European Medicines Agency

London, 23 October 2009
Doc. Ref. EMEA/666809/2009

Questions and answers on the CHMP review of the recommendations on the use of pandemic H1N1 vaccines

The Committee for Medicinal Products for Human Use (CHMP) at the European Medicines Agency has reviewed early data from clinical studies for the three authorised pandemic vaccines. The Committee concluded that its recommendations adopted in September, that the three vaccines be preferably used as two doses, at least three weeks apart, be maintained. However, for Pandemrix and for Focetria, the limited data currently available indicate that one dose may be sufficient in adults.

Which pandemic vaccines have been reviewed?

The Committee reviewed the three vaccines that have received an authorisation from the European Commission[1] valid in all European Union Member States, to protect against infection with the virus that is causing the current pandemic (H1N1) 2009, also known as 'swine flu':

- Celvapan, from Baxter AG;
- Focetria, from Novartis Vaccines and Diagnostics S.r.l.;
- Pandemrix, from GlaxoSmithKline Biologicals S.A.

Because vaccines are a key element to control the impact of the pandemic, which is rising again now that the colder weather season has started in the Northern hemisphere, Member States are starting vaccination, according to their national strategies.

Why are these vaccines being reviewed?

At the time of the marketing authorisation for the pandemic vaccines in September 2009, the recommendation of the Committee was that the H1N1 pandemic vaccines be used as two doses given at least three weeks apart. This recommendation stemmed from the data generated as part of the authorisation of the vaccines: all three vaccines have been authorised using the concept of a 'mock-up' vaccine, authorised in advance of a pandemic using data relating to another strain of the flu virus (the H5N1 strain, also known as 'bird flu'). These H5N1 vaccines were approved as a two-dose schedule.

In September, the Committee already acknowledged that there were preliminary data for Pandemrix suggesting that one dose may be sufficient in adults.

Because there were only limited data on the use of the H1N1 vaccines in clinical studies, the CHMP has requested that the vaccine manufacturers supply the data from their ongoing clinical trials with the H1N1 as soon as they become available. All three vaccine manufacturers have now supplied the early results of their clinical trials in adults to the Committee.

[1] See previous press releases and question-and-answer document on the Agency website:
http://www.emea.europa.eu/pdfs/general/direct/pr/60258209en.pdf
http://www.emea.europa.eu/humandocs/PDFs/EPAR/celvapan/62290809en.pdf
http://www.emea.europa.eu/pdfs/human/pandemicinfluenza/60132109en.pdf

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What data has the CHMP reviewed?
The data supplied come from clinical trials that are looking at the immunogenicity of the vaccines. This is the ability of the vaccines to trigger a response from the immune system, the body's natural defences, which will allow the vaccinated person to fight infection with the H1N1 virus.
The Committee reviewed immunogenicity results in vaccinated subjects three weeks after the first injection of the vaccines. These studies can help provide information on how effective a single dose of the vaccine could be in protecting against the flu pandemic.

What are the recommendations of the Committee?
The CHMP noted that the data supplied to date are still limited and do not allow the Committee to recommend the general use of a single-dose vaccination schedule. Looking at each vaccine in particular, the CHMP stated the following:

- For **Pandemrix**, the additional data with the H1N1 vaccine confirmed the recommendation made in September. The vaccine should preferably be used as a two-dose schedule, but a single dose may be sufficient in adults aged 18 to 60 years. The immunogenicity results in healthy adults show that one dose of Pandemrix brought about an appropriate level of protection, according to all the criteria laid out for influenza vaccines[2]. Consideration can be given to using the same one-dose schedule in adolescents and children (over the age of ten years).
- For **Focetria**, the data are sufficient to conclude that the vaccine should preferably be used as a two-dose schedule, but a single dose may be sufficient in adults aged 18 to 60 years. Again, this is based on immunogenicity results in healthy adults three weeks after vaccination that satisfied all of the Committee's criteria. Consideration can be given to using the same one-dose schedule in adolescents and children (over the age of nine years).
- For **Celvapan**, while the CHMP awaits further data, the dosage schedule remains as two doses, with a three-week interval, in all populations.

The CHMP also noted that:

- At this stage, while the clinical trials with the mock-up H5N1 vaccines included large numbers of subjects, the numbers of adults or elderly subjects in the current trials who have received the H1N1 vaccines are still limited.
- The significance, in the longer term, of the early results is not yet fully known. Studies are ongoing that look at the persistence of the immune response after a single dose of the vaccine. These studies will help understand how long after a single dose the levels of antibodies against H1N1 remain high enough to fight the pandemic flu.
- More data are still expected from these clinical trials, and the Committee will review them as and when they become available. As a result, the dosing recommendations may change in the future.

Where available, the manufacturers have also supplied the Committee with the early safety results from the clinical trials, recording the side effects experienced by the subjects vaccinated with the pandemic vaccines. The CHMP has reviewed these data, and concluded that they confirm the safety profile of the vaccines, as foreseen with the mock-up vaccines.

What will happen next?
The opinions of the CHMP on the dosing schedules for Pandemrix and Focetria are being transmitted to the European Commission for the granting of a variation to the marketing authorisations.

The current recommendations for all pandemic vaccines can be found on the Agency's website. The Agency will provide updates as new information becomes available.

[2] These criteria are described in the Note for guidance on harmonisation of requirements for influenza vaccines (CPMP/BWP/214/96) and are based on seroconversion (when the patient's serum is shown to contain much more antibodies to the virus than it contained before vaccination) and serum levels of antibodies against H1N1 as measured in laboratory tests.