CBG MEB
MEDICINES EVALUATION BOARD

Pharmacovigilance

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RSNN-EMA Workshop
17 November 2020

GOOD MEDICINES USED BETTER

Pharmacovigilance

Pharmacovigilance includes…

- Safety monitoring of medicines
- Identification of new safety issues post-marketing
- Deciding on and implementing risk minimisation measures

- Assessment of effectiveness of regulatory actions on the use of medicines and patient outcomes
  - may trigger new or adjusted risk minimisation measures for **clinical practice**

➢ Different methods, type of data and stakeholders involved

Example: EU review of valproate 2017-2018

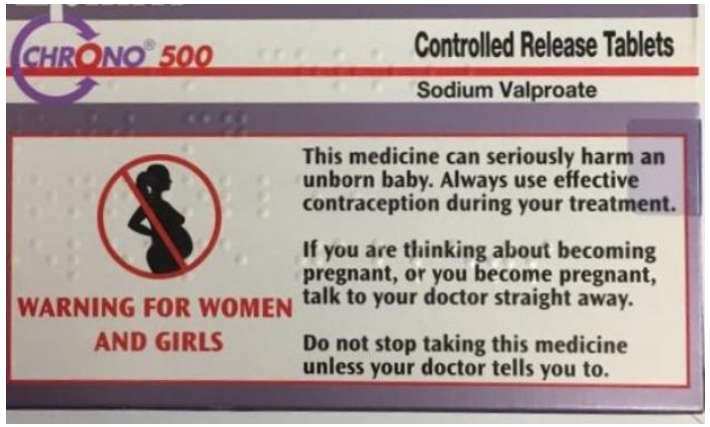
Valproate indicated to treat epilepsy and manic episodes in bipolar disorders.

Risk minimisation measures

- Congenital malformations (10%) and neurodevelopmental disorders (30-40%) after use during pregnancy.

In 2014 updated measures and warning regarding use in WCBP and use during pregnancy

- DHPC, HCP brochure, HCP checklist, patient material.
- Advice to use contraceptive measures
- Valproate should not be used as first choice treatment in young women



EU review of valproate 2017-2018


EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

10 March 2017
EMA/144306/2017

New review of valproate use in pregnancy and women of childbearing age

EMA to consider if risks of these medicines require further restrictions of use

The European Medicines Agency (EMA) has started a review looking at the use of valproate-containing medicines in the treatment of women and girls who are pregnant or of childbearing age. These medicines are approved nationally in the EU to treat epilepsy, bipolar disorder and in some countries, migraine, and have been previously reviewed by the Agency.

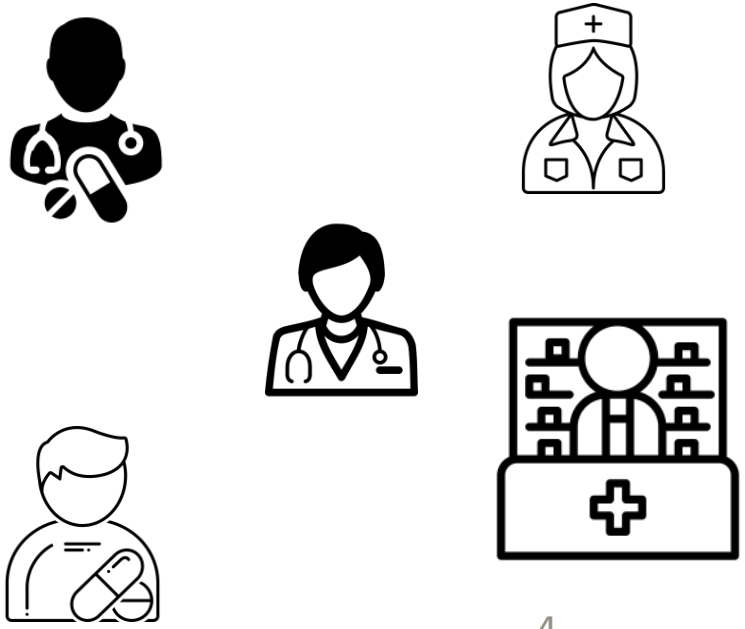
An EMA review in 2014[1] resulted in measures to strengthen the warnings and restrictions on the use of

Exposed pregnancies occured

Assess the effectiveness of measures from 2014

Different type of data and stakeholders involved

- Results of the formal requested HCP Survey and DUS
- Input from clinical practice
    - Neurologists
    - Psychiatrists
    - Stakeholders meeting (GPs, Pharmacists, gynecologists, other HCPs)
- Public Hearing



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An EMA review in 2014[1] resulted in measures to strengthen the warnings and restrictions on the use of

Despite the measures, exposed pregnancies occured!

