Briefing

Your guide to the new vaccine

The UK has taken delivery of the first doses of a coronavirus vaccine. How does it work and who will get it when? **Graham Lawton** reports

IMMUNISATIONS using the vaccine created by Pfizer and its partner BioNTech have begun in the UK. Here, we answer questions about the science of the vaccine, who will get it first, how confident we can be in the authorisation process and the logistics of vaccinating everyone in the UK.

STEVE PARSONS/PA WIRE/PA IMAGES

Nurses undergo covid-19 vaccination training at University Hospital Coventry

Science

How effective is the vaccine?
About 95 per cent. The phase III trials of the Pfizer/BioNTech vaccine involved 42,000 people, about half of whom got the experimental vaccine and the rest a placebo. In total, 170 people fell ill with covid-19. Only eight of them were in the vaccine group; 162 had received the placebo. So around 5 per cent of cases were in the vaccine group, which is where the 95 per cent figure comes from. That is a very healthy number: the World Health Organization (WHO) said it would accept 50 per cent.

What is in the vaccine?
The active ingredient is messenger RNA that carries instructions for making the virus's spike protein, which it uses to enter cells. The mRNA is synthetic, not extracted from actual viruses, and delivered in a sphere of inert fatty material called a lipid nanoparticle.

The RNA-bearing nanoparticles are suspended in saline solution and injected into muscle tissue in the upper arm. The mRNA is then taken up by specialist immune cells, which follow its instructions, just as they would if they were infected with the actual virus.

The spike protein that is made is recognised as foreign by the immune system, which mounts an attack against it. Antibodies, B cells and T cells are activated, according to Uğur Şahin, the chief executive of BioNTech. An immune memory is also laid down, he says, meaning the immune system has learned how to defeat the pathogen and is primed to mount a swift response if it encounters the coronavirus for real.

How long does the immune memory last?
It is hard to say at this point, because the clinical trials weren't set up to answer that question, and in any case, they only began dispensing second doses of the vaccine four months ago. The WHO says that a minimum of six months would be acceptable. It will become clearer as the volunteers continue to be monitored. Şahin says he expects protection to last "months or even years".

Given what we know about natural immunity, that looks about right, says Eleanor Riley at the University of Edinburgh in the UK. She envisages people needing annual boosters, at worst.

> "We don't know how long immunity will last, but people may need annual booster shots at worst"

How long does it take for immunity to develop fully after vaccination?
The trial began assessing immunity seven days after the second shot. We know that protective immunity builds up within four weeks of the first dose, but Şahin says that it appears to develop earlier than that. Further details will be published in a matter of days, he says.

What happens to the mRNA in the body?
It is active for a few days then decays rapidly.

It is a two-shot vaccine, so what happens if people miss their second shot? Is a single shot still protective?
Two shots are needed, and the second shot is required to attain immunity. The gap between doses in the trial ranged between 19 and 42 days. Only 2 per cent of people in the trial missed their second dose so it isn't entirely clear what happens under those circumstances.

Are there any side effects?
Sometimes, but they are mild. In the trial, the vaccine was generally well-tolerated, and an independent data monitoring committee reported no serious safety concerns. The worst side effects were fatigue and headaches after the second dose. About 4 per cent of people reported fatigue and 2 per cent a headache. Other side effects were pain at the injection site and muscle pain. These are "common reactions you would have with vaccination", says Özlem Türeci, chief medical officer at BioNTech. Older adults reported fewer and milder side effects.

Does it work in older people?
Yes. Trial participants were aged up to 85, and the efficacy in people over 65 was 94 per cent – a tiny bit lower than the overall number but still very protective, and much higher than some vaccine experts feared. The vaccine hasn't been tested in people aged over 85.

And in other vulnerable groups?
The vaccine appears to be equally effective regardless of recipients' age, sex and ethnicity, according to BioNTech. It has been tested extensively in people who have already had the virus and doesn't cause any ill effects. It has also been tested in people with "stable" pre-existing conditions – known as comorbidities – including diabetes, cancer, hepatitis B, hepatitis C and well-managed HIV. Their response was as good as anyone else's. People with serious or worsening comorbidities will also be eligible for the vaccine. BioNTech says it has data on this group and will release it imminently.

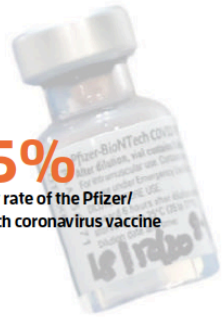
Does it protect everyone?
No. In the trials, out of about 20,000 people who were given the vaccine, eight caught covid-19 and one became seriously ill; 162 people who received the placebo fell ill, nine severely. It isn't known why some people didn't respond to the vaccine. But a success rate of 95 per cent is about as good as it gets with any vaccine.

Does it stop people from catching and transmitting the virus?
We still don't know. The trial was designed to test for symptomatic covid-19 and confirmed infection with the virus. Assessing whether the vaccine prevents transmission – which is probably a prerequisite for attaining vaccine-induced herd immunity – is much harder. But Pfizer says it is carrying out more studies on this question and will release information soon.

Some vaccines can paradoxically make a disease worse through a process called antibody-enhanced disease. Is that a risk?
Yes, theoretically. But it hasn't been seen with this vaccine or any other against covid-19, and hasn't occurred naturally, as sometimes happens with other viruses.

Has the full data from the trial been published yet?
No, it hasn't, but there is nothing sinister about that. Companies can release news to the market as soon as they have it, which is a much speedier process than preparing a scientific manuscript. According to Pfizer, every detail of the science will be submitted to a top-ranking peer-reviewed journal as soon as it is ready. It will be up to the journal how long it takes to publish.

