

# 12<sup>th</sup> Pharmacovigilance Stakeholder Forum

Listening to the Public. Case History - Valproate.  
Pharmacists Perspective

# Overview

1. Reflections on the 2014 review
2. UK Experience post 2014 review
3. PGEU survey of member organisations
4. Issues identified at the public hearing
  - General
  - Pharmacist
5. Important outcomes from the 2017 review.

# From the 2014 referral

- Recommendation to strengthen restrictions on the use of Valproate
- Doctors who prescribe Valproate provide women with full information to ensure full understanding of the risks
- Risks identified
- Recommendation for education materials to be provided to HC Professionals and to women prescribed valproate to inform them of the risks
- Doctors required to review treatment on a regular basis -inc. at puberty and when planning a pregnancy.

- **Outcomes:**

Education measures to ensure HCP's & patients informed

A guide for prescribers

A patient booklet

Drug Utilisation study to assess effectiveness of RMM's

Changes to SmPC

DHPC

# Actions in UK post 2014 referral

- Outcome of referral was communicated in UK through NHS cascade in January 2015
- Ongoing discussions with stakeholders about the role of the 'record of discussion form'
- Initial feedback from health professional and patient groups suggested message not getting through
- Importance of pharmacy profession in highlighting risks to women stable on treatment and under GP care led to consideration with Sanofi of a patient card and carton warning
  - MHRA July 2016

On Feb 8<sup>th</sup> 2016  
the Valproate  
toolkit was  
launched in the UK

### Valproate package warning label

“This medicine can seriously harm  
an unborn baby.  
Always use effective contraception  
during treatment.  
If you are thinking about becoming  
pregnant or you become pregnant  
talk to your doctor straight away .”

**UK Case study: sodium valproate (example of materials provided for use in pharmacy) <sup>9</sup>**

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Communication to Pharmacist

  
Letter to Pharmacists

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Educational Materials for Pharmacist

 HCP Card       HCP Booklet

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Prompts/Reminders in the Pharmacy

 Dispensary Shelf Sign       Dispensary Poster

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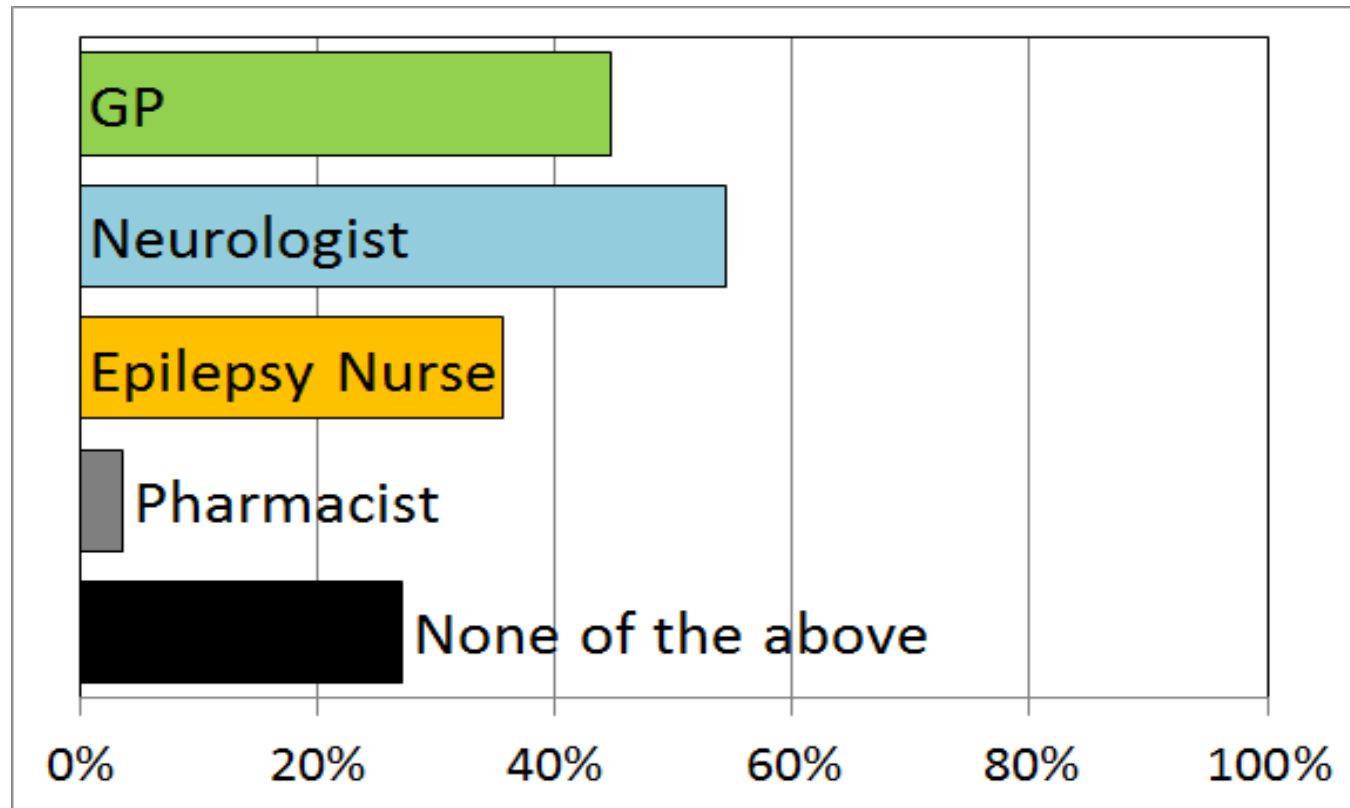
Educational Materials for Patient

