Pharmacovigilance during the Pandemic

PHV platform meeting 30/10/2020
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EMA Approach to the Pandemic

**COVID-19 EMA pandemic task force (COVID-ETF):**

- EMA scientific committee and working party members expert in vaccines, infectious diseases, preclinical and clinical trial design, paediatric aspects, quality of biological medicinal products
- Support to the development, authorisation and supervision of medicines and vaccines
- Deal with the scientific, regulatory and operational challenges created by the COVID-19 pandemic
EMA Approach to the Pandemic

➢ Regulatory procedures adapted to grant marketing authorisation (MA) of safe, effective and high-quality COVID-19 vaccines and therapeutics as soon as possible

➢ Fast reviews supported by COVID-ETF coordinates and enables fast regulatory actions on development, authorisation and safety monitoring of treatments and vaccines intended for COVID-19:

- **Rapid scientific advice:** guidance on best methods and study design to generate valid data on efficacy, safety and quality
- **Rapid agreement of paediatric investigation plans (PIPs)**
- **Rolling review:** data assessed in 15-day cycles as they become available
- **Accelerated assessment of MA applications:** minimum timetable with flexibility depending on amount of data and public health importance
Summary of activities

165 therapeutics in discussion with EMA
40 vaccines identified for interaction

Rapid scientific advice proceeding for advanced vaccines and therapeutics (43 completed – 18 ongoing)

2 Rolling reviews started (AstraZeneca/Oxford and BNT162b2, BioNTech/Pfizer)
Enhanced Safety Monitoring of Medicines Used In Treatment of COVID-19

A range of pharmacovigilance measures have been put in place:

✓ Dedicated eRMRs (EudraVigilance safety monitoring reports) with increased frequency
✓ Close monitoring of ongoing observational studies and sharing information to network on a weekly basis
✓ Reduced timeframe for confirming urgent COVID-19 related signals
✓ Periodicity of PSURs for COVID-19 relevant products reviewed
✓ Call for ADR reporting to HCP and patients
✓ Extension of EMA Medical Literature Monitoring service to cover active substances of interest in treatment of COVID-19
✓ Updated guidance on conduct of clinical trials during pandemic to stimulate SUSAR reporting in EV
✓ Stimulate reporting in EudraCT: reminders sent to NCAs, sponsors reminded to include “COVID-19” in titles
✓ Encouraged registration of observational studies related to the pandemic in EU-PAS Register
COVID-19 Vaccines Monitoring Preparedness

- Potentially many different vaccines, **new technologies**
- **Accelerated** development and approval
- **Rapid vaccination** to occur in millions or billions
- **Safety critical**: Unexpected or rare serious ADRs could negatively affect vaccination campaigns and increase vaccine hesitancy
- Regulators need to demonstrate to have systems in place to rapidly **detect** and **minimise** serious risks to patients
- **Transparency** and **communication** will be key
Lessons have been learned from A/H1N1 pandemic vaccination campaign, but more uncertainties and fast introduction of COVID-19 vaccines after approval.
COVID-19 Vaccines Monitoring Preparedness Plan

Enhanced monitoring activities to be carried out in the EU for COVID-19 vaccines, including roles, responsibilities and interactions of stakeholders involved.

**Lessons Learned H1N1**

Lessons learned from A/H1N1 pandemic adapted to current emergency situation.

- Rapid detection, exchange, prioritisation and assessment of safety signals
- Testing of existing and new methodologies specific for COVID-19

**Signal Detection Methods**

- Active surveillance of vulnerable populations:
- Active data collection on rare and severe risks
- ACCESS, ICMRA, pregnancy studies, int. cohorts

**COVID-19 Vaccines Monitoring Preparedness Plan**

- Engage and communicate with public, patients and HCP.
- Enhanced communication and transparency measures

**International And Research Centres Collaboration**

**Transparency & Communication**
Real-World Monitoring of COVID-19 Treatments and Vaccines

**EMA review of study results**
- **Daily triage** of published studies
- **Reviews** e.g. ACEi/ARBs and HCQ to support regulatory decision making
- Use of **EU PAS Register** to support collaborations and quality of studies

**EMA-funded projects**
- Framework for COVID-19 vaccine monitoring
- Framework for **multi-centres collaboration** for observational studies
- **Pregnancy** study on effects of COVID-19 infection and treatments

**International Collaboration (ICMRA, WHO)**
- Preparation for **vaccine safety monitoring** (lead MHRA/TGA)
- Building **international cohorts** facilitating multicentre observational studies (lead Health Canada)
- **Pregnancy research** to support regulatory decision-making (lead EMA)
- WHO Europe Regional Working Group on COVID-19 vaccination
Transparency and Communication

