EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Signal Management GVP IX: pilot on signals from MAHs

12th industry stakeholder platform – operation of EU pharmacovigilance
24 November 2017

Agnieszka Szmigiel– Signal & Incident Management Service
Pharmacovigilance & Epidemiology Department, EMA

Disclaimer

Scope of the revision

- Guidance on signals detected by MAHs based on EV monitoring
- Terminology, including emerging safety issues (previously GVP VI)
- Streamlined guidance on scientific aspects
- Monitoring periodicity and analysis of EV data
- Roles and responsibilities within EU process, flowcharts
- Addendum: *“Methodological Aspects of Signal Detection from Spontaneous Reports of Suspected Adverse Reactions”*

Legal provisions for MAHs: implementation about to start

- EV shall also be accessible to MAHs to the extent necessary for them to comply with their pharmacovigilance obligations *[REG Art 24(2)]*
- MAHs shall monitor EV data to the extent that they have access to the database *[IR Art 18(2)]*
- MAHs shall ensure the continuous monitoring of EV data with a risk-based frequency *[IR Art 18(3)]*
- Where a MAH detects a new signal when monitoring the EV database, it shall validate it and shall forthwith inform EMA and NCAs. *[IR Art 21(2)]*

EV monitoring

- Periodicity should be determined by the MAH based on the risk profile of the medicinal product and it should be documented.
- Minimum: 6 monthly; more frequent for active substances included in the additional monitoring list (except PASS).
- Selection of DECs for further review should be based on scientific judgement: not all SDRs should be further investigated and some DECs not showing disproportionality may warrant further investigation.
- EV outputs provided at active substance level, MAHs to consider all ICSR data relevant to the safety profile of their medicinal product.
- Record management should be in line with the organisation's procedures.

Transitional arrangements

- To streamline the involvement of MAHs in the monitoring of EV data, a phased implementation has been agreed with the European Commission:
  - focus on active substances on the additional monitoring list for a pilot period of one year
  - start on 22 February 2018 (i.e. grace period of 3 months)
- EMA will report back to the Commission after one year to discuss next phase of the implementation.

Active substances involved in the pilot

- Pilot list published separately on the Agency's signal management webpage
- Reference: additional monitoring list in force as of 22 November (rev. 49)
- Inclusive:
  - ✓ all active substances (or combinations) on the list (not only products)
  - ✓ irrespective of reason for inclusion
- Changes to the additional monitoring list after 22 November will not affect the pilot.

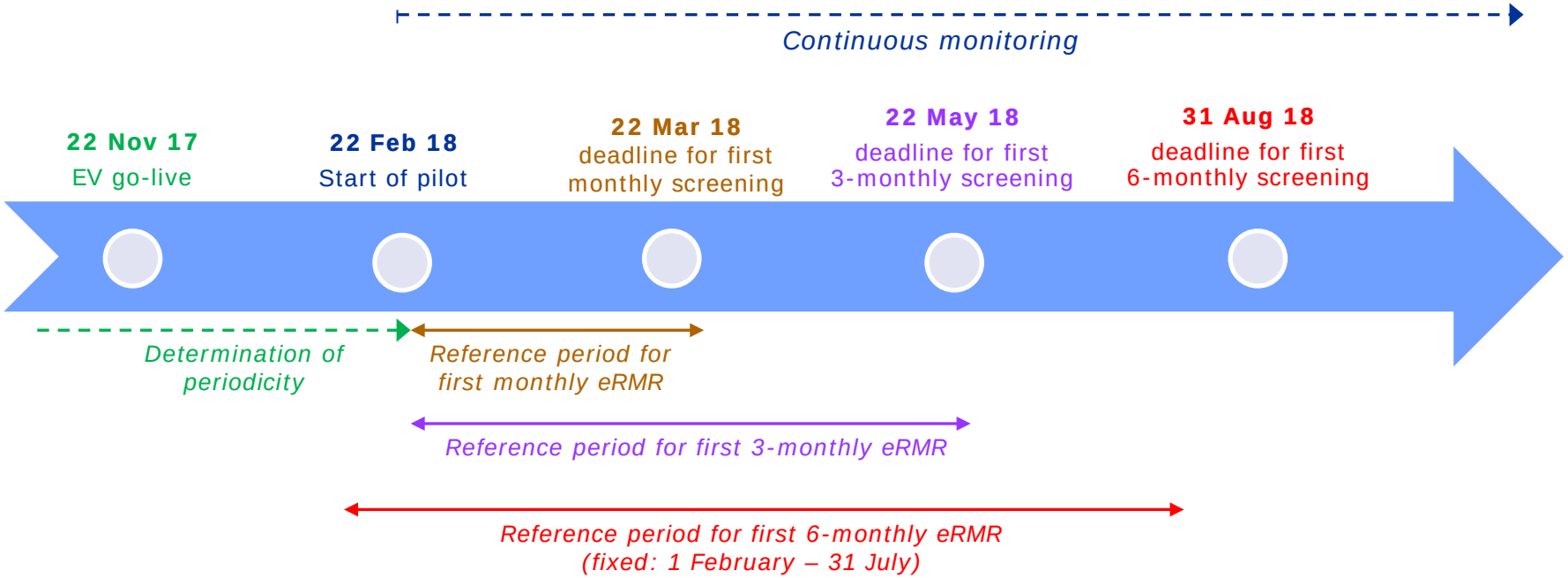
Active substances not included in the pilot