 Patient Card       Patient Guide

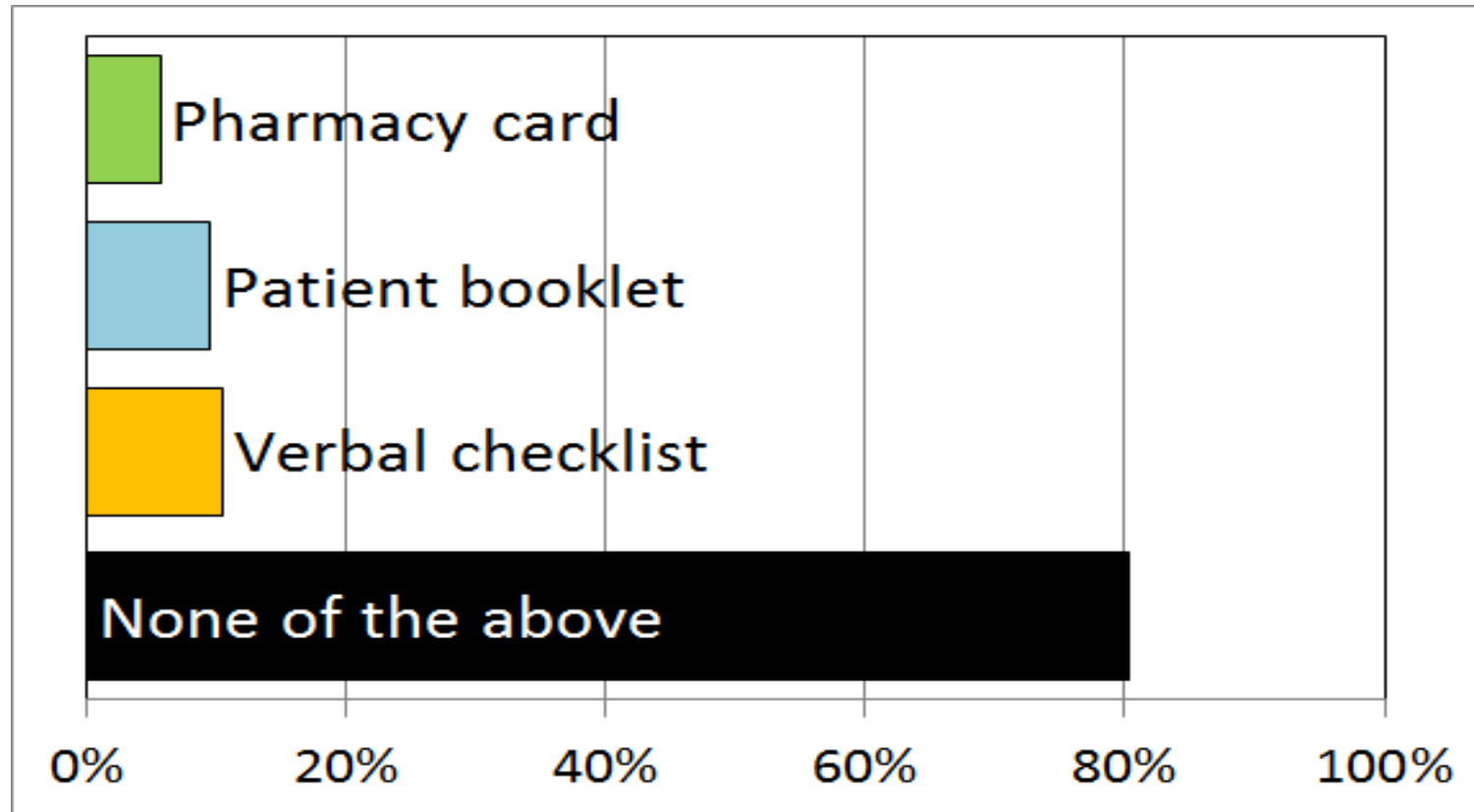
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<sup>9</sup> <http://www.medicines.org.uk/emc/medicine/23020>

