EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Good Pharmacovigilance Practices (EU-GVP)

GVP PIII update after public consultation

Pharmacovigilance Platform Meeting
30 October 2020

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High level contents:

- Part A: scope, outlining the issues
- Part B: guidance to address the issues outlined in part A
- Part C: guidance that is specific to the EU

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Working principles we tried to adhere to:

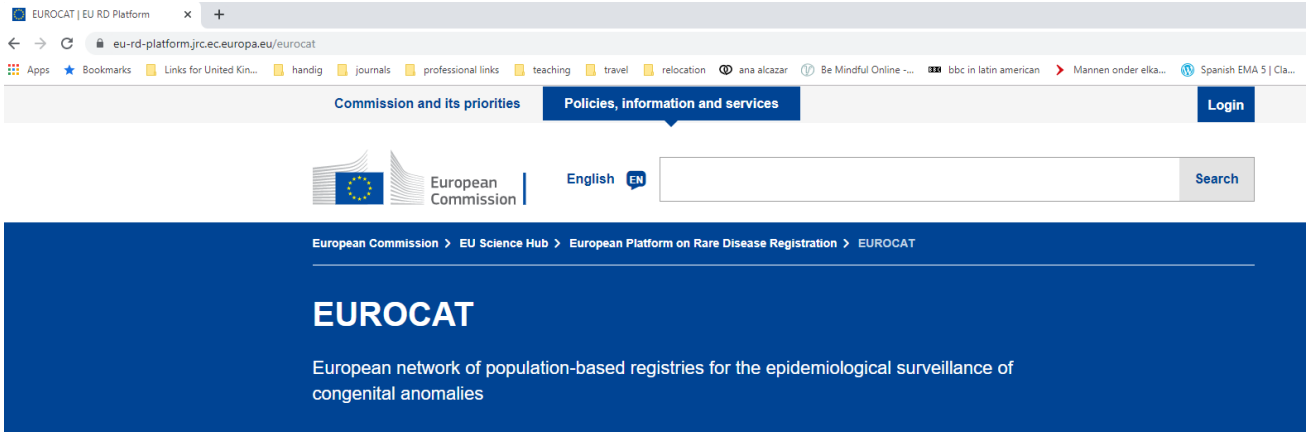
- Encourage a 'step up' from current practice. More proactive data collection & evaluation of safety in this vulnerable population. 'If you don't ask, you don't get.'
- Order of contents in line with all other GVP
- No repetition of, or conflict with, guidance written elsewhere (e.g. requirements for PSUR, AE reporting, PASS, risk minimisation)
- If concerns are theoretical only, we do not issue guidance on those
- It is not our role to highlight benefits of breastfeeding
- Minimal use of examples

Discussion items – part A

Part A

- Terminology section - CHMP guideline or EUROCAT definitions?
- Possibility of harm by exposure through semen
- Need to 'state the obvious' given experience with MAH's submissions

EUROCAT:



- Congenital malformations only
- Detected at any time – but the later the detection, the less likely to be reported
- Rates & data quality vary between centres
- Focus on outcomes; medicine exposure information is limited. Hence EUROmediCAT
- Focus on ‘major malformations’ – for reasons of pragmatism

Discussion items – part B

- **PSURs**
  - sales data only or also age & sex specific utilisation data?
- **PASS**
  - When there is a ***DUS***, ensure insight is obtained on confounders
  - Product specific ***registries*** vs hybrid study designs – everyone seems to agree on what is needed; the challenge is what can be required
  - Information on existence of registries in the PI & SmPC?
  - ***Distinction between the implications of risk*** in pregnancy & risk in breastfeeding

Observation from our analysis of registries

- On the surface: reassuringly, no major teratogen found.
- Scratch a little bit below the surface:
  - No protocol
  - No detailed data
  - Selective recruitment & eligibility, with

    as a result, low numbers & ??generalisability

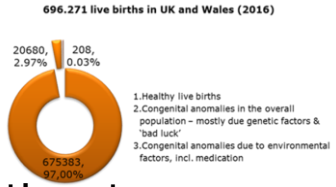
⇒ For all we know, there may still be a major teratogen here.

Better use of existing methods & data sources

- Pre-authorisation: PK studies in breastfeeding
- Routine pharmacovigilance: PSURs, Eudravigilance
- Additional pharmacovigilance: hybrid approaches
- Translated into good risk minimisation measures
  - ✓ further developed in GVP XVI

Please consider

- PSURs should provide age & sex specific utilisation data where available
  - Is there really no further information available? E.g. drug utilisation studies / safety studies that are not product-specific
- If there is a signal,
  - What, if any, is the impact of missing information e.g. on competing endpoints?
- No evidence of harm is not the same as evidence of no harm. Remember the numbers
- In terms of PASS, a lot more is possible today than 10 years ago
- Study requests & risk minimisation measures need to remain risk proportionate
- It is an emotive subject – with potentially impactful consequences. Careful consideration & good communication is crucial.



Discussion items – part B

- **Risk minimisation**
  - Avoiding pregnancy, avoiding exposure (pregnancy & breastfeeding) , risk mitigation when pregnancy unplanned
  - Effective communication of risk & uncertainty (not 'lost' in large info packs, risk proportionate), empowering HCPs with information & skills
  - Exposure through semen – theoretical only? Or solid evidence of risk?
  - Effective contraception – how prescriptive do we want to be?
  - Pregnancy prevention programmes (PPP) – at present, ***a lot of inconsistency*** between products.
    - To clarify the needs & achieve harmonisation. Driving factor: known teratogenicity in humans
    - Full PPP to have routine & additional RMMs. Most elements will be 'standard'; some decided on case-by-case basis
    - How the elements are to be implemented may depend on what is appropriate in each Member States (e.g. 'visual reminder' could be a pictogram or a text in colour on the pack)

Thank you for your attention

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