- There will be no requirement to continuously monitor EV data and inform EMA/NCAs of validated signals for the duration of the pilot.
- MAHs will still have access to EV and will be able to use the data as an additional source for their existing signal management activities.
- This may include signals from other sources discussed in PSURs, for which MAHs will be expected to analyse data available in EV to complete their evaluation as appropriate.

Preparation for the pilot

- Between 22 November 2017 and 22 February 2018, MAHs involved in the pilot should familiarise themselves with the EV data and tools and the new process outlined in GVP.
- By 22 February, MAHs should have determined the frequency at which they will monitor EV data.
- The frequency will determine the date of the first screening, which should cover DECs with new cases reported to EV on or after 22 February 2018.
- No obligation to include in first analysis DECs for which no new case is received on or after 22 February 2018.

Getting into the pilot using eRMRs



EU signal management process: until now the full picture

Signal detection (EV) & validation
EMA, NCAs
MAHs

Confirmation
PRAC Rapp / Lead MS

Initial analysis & prioritisation, assessment, recommendation
PRAC (with MAH input)

Conclusion

- The involvement of MAHs in the monitoring of EV data will complement the activities already performed by EMA and NCAs, and thus should strengthen the early detection of safety signals.
- It is however a major new process which will require adjustments of practices for MAHs and across the EU regulatory network.
- GVP IX revision 1 provides requirements for the handling of signals detected by MAHs based on their continuous EV monitoring; for signals detected through other sources, existing obligations and processes still apply.
- While the revised module will come into effect on 22 November when the new EV system goes live, transitional arrangements will apply to EV monitoring by MAHs.

Thank you for your attention

Further information

Contact me at: agnieszka.szmigiel@ema.europa.eu

European Medicines Agency
30 Churchill Place • Canary Wharf • London E14 5EU • United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Follow us on **@EMA_News**

Abbreviations

ADR: Adverse Drug Reaction

CAT: Committee for Advanced Therapies

CHMP: Committee for Medicinal Products for Human Use

CMDh: Co-ordination Group for Mutual Recognition and Decentralised procedures - Human

DEC: Drug-Event Combination

DIR: Directive 2001/83/EC

EMA: European Medicines Agency

EPITT: European Pharmacovigilance Issues Tracking Tool

eRMR: electronic Reaction Monitoring Report

ESI: Emerging Safety Issue

EU: European Union

EURD list: List of EU reference dates and frequency of submission of PSURs

EV: EudraVigilance

GVP: Good pharmacovigilance practices

IR: Commission Implementing Regulation (EU) No 520/2012

MAH: marketing authorisation holder

MS: Member State

NCA: national competent authority

PRAC: Pharmacovigilance Risk Assessment Committee

PV: Pharmacovigilance

Q&A: Questions and Answers

QPPV: Qualified Person Responsible for Pharmacovigilance

REG: Regulation (EC) No 726/2004

PASS: Post-authorisation Safety Study

PSUR: Periodic Safety Update Report

SDR: Signal of Disproportionate Reporting

SMART: Signal Management Review Technical Working Group

SPC: Summary of Product Characteristics