Have any of the following ever started a discussion with you about Pregnancy and Sodium Valproate  
(Number taking Valproate 624)



Have you received any of the following items or advice from healthcare professionals in 2016? (Number responses = 557)





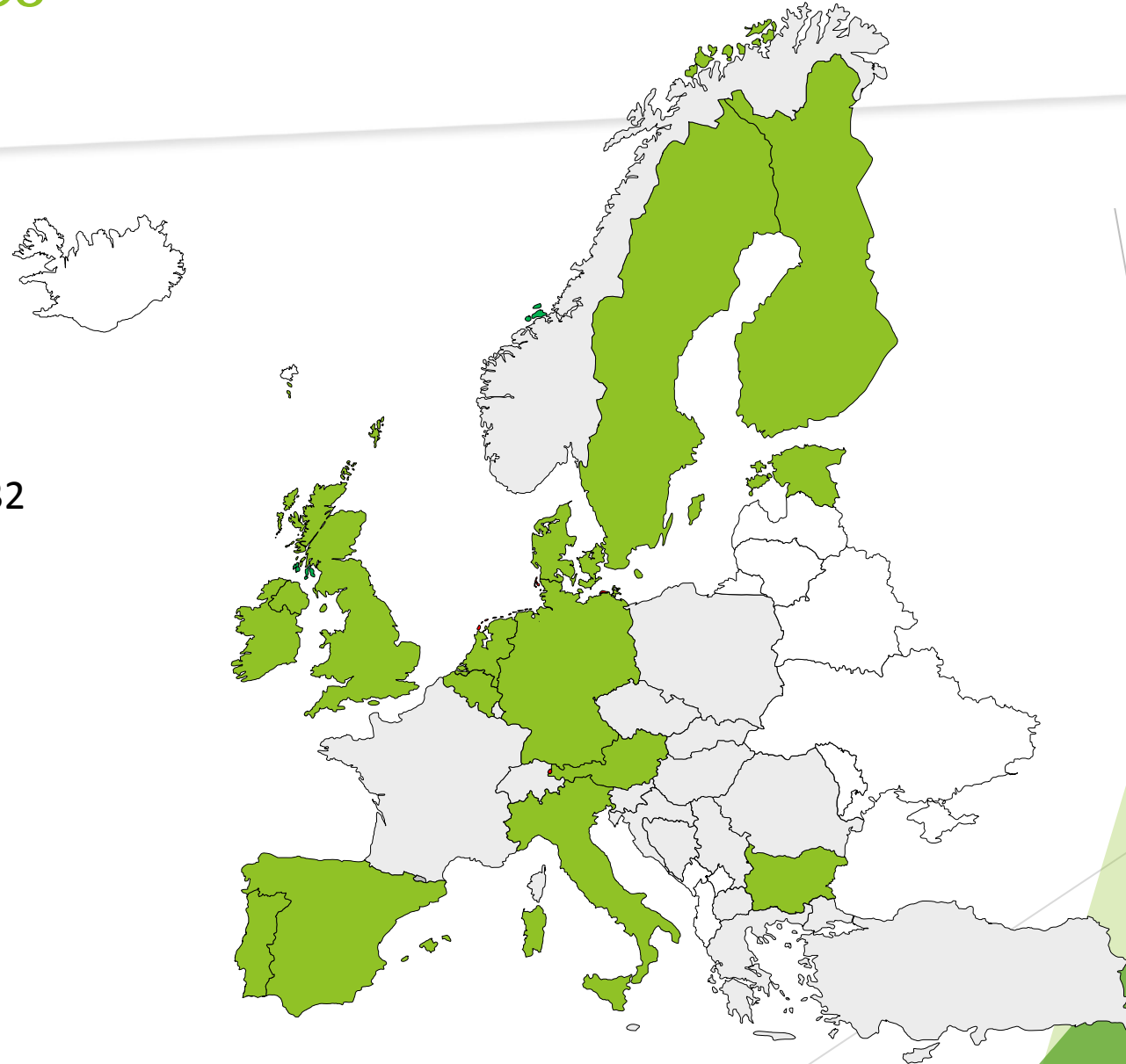
# PGEU Survey of Pharmacists in 2017

- Percentage of pharmacies that received material
- *Response rate 14/32 Countries (44%)*
- *More than 90% of pharmacies/pharmacists received the material in:*
  - > *Austria, Belgium, Estonia, Ireland, Netherlands, Portugal - (Total 6 countries)*
- *The material was spread mainly through online sources.*

