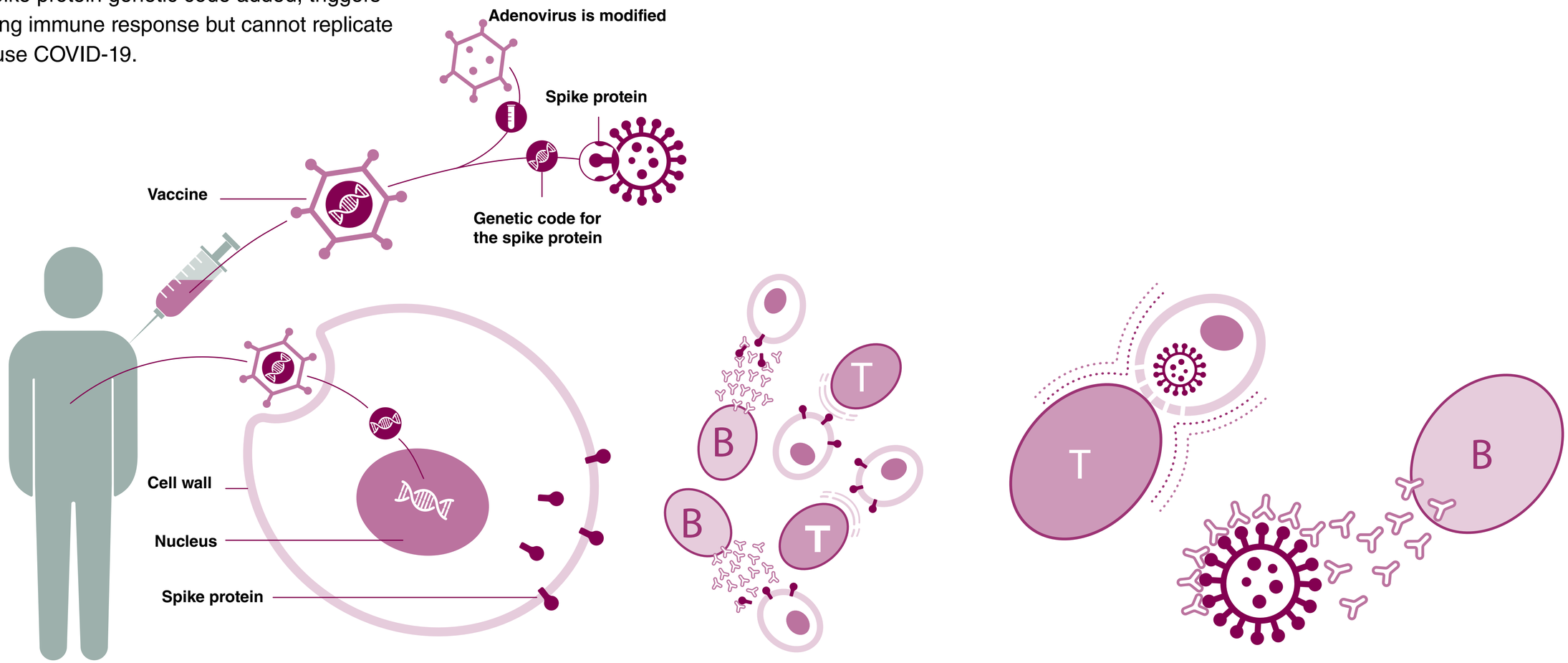
## How this vaccine works

A non-human modifed adenovirus vector, with the spike protein genetic code added, triggers a strong immune response but cannot replicate or cause COVID-19.




The viral vector enters the body's cells and delivers the genetic code for the spike protein. The human cells then produce the spike protein but there are no changes to the human DNA.

T-cells and B-cells recognise the spike protein and multiply. B-cells start releasing antibodies.

The immune system also produces memory cells. If they spot SARS-CoV-2 in the future, antibodies and T-cells are rapidly produced in response.

T-cells destroy cells infected with the virus. Antibodies bind to the spike proteins, blocking the ability for viruses to enter cells. Together they can prevent disease.

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# More details on what the vaccine is

## Vaccine ingredients

As in all vaccines, COVID-19 Vaccine AstraZeneca consists of an active ingredient plus inactive ingredients which facilitate administration by injection. These inactive ingredients also stabilize the product. The vaccine does not contain any preservatives.

The **active ingredient** is the modified adenovirus (ChAdOx1) containing spike protein genetic code. It is a genetically modified organism (GMO).

