EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

COVID-19 vaccines' extra doses

PHIRI meeting on information exchange on COVID-19 between countries

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Outline

- EMA's role in COVID-19 vaccine booster doses
- Comirnaty's boosters
- Spikevax's boosters
- Comirnaty and Spikevax - extra dose for immunocompromised
- Update on Janssen's vaccine and extra doses
- Update on heterologous vaccination in the context of booster doses
- Conclusions

How EMA works to evaluate booster doses

EMA

- **Evaluates benefits and risks** of COVID-19 vaccines - initially and during lifecycle
- **Carries out pharmacovigilance and risk management** activities for all EU medicines
- **Its Pandemic Task Force (ETF)** supports the scientific evaluation by EMA committees & supports developers
- **Reviews the data submitted by companies** when applying to change the terms of their COVID-19 vaccine marketing authorizations (e.g. authorization of extra doses)
- **Reviews Real World Evidence** as important data source to complement clinical trial data
- If changes to marketing authorization are approvable, **updates the EU product information**
  - Summary of Product Characteristics – or SmPC - and Package Leaflet
- **Exchanges information with national authorities and the European Centre for Disease Prevention and Control** (ECDC) to evaluate available data and support campaigns to protect the public during the ongoing pandemic

Comirnaty / Spikevax – approved use of booster doses

- Booster doses are for people with normally functioning immune systems

Comirnaty (Pfizer COVID-19 vaccine)

- Primary course of 2 doses given 3 weeks apart - one dose contains 30 micrograms
- A **booster dose (30 micrograms)** of Comirnaty may be administered intramuscularly **at least 6 months after the second dose in adults (18 years of age and older)**

Spikevax (Moderna COVID-19 vaccine)

- Primary course of 2 doses given 28 days apart - one dose contains 100 micrograms
- A **booster dose (50 micrograms**, half the dose used in primary series) may be administered intramuscularly **at least 6 months after the second dose in adults (18 years of age and older)**

*The decision **when and for whom to implement a third dose** should be made based on **available vaccine effectiveness data, taking into account limited safety data** (product information, SmPC sections 4.4 and 5.1)*

Comirnaty – evidence base for use of booster doses

- Based on interim safety and immunogenicity data of a third booster dose of Comirnaty from **study C4591001**, a Phase 1/2/3, placebo-controlled, observer-blind, interventional, dose-finding, study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals
- **Further evidence - published real-world effectiveness data from Israel and the US** [1]
- The safety and immunogenicity of a booster dose (third dose) of Comirnaty in individuals 65 years of age and older is based on **safety and immunogenicity data in adults of 18 to 55 years of age**
- The summary of the scientific evaluation can be found in the **assessment report**: https://www.ema.europa.eu/en/documents/variation-report/comirnaty-h-c-5735-ii-0067-epar-assessment-report-variation_en.pdf

- 1. Hause et al, MMWR Morb Mortal Wkl. 2021 Oct 1;70(39):1379-1384. doi:10.15585/mmwr.mm7039e4; Bar-on et al, N Engl J Med 2021 Oct 7;385(15):1393-1400. doi: 10.1056/NEJMoa2114255

Spikevax – evidence base for use of booster doses

- Current **trial data** show that a booster of Spikevax 6 to 8 months after the second dose leads to a rise in antibody levels in adults whose antibody levels were waning

- The safety and immunogenicity of a booster dose of Spikevax are evaluated in an ongoing Phase 2, randomised, observer-blind, placebo-controlled, dose-confirmation study in **participants 18 years of age and older** (NCT04405076).
- The summary of the scientific evaluation will be found in the **assessment report**, once published

Extra doses for immunocompromised

Comirnaty and Spikevax

- **An extra dose** (considered the third dose of the primary series) **of Comirnaty / Spikevax may be given at least 28 days after the second dose**
- Indicated for individuals who are **severely immunocompromised aged 12 years and older** (SmPC section 4.4)
- Studies showed that **an extra dose of these vaccines increased the ability to produce antibodies** against the virus that causes COVID-19 in organ transplant patients with weakened immune systems[1,2]
- Although there is no direct evidence that the ability to produce antibodies in these patients protected against COVID-19, it is **expected that the extra dose would increase protection at least in some patients**
- EMA will continue monitoring any data that emerges on its effectiveness

1. Kamar N, Abravanel F, Marion O, Couat C, Izopet J, Del Bello A. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med 2021;385:661-662

2. Hall VG, Ferreira VH, Ku T, et al. Randomized trial of a third dose of mRNA-1273 vaccine in transplant recipients. N Engl J Med 2021;385:1244-1246

Safety of booster doses – effect on myocarditis and pericarditis

- Current data indicate that the pattern of **side effects after the booster is similar to what occurs after the second dose** for Comirnaty and Spikevax
- **Limited data on safety of third dose** for both vaccines, however **no specific safety signal** has been identified following 3rd dose of Comirnaty/Spikevax
- **Real World Evidence** from Israel / US on the safety of the 3rd dose is **reassuring**
- The risk of inflammatory heart conditions or other **very rare side effects after a booster are carefully monitored**
  - Risk of **myocarditis/pericarditis with mRNA vaccines after a third dose has not been characterised**
  - EMA's Pharmacovigilance and Risk Assessment committee (PRAC) is currently evaluating **a safety signal on risk of myocarditis/pericarditis for Comirnaty / Spikevax**
- **Younger people may suffer from severe COVID-19**, including infection-induced myocarditis/pericarditis
- On the basis of existing evidence, the CHMP considers there is **no reason to restrict the use of booster doses in certain age groups, instead it has granted approval for all adults** with a warning in the SmPC