Need to assess the effectiveness of measures from 2014 and

how valproate is used young women in clinical practice

Different type of data and stakeholders involved

HCP Survey + DUS

Results from imposed studies requested by PRAC performed by industry

Public hearing

Learned societies

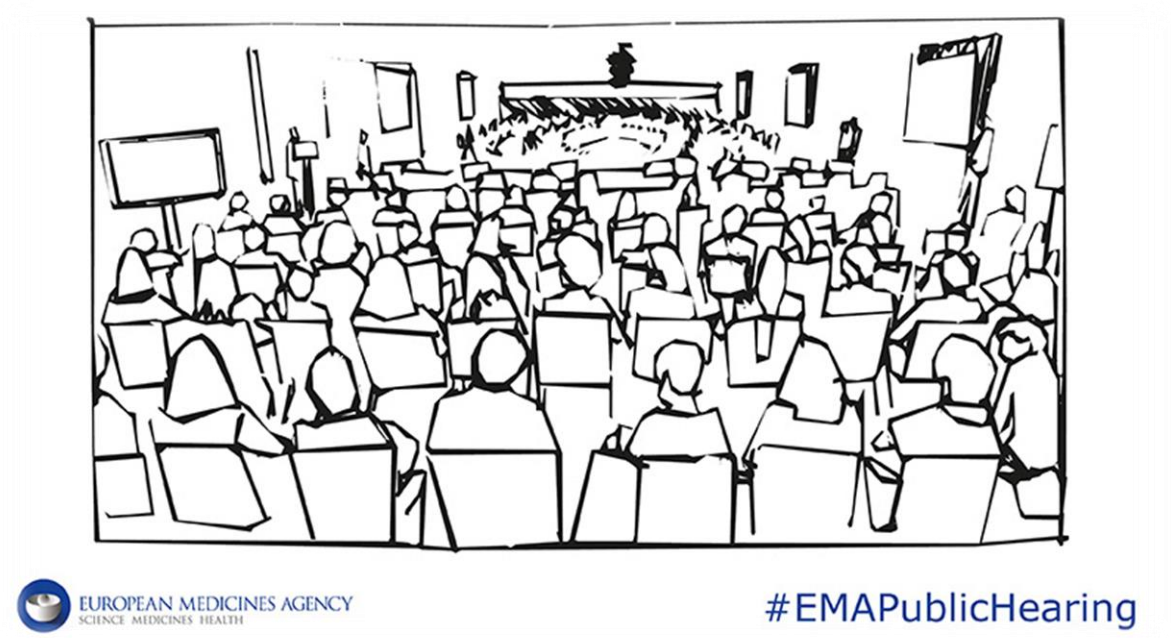
Representatives from clinical practice

EMA organised meetings with:
neurologists,
psyciatrists,
Other stakeholders: pharmacists, GPs, gynecologists, other HCP

Public hearing

Engaging with patients and healthcare professionals in the assessment of medicines

What are your experiences with valproate and the existing risk minimisation measures



Topics of included in the review…

- Discussion on the medical need of valproate for epilepsy and bipolar disorders during pregnancy
- Level of knowledge and awareness of the valproate risks among the different type of HCP and how they educate their patients
- Suggestions for improvement of the measures to avoid use during pregnancy
- How patients experieced the received education on the harmfull effects of valproate and the need for improvement

Review of the data

Joint DUS

- Period after implementation of the RMM (2015-2016) is short. No strong conclusions can be drawn.
- Overall, valproate use among WCBP decreased after Referral 2014, less pronounced for BP.
- Concomitant contraception was difficult to study

HCP Survey

- Educational materials did not reach all relevant HCPs (only 60%)
- Knowledge is better in those HCP that acknowledge receipt.

Other data

- Educational materials were not provided to all patients.
- There might be a different perception between HCP and patients about the information provided by the HCP and received/understood by the patient

Conclusion of Referral 2018

Benefit-Risk positive provided that :

Implementation of the measures should be improved

- Improved (online) materials, consistency
- Better defined target groups
- More frequent distribution to target group
- Patient card in pharmacy

Stricter measures should be implemented:

- Contraindication for use in pregnancy
- A pregnancy prevention plan
- Updated materials for HCP and patients
- Warning on all outer packagings

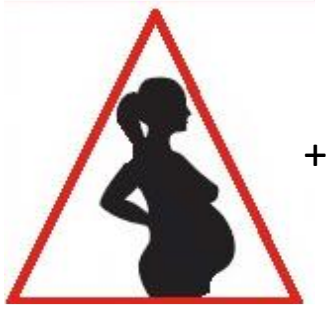
\+ effectiveness of updated measures to avoid valproate exposure during pregnancy will be evaluated

National implementation in NL

Pictogram for the outer packaging reviewed by 10 women via Pharos (Dutch Centre of Expertise on Health Disparities)

- Consulted NL Epilepsy and psychiatric patient organisations
- Consultedm NL professional associations for psychiatrists, pharmacy, and GPs

OR



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Warning for women and girls
This medicine can seriously harm an unborn baby.
Always use effective contraception during treatment with valproate.
If you are thinking about becoming pregnant, or if you are pregnant, contact your doctor urgently.
Do not stop valproate unless your doctor tells you to.

Lessons learned

1. Input from different stakeholders reflecting clinical practice was essential during the EU review of valproate

2. Combine various type of data and involve all relevant stakeholders can be very helpful
   - Complimentary
   - Confirmatory
   - Possibility to identify difference between countries / national implementation / type of HCP

3. Requested studies that evaluated RMM are useful

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Questions?

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