The **inactive ingredients** are L-Histidine (an amino acid); L-Histidine hydrochloride monohydrate (an amino acid); magnesium chloride hexahydrate (supports many activities inside cells); polysorbate 80 (a stabiliser); ethanol (alcohol); sucrose (sugar); sodium chloride (salt); disodium edetate dihydrate (EDTA, a binding agent); water for injection.
**Latex:** There is no latex in the vial or stopper.

## Origin of ingredients

- This vaccine does not contain milk, lactose, soya, egg, maize/corn starch, peanuts, gluten.
- None of the ingredients are of human or animal origin.
- The active ingredient, the modified adenovirus, is grown using cells that are of human origin, called human embryonic kidney cells (HEK293). None of these cells remain at the time the vaccine is administered.

## Ruling on vaccine uptake

The Special Muzakarah (discussion) of National Council for the Islamic Religious Affairs (MKI) had decided that the use of the COVID-19 vaccine is permissible (harus). The use of vaccines to protect mankind from dangerous diseases is unusual in Islam but has been in practice since 1988. Besides Malaysia, other world fatwa institutions have also decreed the need for vaccine use, among them are the leading institutions of al-Azhar al-Sharif; Fatwa Council of the United Arab Emirates Government; and Majma 'Fuqaha' al-Shari'ah United States (Source: Department of Islamic Development Malaysia)

## "Genetically modified organisms (GMOs)

COVID-19 Vaccine AstraZeneca contains a genetically modified adenovirus. Two genetic alterations have been made in order to make the vaccine.

- Genes essential for adenovirus replication have been deleted.
- The coronavirus (SARS-CoV-2) spike protein gene has been added.

The result is a genetically modified organism (GMO) with a new combination of genetic material. These changes to the adenovirus allow the vaccine to deliver the spike protein genetic code to the cells without causing COVID-19.

**Click to see more details on:**

▶ *Disposal*

# Before vaccination

## Indication

COVID-19 Vaccine AstraZeneca is indicated for active immunisation of individuals 18 years or older for the prevention of coronavirus disease 2019 (COVID-19).


Consult local guidelines on who is included in local vaccination programs.

## Contraindications

**Do not give** the vaccine to anyone with **hypersensitivity** to any of the vaccine ingredients.

See What **the vaccine is - vaccine ingredients**

As with all injectable vaccines, always be prepared in case of **anaphylaxis** following the administration of the vaccine.

## Precautions

### Children

- The safety and efficacy of COVID-19 Vaccine AstraZeneca in children and adolescents (aged <18 years old) have not yet been established. No data are available.

### Pregnancy

COVID-19 Vaccine AstraZeneca is not recommended during pregnancy. Do not give to a pregnant woman unless the potential benefit of vaccination outweighs the potential risks.

- There are limited data from the use of COVID-19 Vaccine AstraZeneca in pregnant women, or women who became pregnant after receiving the vaccine. The data are in sufficient to inform on vaccine-associated risk.
- Animal reproductive toxicity studies have not been completed.

### Breast-feeding

As a precaution, it is preferable to avoid vaccination with COVID-19 Vaccine AstraZeneca in women who are breast-feeding.

- There are no or limited data on the use of COVID-19 Vaccine AstraZeneca in lactating women.
- A risk to breast-fed newborns and infants cannot be excluded.

### Elderly

- No dosage adjustment is required in elderly individuals (65 years or older).

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# Before vaccination

## Precautions (continued)

### Medical history

- Use caution when vaccinating anyone with **thrombocytopenia**, **any coagulation disorder** and/or receiving **anticoagulation therapy**. This is because, as with other intramuscular injections, **bleeding or bruising** may occur following administration.
- It is not known whether recipients with impaired immune responsiveness will exhibit the same response as immunocompetent individuals.

### Neurological events

Very rare events of demyelinating disorders have been reported following vaccination with COVID-19 Vaccine AstraZeneca. A causal relationship has not been established.

### Concurrent illness

- Postpone administration of COVID-19 Vaccine AstraZeneca in individuals suffering from an acute severe febrile illness (objective measure of ≥38° [100.4°F]).
- Vaccination should not be delayed because of a minor infection, such as a cold and/or low-grade fever.

See other *Precautions* on page 8.

**Important!** Consider the potential *risks and benefits* of vaccination with COVID-19 Vaccine AstraZeneca for each individual.

**Click to see more details on:**


- *Fertility*
- *Administration with other vaccines*
- *Administration with other medicines*
- *Vaccine interchangeability*
- *Duration and level of protection*
- *Vaccination of individuals with previous COVID-19 infection*


*Continued*

# More details on before vaccination

## Fertility

It is unknown whether COVID-19 Vaccine AstraZeneca may impact fertility. No data are available.