Janssen's – use of booster doses

- **Some Member States have started recommending a second vaccine dose with an mRNA vaccine following a first vaccination with Janssen**
- This is because, as more data on effectiveness become available, **one dose of Janssen does not seem to provide longer term protection**
- Over coming weeks, **the Agency expects to receive data on additional/booster doses of Janssen's vaccine given 2 to 6 months after the first dose**
- This will help EMA determine if data are sufficient to recommend a booster dose
- **EMA will communicate** as the situation develops

Heterologous vaccination for booster doses

- Use of a different vaccine than the one used for the primary series for boosting the immune response
- This '**mix and match' boosting strategy is being used and considered by some EU Member States**
- Also **approved by FDA** (for heterologous boosters)
- Several studies prove that **certain vaccine combinations would trigger a strong immune response**
- **EMA is currently evaluating these data** and will consider if clinical data is sufficient to update the product information for each individual vaccine
- At present, the product information for Comirnaty/Spikevax states that *Interchangeability with other COVID-19 vaccines to complete the primary vaccination course or the booster dose (third dose) has not been established*.

Transparency and data

Use of booster doses

- EMA is publishing the Assessment Reports summarizing the evaluation on use of booster and extra doses

Comirnaty

- Booster doses: https://www.ema.europa.eu/en/documents/variation-report/comirnaty-h-c-5735-ii-0067-epar-assessment-report-variation_en.pdf
- Extra doses for immunocompromised: https://www.ema.europa.eu/en/documents/variation-report/comirnaty-h-c-5735-ii-0062-epar-assessment-report-variation_en.pdf

Spikevax

- Booster doses: to be published here under 'assessment history – changes since initial authorization of the medicine': https://www.ema.europa.eu/en/medicines/human/EPAR/spikevax
- Extra doses for immunocompromised: https://www.ema.europa.eu/en/documents/variation-report/spikevax-previously-covid-19-vaccine-moderna-h-c-5791-ii-31-epar-assessment-report-variation_en.pdf

- EMA has put extra transparency measures in place for COVID-19 medicines
  - the relevant clinical data will be put in the public domain

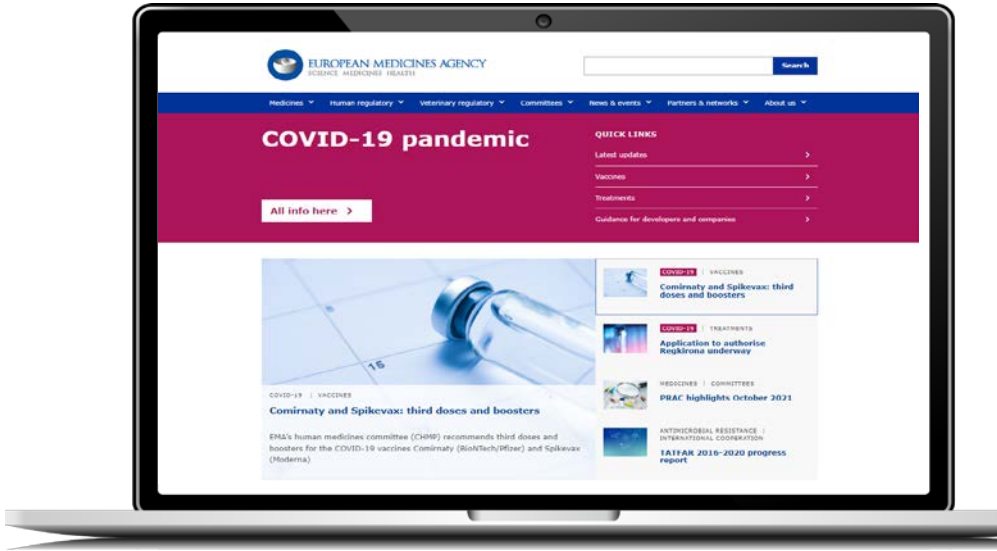
Conclusions

Use of booster doses

- Most Member States have started giving booster doses
- **EMA has assessed and made recommendation for third doses for mRNA vaccines**, which are the basis for national vaccination decisions. **Transparency measures ensure clinical data will be published**
- Advice on how vaccinations should be given remains the **responsibility of the national immunisation technical advisory groups** (NITAGs). EMA and ECDC are already collaborating with NITAGs
- **Real world effectiveness data** from Europe and other parts of the world are of particular interest to supplement data from clinical trials investigating booster doses
- **More data from companies marketing the vaccines are expected in the coming weeks** and EMA will keep reviewing the information. EMA is engaging with vaccine developers to coordinate submission of these data
- **Close monitoring of breakthrough infections and vaccine effectiveness** (against infections, severe disease and deaths), should be continued
- **Member States need to prepare for possible adaptations to their vaccination programs** in case of a substantial decrease in vaccine effectiveness is noted in specific population groups or in the population at large

Latest updates on EMA's corporate website:

COVID-19 pandemic



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Vaccination of people recovered from COVID-19

- Data suggest that **natural immunity, while effective, wanes over time**

- For individuals who have already recovered from the infection with natural immunity, evidence shows that **vaccination helps develop an increased ability to fight future infection**

- The optimal schedule for these individuals to be vaccinated has not been identified, and **more data are needed to understand how to maximise protection**

- From data on severe disease, hospitalisation and death caused by COVID-19, as well as from the incomplete understanding of so-called “long-Covid”, it is clear that **the cost of natural immunity is not tolerable**