FRANK AUGSTEIN/POOL/GETTY IMAGES



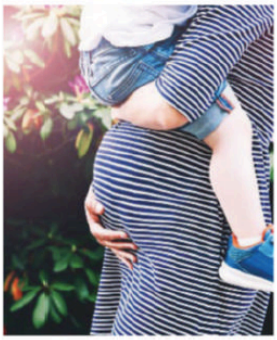
95%
Efficacy rate of the Pfizer/BioNTech coronavirus vaccine

2
Vaccine doses needed to protect against symptomatic covid-19

-70°C
Temperature the vaccine must be kept for long-term storage

5
Days the vaccine is stable in an everyday fridge

Pregnant women and children under 16 won't be eligible for the Pfizer/BioNTech vaccine in the UK until further trials take place



SHUTTERSTOCK/NATALIA DERABINA

Eligibility

Who is first in the queue in the UK?
When a vaccine is approved it is customary to first offer it to people who took part in the clinical trial but received the placebo. However, as the trial wasn't done in the UK, there is nobody in this category.

Care home residents and their carers have the highest priority, according to a priority system devised by the UK's Joint Committee on Vaccination and Immunisation. But there are problems with delivering this particular vaccine to care home residents because it needs to be transported at very cold temperatures in special cases.

Next in line are people over 80 and frontline healthcare workers, followed by people aged over 75, then people in increasingly younger age groups and/or with underlying health conditions.

Will anyone be excluded from the vaccine programme?
Yes. Pregnant women and children under 16 won't be eligible, at least at first. The vaccine hasn't been tested on pregnant women or children under 12, and there isn't enough data on children aged 12 to 15. But trials in those groups are ongoing or planned.

Everyone else can get it?
Yes, but most will have to wait their turn. Sean Marett at ›

BioNTech says the exact delivery schedule depends on how fast the factories can churn it out and where else the vaccine is approved, as the company is committed to equitable access. "We will deliver as many doses as we can as quickly as we can," he says.

Regulatory process

What does "temporary authorisation for emergency use" mean?
Exactly what it says on the tin. The UK's Medicines and Healthcare products Regulatory Agency (MHRA) has expedited the approval process in recognition of a public health emergency, and could rescind the approval just as quickly. But that is highly unlikely as it says it has done a thorough assessment of the safety and efficacy data and has seen nothing to give it reason not to approve.

Will the vaccine inevitably progress from temporary to full authorisation?
Probably, but it isn't a given. Pfizer says it expects so, but that is in the hands of the regulators.

It all happened very quickly, can we be confident corners weren't cut?
Yes. The MHRA is an independent body and so is the Commission on Human Medicines, which also had

"If there is disruption in the supply chain due to the UK leaving the EU, we will find another route"

a say in the approval decision. The MHRA only received the full clinical trial data a couple of weeks ago, but the vaccine developers have been submitting information since October, which has been subject to ongoing review.

DANIEL ROLAND/AFP VIA GETTY IMAGES

The Pfizer/BioNTech vaccine will travel in trucks at -70°C

The European Medicines Agency, the group that approves covid-19 vaccines for the European Union, said in a statement that its process for assuring the safety and efficacy of the vaccine is based on more evidence and more checks than the process used in the UK. According to the vaccine developers, the MHRA asked for the same amount of information as any other regulatory agency.

Are other countries likely to approve the vaccine soon as well?
Yes. Pfizer/BioNTech have applied for approval in the US, Australia, Canada, EU, Japan and New Zealand, and say they are preparing to submit applications to other regulatory agencies. Decisions are expected from the US and EU this month.

Logistics

How many doses is the UK getting?
In total, the UK government has pre-ordered 40 million single doses, which is enough for 18 million people assuming two doses per person and about 10 per cent wastage. But it won't get all 40 million at once. The full order will be delivered in batches over the course of 2020 and 2021.

Doesn't the vaccine require complicated cold storage?
Yes and no. For long-term storage – meaning for six months or so – the vaccine has to be kept at -70° C, which requires specialist cooling equipment.

But Pfizer has invented a distribution container that keeps the vaccine at that temperature for 10 days if unopened. These containers can also be used for temporary storage in a vaccination facility for up to 30 days as long as they are replenished with dry ice every five days.

Once thawed, the vaccine can be stored in a regular fridge at 2°C to 8°C for up to five days.

Could the supply chain be disrupted on 1 January by the end of the Brexit transition period following the UK leaving the EU?
Possibly. But according to Marett, "if there is disruption we will find another route".

Where will people be vaccinated?
The usual places: GP surgeries, health centres and hospitals. Once logistical challenges have been met, it will also be done in care homes, starting in Scotland in mid-December. People will be invited by the NHS. The entire supply is going to the various NHS bodies in the UK and nobody can jump the queue by buying a vaccine privately, according to Pfizer.

Could something still go wrong?
Yes, but that is highly unlikely. Vaccine effectiveness in the real world is almost always lower than efficacy in trials, but the drop-off would have to be spectacular to dip below the 50 per cent threshold considered acceptable by the WHO.

There could still be rare severe adverse effects down the road, especially as mRNA vaccines are a new technology and have never been rolled out on a massive scale.

Vaccine clinical trials aren't big or long enough to rule out rare but serious side effects, which can appear months or even years after vaccination. People who have been vaccinated will be followed up for two years to ensure that there are no serious adverse effects waiting in the wings.

But these are small, theoretical risks. As Fiona Watt at the UK Medical Research Council, said: "This is great news." ▮