## Administration with other vaccines

- The safety, efficacy and immunogenicity (strength of immune response) of co-administration of COVID-19 Vaccine AstraZeneca with other vaccines have not been evaluated.
- In the clinical trials, other vaccines were not permitted during the 30 days before or after administration of COVID-19 Vaccine AstraZeneca.
- Further studies are planned to evaluate use with other vaccines.

## Administration with other medicines

- Drug-drug interaction studies have not yet been conducted.
- Refer to *Precaution* for guidance on medical history.

## Vaccine interchangeability

- There are no safety, immunogenicity or efficacy data to support interchangeability of COVID-19 Vaccine AstraZeneca with other COVID-19 vaccines.

## Duration and level of protection

The duration of protection has not yet been established. As with any vaccine, vaccination with COVID-19 Vaccine AstraZeneca may not protect all vaccine recipients.

## Vaccination of individuals with previous COVID-19 infection

Subjects with previous COVID-19 infection can be vaccinated with COVID-19 Vaccine AstraZeneca.

# Before administration

- Consider the potential risks and benefits of vaccination with COVID-19 Vaccine AstraZeneca for each individual.
  See *Risks and benefits* and *Contraindications* and *Precautions.*

- When a recipient is due the second dose, ensure the first dose was with COVID-19 Vaccine AstraZeneca.

**Do not give** the vaccine to anyone with **hypersensitivity** to any of the vaccine ingredients - see *Vaccine ingredients.*

## At administration

- Ensure appropriate medical supervision and treatment is available in case of anaphylaxis following the administration of the vaccine.

- Educate the vaccine recipient on key points in the Patient Information Leaflet (RiMUP) related to vaccination with COVID-19 Vaccine AstraZeneca, including:
  - ☐ benefits of vaccination, including time to protection
  - ☐ risks, including injection site reactions and other vaccine related adverse reactions (including signs, symptoms and duration of effects)
  - ☐ flu-like symptoms are to be expected
  - ☐ the vaccine cannot cause COVID-19
  - ☐ analgesic and/or anti-pyretic medicines (e.g. paracetamol) may be used for relief from post-vaccination side effects
  - ☐ when to call a doctor or healthcare professional
  - ☐ when they need to come back for their next vaccination.

- Inspect the vaccine for particulate matter or discolouration. It is a colourless to slightly brown, clear to slightly opaque solution. Discard if the solution is discoloured or visible particles are observed.

- Withdraw 0.5 ml into a syringe. Choice of needle length/gauge must be made by each healthcare professional based on individual patient needs.

- Use a separate sterile needle and syringe for each recipient.
  - Multidose vials contain 10 vaccine doses.
    See *Multidose vials.*
  - It is normal for liquid to remain in the vial after withdrawing the final dose. This will not be enough for a full dose and should be discarded.

- Administer the vaccine by **intramuscular** (IM) injection, preferably into the deltoid muscle.

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# Administering the vaccine

## Administer two injections, between 4 and 12 weeks apart

Advise the recipient to:

- return between 4 and 12 weeks after the first dose
- complete the full 2-dose treatment with COVID-19 Vaccine AstraZeneca.

**Click to see more details on:**

- ▶ *Multidose vials*
- ▶ *Storage and stability details*
- ▶ *Shelf life*
- ▶ *What to do if a vial has been shaken*
- ▶ *Disposal*
- ▶ *Vaccine interchangeability*

## After administration

Monitor vaccine recipients for anaphylactic reaction for **at least 15 min** or as directed by local guidelines.

- Refrigerate any unused vaccine as per storage guidance.
- Advise vaccine recipients:
  - ☐ to retain records of vaccine name, vaccination dates and batch/lot number. These will be needed if they report an adverse event
  - ☐ to contact you or another healthcare provider if they have any health concerns they think may be related to the vaccine
  - ☐ to return for their next vaccination in 4 to 12 weeks' time
  - ☐ Reminder materials: MySejahtera App, Vaccination Card
  - ☐ Further information is available at http://covid-19.moh.gov.my/ or https:// www.vaksincovid.gov.my or https://www.facebook.com/kementeriankesihatanmalaysia/
- Retain appropriate vaccination records, including vaccine name, date of vaccination and batch/lot number.

**Click to see more details on:**

- ▶ *COVID-19 restrictions following vaccination*
- ▶ *COVID-19 tests following vaccination*
- ▶ *Reporting side effects*

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# More details on administering the vaccine

## COVID-19 restrictions following vaccination

Advise vaccine recipients to follow local public health/government guidance to reduce transmission of COVID-19, such as mask wearing, handwashing and social distancing.