- **Timely communication** and high level of **transparency** critical to ensure public trust in vaccines and protect public health
- Engage and communicate with public, patients and HCP
- Exceptional transparency measures
- Pharmacovigilance updates

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<th>Regulatory procedure</th>
<th>Standard practice</th>
<th>COVID-19 medicines</th>
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<tr>
<td>Compassionate use opinion</td>
<td>Published in Compassionate use after CHMP opinion</td>
<td>News announcement published within 1 day of CHMP opinion</td>
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<td>Start of rolling review</td>
<td>Not applicable</td>
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<td>Marketing authorisation application</td>
<td>Active substance and therapeutic area listed in Medicines under evaluation</td>
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<td>Application for extension of indication</td>
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<tr>
<td>Publication of European public assessment report (EPAR)</td>
<td>Published at least 2 weeks after marketing authorisation</td>
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<tr>
<td>Product Information</td>
<td>Published in all EU languages with EPAR</td>
<td>Published (in English) within 1 day of positive CHMP opinion; published in other EU languages with EPAR</td>
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<tr>
<td>Risk management plan (RMP)</td>
<td>Summary of RMP published</td>
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<td>Clinical trial data</td>
<td>Publication suspended until further notice</td>
<td>Published on Clinical data website after marketing authorisation</td>
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Clarifications on received questions - Rapid signal assessment coordination and communication

- Validated signals that are not an ESI should be submitted in monthly summary safety reports and PSURs

- List of confirmed signals on PRAC agenda (i.e. to be discussed at PRAC) and list of non-confirmed signals are sent to all QPPVs prior to each PRAC meeting

- PRAC signal assessment report is shared with concerned MAHs at both the preliminary and final stages

- Emerging safety issues to NCAs and EMA “P-PVemerging-safety-issue@ema.europa.eu”. This should be done as soon as possible and no later than 3 working days after establishing that a validated signal or a safety issue from any source meets the definition of an emerging safety issue.
Clarifications on received questions – core RMP

- core RMP in 2009 defined all the requirements for H1N1 vaccines (+lessons learned)

- Since then, EMA developed: GVP guidance (rev 2 for RMP), RMP template (rev 2.0.1), GVP PI vaccines, CHMP influence vaccines clinical guidance

Manufacturers: Pre-submission interaction, scientific advice requests on PhV

Unified view from EMA Committees on RMP requirements for COVID-19 vaccines:

• Additional guidance, no duplication (existing guidance applies)
• Requirements & recommendations = more than a list of possible options
• Reflects current understanding of the pandemic and the vaccines development
  • Will be a living document, integrating outcomes of EMA/EU funded projects and other international collaborations
Clarification received questions – core RMP

Main topics:

- Additional COVID-19 specific topics to be addressed in the safety specification, including missing information and AESI.
- Methods for signal detection adapted to pandemic use (to be described in RMP);
- Content and periodicity of Summary Safety Reports (monthly at start);
- Use of stickers for traceability, additional electronic methods to be considered;
- Key elements of PASS design: e.g. rapid start, fast data generation, frequent reports, using results of ongoing EU efforts;
- Additional guidance on section of the RMP template, with a different level of detail.
Clarification based on received questions - ACCESS

- Focused on **preparedness** prior to vaccine introduction (e.g. background rates) and **readiness of hospital sites and data sources** post licensure by providing protocols and the establishment of a European network of hospitals/data sources that are able to provide high quality data/robust sample sizes. By establishing this network, ACCESS prepares countries to do this in a harmonized (common protocols) and collaborative manner (European network of data sources).

- Within the ACCESS contract, **it is not envisioned that studies will be performed** using the protocols and identified data sources, but it provides an opportunity for data providers, vaccine manufacturers and public institutions to use the outputs of ACCESS (protocols, background rates) and to perform studies on effectiveness, safety and coverage.

- The common protocols and platform/infrastructure of data sources **will be disseminated** through the VAC4EU (Vaccine monitoring Collaboration for Europe) being a partner of the ACCESS project and will guarantee a continuous monitoring through their website [https://vac4eu.org/](https://vac4eu.org/) and hosting of the ACCESS deliverables, including a tool/dashboard for accessing background rates and common protocols and training manuals. ACCESS includes a code of conduct and governance principles for collaborative studies using the ADVANCE code of conduct endorsed by VAC4EU.
Key messages

- COVID-19 is a major public health challenge
- Unprecedented collaboration and unprecedented interest and scrutiny
- Regulators and companies need to rise to the challenge and demonstrate to have systems in place to rapidly detect any safety issues and minimise serious risks to patients
- Timely exchange of information, transparency and communication are critical
- We need to be prepared and we are all committed to a common goal
Any questions?

Thank you for your attention

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