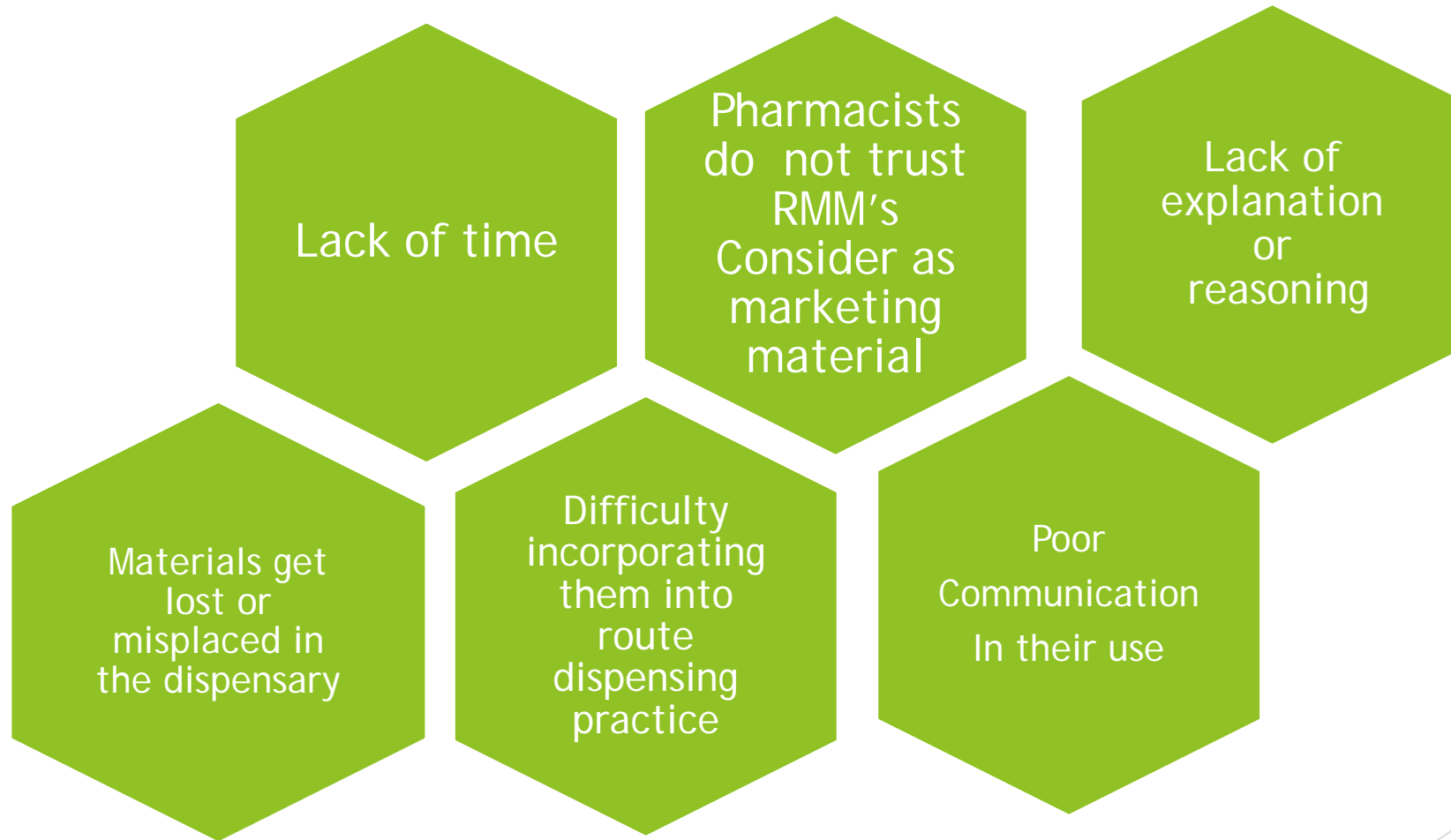


# Responses

-  Response 14/32
-  No response



# Barriers to implementation



# Facilitators to Implementation

Training

Support to  
incorporate  
into the  
dispensing  
process

Dispensing  
software  
updates /  
integration  
(e.g. for pop-  
up alerts)

Integration into  
medication  
reviews / new  
medicine  
services /  
counselling

# Key take home messages

- ▶ Full possible range of RMM materials has not been systematically distributed to pharmacists / pharmacies
- ▶ Biggest barrier was materials getting lost in dispensaries (mitigate by incorporating into e-communication / software / pharmacy services)
- ▶ RMM materials could be incorporated into pharmacists' CE/CPD/training
- ▶ RMMs could also feature in professional journals / articles / publications
- ▶ NCAs could facilitate interprofessional collaborations / groups
- ▶ Design of new RMMs / evaluation and review of existing measures should include early feedback from pharmacists to ensure effective implementation is achieved before further regulatory action is taken by EMA / NCAs

# Issues Identified during the Public Hearing

- ▶ 70% of women still not aware of the risks
- ▶ From 2007-2014 14,322 women got pregnant taking Valproate
- ▶ Dispensing - Packaging in Plastic Bags.
- ▶ Lack of PIL with product when dispensed
- ▶ 56% of women say they had discussion with HCP ( 44% did not)
- ▶ No box warning - (not mandated in 2014 outcome)
- ▶ Pack sizes (not aligned to prescribing quantities)
- ▶ Use of the toolkit disappointing (64% Of public never heard of it)

# Role of the Pharmacist presented at the public hearing

## Ways to improve the present system suggested:

- ▶ Professional development through professional publications
- ▶ Point of dispensing warnings
- ▶ R/v patients through enhanced services e.g. medicine use review or new medicine service.
- ▶ Need for multidisciplinary communication/collaboration
- ▶ Pharmacist having access to patient record
- ▶ Implementation of training on toolkit and raising awareness
- ▶ Include in CPD programmes
- ▶ Maximize pharmacists input into safety measures

## Remember

Pharmacists generally only have the information on a prescription available to them along with a dispensing record.