## COVID-19 tests after vaccination

**Polymerase Chain Reaction (PCR) tests**
The vaccine does not contain live coronavirus or the part of the virus this test looks for.

**Antibody tests**
The antibodies produced following vaccination may affect the result of a COVID-19 antibody test, but only if the test looks for antibodies against the spike protein of the coronavirus.

## Reporting side effects

- Reporting suspected side effects is important. It allows continued monitoring of the benefit and risk balance of the medicine.

- Side effects can be reported at:
  https://www.npra.gov.my/index.php/en/health-professionals/reporting-adr
  OR http://www.azcovid-19.com

Please do not report the same adverse event(s) to both NPRA and AstraZeneca as all reports will be shared between AstraZeneca and NPRA (in an anonymised form) and dual reporting will create unnecessary duplicates.

When reporting side effects, provide as much information as possible including:

- ☐ recipient's medical history
- ☐ any other medicines they are taking
- ☐ date and batch/lot number of vaccination(s).

## Multidose vials

- COVID-19 Vaccine AstraZeneca multidose vials come in 10 doses (5 ml vial)

- It is normal for liquid to remain in the vial after with drawing the final dose. Discard any unused vaccine.

## Storage and stability details

- The vaccine does not contain any preservative.

- **Unopened (unpunctured) multidose vial**
  – Store in a refrigerator (2 to 8°C [36 to 46°F]) for up to 6 months.
  – Do not freeze.
  – Store in outer carton in order to protect from light.

- **Opened multidose vial**
  After first opening, chemical and physical in-use stability has been demonstrated from the time of vial puncture to administration for no more than:
  – 6 hours at room temperature (up to 30°C [86°F]).
  – 48 hours in a refrigerator (2 to 8°C [36 to 46°F]).

After this time period, the product must be discarded. Do not return it to the refrigerator.

*COVID-19 Vaccine AstraZeneca is not provided in pre-filled syringes. There are no available data on storing COVID-19 Vaccine AstraZeneca in syringes filled in advance.*

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# More details on administering the vaccine

## Shelf life

- Unopened multidose vials of COVID-19 Vaccine AstraZeneca have a shelf life of 6 months. Refer to the expiration date on the pack.

## What to do if a vial has been shaken

- The vial does not need to be shaken but can still be used if it has been shaken.

## Disposal

- COVID-19 Vaccine AstraZeneca contains genetically modified organisms (GMOs). Any unused vaccine or waste material should be disposed of in accordance with local requirements.

- Spills should be disinfected with an appropriate antiviral disinfectant.

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# Risks and benefits

Refer to the Prescribing Information for a detailed description of the benefits and risks. A high-level summary is included below.

## Background to safety analysis

- The overall safety of COVID-19 Vaccine AstraZeneca is based on an interim analysis of pooled data from four clinical trials conducted in the United Kingdom, Brazil and South Africa.

- At the time of analysis, 23,745 participants ≥18 years old had been randomised and received either COVID-19 Vaccine AstraZeneca or control. Out of these, 12,021 received at least one dose of COVID-19 Vaccine AstraZeneca.

- The majority of participants were white (75.5%), black (10.1%) or Asian (3.5%).

**Gender and age of study participants**

| | | % |
|---|---|---|
| **Gender** | Male | 44.2 |
| | Female | 55.8 |
| **Age** | 18 to 64 years | 90.3 |
| | 65 years of age and older | 9.7 |

## Side effects

- Most side effects were mild to moderate and usually resolved within a few days.

- When compared with the first dose, side effects were milder and reported less often after the second dose.

- Side effects were generally milder and reported less frequently in older adults (≥65 years old).

- Analgesics and/or anti-pyretic medicines (e.g. paracetamol) may be used for relief from post-vaccination side effects.

**Very common** (may affect more than 1 in every 10 people):

- Side effects where the injection is given (injection site reactions):
  – tenderness
  – pain
  – warmth
  – redness
  – itching
  – swelling.

- Other general side effects (systemic reactions):
  – generally feeling unwell (malaise)
  – feeling tired (fatigue)
  – chills or feverishness (temperature not measured)
  – headache
  – feeling sick (nausea)
  – joint pain or muscle ache.

**Common** (may affect up to 1 in every 10 people):

- fever (measured temperature is 38°C [100.4°F] or higher).