# Outcome from the 2017 referral

## New Must do's

- ▶ For Migraine and Bipolar disorder - Valproate now C/I in pregnancy
- ▶ Introduction of the Pregnancy prevention Programme
- ▶ Visual boxed text warning on the outer packaging with option of visual symbol/pictogram to be agreed at NCA level
- ▶ Patient reminder card to be attached to the outer packaging - a tool to aid discussion with patient at each time of dispensing
- ▶ Updated educational materials
- ▶ Packaging and pack sizes?

## Reflection on the difference from 2014

Tools to facilitate the process rather than simply imparting information

Need to ensure a timely implementation engaging professional bodies and stakeholders.

Pharmacies - public space, need to understand the way interactions take place with the patient. Consultation rooms now available in more pharmacies in more countries facilitating a private conversation/consultation.

FOR DISPENSARY USE ONLY

**prevent**  
valproate pregnancy prevention programme

**Valproate (Epilim):  
Pregnancy Prevention Programme**



Valproate should not be used in female children and women of childbearing potential unless other treatments are ineffective or not tolerated. Valproate must be prescribed and dispensed according to the Valproate Pregnancy Prevention Programme.

Children exposed to valproate are at a high risk of serious developmental disorders (in up to 30-40% of cases) and congenital malformations (in approximately 10% of cases).

**IMPORTANT ACTIONS FOR PHARMACISTS**

- ✓ Every time you dispense valproate to female children or women of childbearing potential, provide a Valproate Patient Card unless you dispense a valproate preparation and advise that the patient exclusively is a child.
- ✓ Explain carefully to the lady of childbearing potential the risks of valproate in pregnancy and advise her about effective contraception.
- ✓ If a woman of childbearing potential reports that she is not taking effective contraception, refer her to her GP.
- ✓ Dispense valproate in the original packaging with the outer carton remaining sealed and unopened. Where repackaging cannot be avoided always provide a copy of the package leaflet and a patient card and add a warning sticker to the bag into which the tablets are placed.
- ✓ Ask if the patient has received a Valproate Patient Guide and provide a copy if necessary.
- ✓ Present patients of this need for special attention.

www.hpra.ie

**Valproate (Epilim, Depakote, Convulex, Episenta, Epival, Kentlim, Orlept, Sodium Valproate, Syonell & Valpal)**

**Contraception and Pregnancy Prevention – Important information to know**

- Valproate is an effective medicine for epilepsy and bipolar disorder.
- Valproate can seriously harm an unborn baby when taken during pregnancy.
- Always use effective contraception at all times during your treatment with valproate.
- It is important to visit your specialist to review your treatment at least once each year.

These medicines are subject to additional monitoring. Report any side effects to [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard)


Keep this card safe so you always know what to do.

# Key Facts – Valproate and Pregnancy

Name:  Date:

- Valproate is an effective medicine used to treat epilepsy and bipolar disorder.
- Valproate can seriously harm an unborn child when taken during pregnancy and should be not taken by women and girls unless nothing else works.
- When taking valproate always use reliable contraception so you do not have an unplanned pregnancy.

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) for how to report side effects.



**WARNING FOR WOMEN AND GIRLS**

*Please read the Package Leaflet, Patient Guide and Patient Card for further information.*

**This medicine can seriously harm an unborn baby. Always use effective contraception during your treatment with Epilim.**

**If you are thinking about becoming pregnant, or if you are pregnant, contact your doctor urgently.**

**Do not stop taking this medicine unless your doctor tells you to.**

**Valproate**  
Patient Guide

This booklet is for you if you are a girl or a woman taking any medicine containing valproate.

It contains key information about the risks of valproate in pregnancy.

This guide was last updated in January 2016.

▼ This medicine is subject to additional monitoring. You will receive quick identification of new safety information. You can help by reporting any side effects you may get. See [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) for how to report side effects.

**Sodium Valproate**

**WARNING FOR WOMEN AND GIRLS**

This medicine can seriously harm an unborn baby. Always use effective contraception during treatment. If you are thinking about becoming pregnant, or you become pregnant, talk to your doctor straight away.



Thank You for your  
attention

Questions ?