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# Risks and benefits

## Background to benefit analysis

- The overall efficacy of COVID-19 AstraZeneca is based on an interim analysis of pooled data from two randomised blinded clinical trials in UK and Brazil.
- This analysis was conducted with 11,636 participants (active and control) who were followed up for a median of 19 weeks (after dose 1) and 9 weeks (after dose 2).
- Participants were excluded if they had severe and/or uncontrolled cardiovascular, gastrointestinal, liver, renal, endocrine/metabolic disease, and neurological illnesses; as were those with severe immunosuppression.
- Participants are planned to be followed for at least 12 months, for assessments of safety and efficacy against COVID-19 disease.
- 2,070 (35.6%) participants who received COVID-19 Vaccine AstraZeneca had at least one pre-existing comorbidity, including:
  – BMI ≥30 kg/m$^2$
  – cardiovascular disorder
  – respiratory disease
  – diabetes.

## Overall benefits

- It has been demonstrated that a two-dose regimen of COVID-19 Vaccine AstraZeneca was 70.42% (95.84% CI: 54.84% to 80.63%) efficacious against COVID-19.
- Complete protection against COVID-19 hospital admission was shown ≥22 days after the first standard dose (0 vs 9 cases in Control group).
- There was a similar level of vaccine efficacy by country and by comorbidity.
- Adults with pre-existing comorbidity showed similar immune responses and vaccine efficacy to the general study population.
- For the two standard-dose regimen, it has been shown that protection begins from 22 days after the first dose.
- The second dose can be given in a flexible window, 4 to 12 weeks after the first dose.

## Duration and level of protection

- The duration of protection has not yet been established. Further studies are planned to evaluate the duration of protection.
- As with any vaccine, vaccination with COVID-19 Vaccine AstraZeneca may not protect all vaccine recipients

**Click to see more details on:**


- *Vaccine development and approval*
- *Scientific publications for COVID-19 Vaccine AstraZeneca*
- *Reporting side effects*

# Vaccine development and approval

## Clinical trials

Adenovirus-vectored vaccines, similar to COVID-19 Vaccine AstraZeneca but targeted for other diseases, have been tested and successfully used as a way to make other vaccines.

Extensive clinical trials to test the safety and efficacy of COVID-19 Vaccine Astra Zeneca have been conducted. The vaccine has undergone the phase I, II and III clinical trials that are expected of all new vaccines. So far, over 55,000 people have taken part in clinical trials, in countries including the USA, UK, Brazil, South Africa, India, Kenya and Japan. Trials include a broad range of ages and co-morbidities, and diverse racial, ethnic and geographic groups.

Clinical trials are continuing to evaluate long term effects and additional studies are planned. See *Planned and ongoing clinical trials* for more detail.


## Accelerated product development

Although the development of this vaccine has been accelerated, it has not been rushed and vaccine safety is of paramount importance.

**How the development of COVID-19 Vaccine AstraZeneca has been accelerated**


*Continued*

# Vaccine development and approval

## Regulatory review and approval

National Pharmaceutical Regulatory Agency (NPRA) has been conducting a 'rolling review' of the COVID-19 Vaccine AstraZeneca clinical trial results for several months, as the data became available, rather than waiting for everything to be finished and submitted at the end.

NPRA has clear and stringent efficacy and safety standards for the approval of any new medicine. All of these standards have been applied to COVID-19 Vaccine AstraZeneca.

During a public health emergency, NPRA can allow the use of medicines and new vaccines more quickly than usual, when there is no alternative available. In this way, COVID-19 Vaccine AstraZeneca has been granted Conditional Registration approval in Malaysia. Read more on how the Conditional Registration process works here.

## Approval Under Malaysia Conditional Registration For Pharmaceutical Products During Disaster

The Drug Control Authority (DCA) in its 354th meeting has granted COVID-19 Vaccine AstraZeneca Solution for Injection a Conditional Registration Approval on the 2nd March 2021.

This was granted in the interest of public health because the medicine addresses an unmet medical need and the benefit of immediate availability outweighs the risk from less comprehensive data than normally required.

AstraZeneca will continue to provide results from the clinical trials, monitor the safety trend, and carry out studies to provide additional assurance on the pharmaceutical quality and testing of the vaccine.

## Planned and ongoing clinical trials

Further clinical studies are planned to evaluate long-term effectiveness and safety, as well as effectiveness in the wider population, including use in groups such as pregnant women and people who are immunocompromised.

**Click to see more details on:**

- *Scientific publications for COVID-19 Vaccine AstraZeneca*

# References and further information

**Scientific publications for COVID-19 Vaccine AstraZeneca**

Phase I and II studies, and phase III interim analysis, are published:

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- Voysey M, Costa Clemens SA, Madhi SA et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet 2020; Dec 8. Online ahead of print.

- Contact AstraZeneca Medical Information for details of further publications and associated data: http://www.azcovid-19.com

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