Kent and Medway
NHS and Social Care Partnership Trust

Protocol for using valproate in women of childbearing potential

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DOCUMENT TRACKING SHEET

Protocol for using valproate in women of childbearing potential

Version	Status	Date	Issued to/approved by	Comments
1	Ratified: 3rd of October 2017	October 2017	Author: Jagdip Bahia	
2	Ratified: 5th December 2017	November 2017	Author: Jagdip Bahia	• New guidance published by the European Medicine Agency public hearing on valporate prescribing in pregnancy on 27th of September 2016 which recommends: **" Regular (at least annual) reviews for all women receiving long-term valproate were supported, to ensure that their understanding of the risks and benefits was updated appropriately as their life plans change"** • Prescriber checklist updated from 6 monthly reviews to annual reviews
3	Ratified: 7th of August 2018	August 2018	Author: Jagdip Bahia	• In May 2018 the MHRA strengthened its regulatory position on valproate medicines. Valproate must no longer be used in any woman or girl able to have children unless she has a pregnancy prevention programme in place. This is designed to make sure patients are fully aware of the risks and the need to avoid becoming pregnant. • Exclude pregnancy in women of childbearing potential (by serum pregnancy test) before the first prescription is issued. • Arrange for highly effective contraception for women of childbearing potential before the first prescription is issued. • Two checklists implemented in the guidance for prescribers. One for new female patients prescribed valproate and the other is for existing patients. • For patients who are assessed to lack capacity to consent to treatment then prescribing of valproate should be avoided. If a decision is made to initiate valproate then it should only be done on a KMPT inpatient ward after getting a second opinion from another Consultant. A best interest meeting needs to be arranged for all patients without the capacity to make an informed decision.

				• New Section 3 Action for pharmacists • Annual Risk Acknowledgment Form updated as per MHRA guidance
4		Dec 2018	Author: Jagdip Bahia	• The Royal College of Psychiatrists have published guidance for prescribers on the withdrawal of, and alternatives to, valproate-containing medicines in girls and women of childbearing potential who have a psychiatric illness.
5	TBC	May 2019	Author: Angie Lehman	• Updated Annual Risk Acknowledgement Form
6	**Final**	Ratified 2nd June 2020	Author: Angie Lehman **Approved by:** Drugs and Therapeutics Committee	• Updated contact details and email addresses • Updated flow chart
6.1			Author: Lola Ogungbangbe **Approved by:** Drugs and Therapeutics Committee	• Section 1 updated with NICE and RCOG guidance on diagnosing menopause in women • Updated to reflect absolute contraindication in pregnancy.
7	**Final**	Ratified 6th of April 2021	Author: Lola Ogungbangbe **Approved by:** Drugs and Therapeutics Committee	• Highlighting the message Valproate should **NEVER** be prescribed to pregnant women for the indication of bipolar disorder. • Detailed information on confirming absence of risk of pregnancy
8	**Final**	Ratified 7th of June 2022	Author: Jagdip Bahia **Approved by:** Drugs and Therapeutics Committee	• Initiation must be done by a Consultant Psychiatrist, but other responsibilities may be carried out by other healthcare professionals as part of a Consultant led team; Non-Medical Prescribers and Advanced Clinical Practitioners.

SUMMARY OF CHANGES

Date	Author	Page	Changes (brief summary)
March 2021	Lola Ogungbangbe	1	• Valproate should not be prescribed to women or girls of child bearing potential unless other treatments are ineffective or not tolerated. • Valproate should **NEVER** be prescribed to pregnant women for the indication of bipolar disorder.
March 2021	Lola Ogungbangbe	5	• New section 2.1.5 confirming absence of risk of pregnancy
July 2021	Jagdip Bahia	2	• Initiation must be done by a Consultant Psychiatrist, but other responsibilities may be carried out by other healthcare professionals as part of a Consultant led team; Non-Medical Prescribers and Advanced Clinical Practitioners in such teams should be considered as specialists for this situation, allowing them to complete annual reviews for continuation of treatment.

CONTENTS

1 BACKGROUND

- Valproate is a medication used in the treatment of epilepsy and bipolar disorder.

- Valproate is available in three formulations in the UK: sodium valproate, valproic acid and semisodium valproate.

- *In utero* exposure to valproate is associated with serious adverse effects for the developing child, including:

    - Congenital malformations. Affecting approximately 10% of cases, these include; neural tube defects (spina bifida, anencephaly), facial dysmorphia and cardiac malformations.
    - Developmental disorders. Affecting approximately 30-40% of cases, these can include an increased risk of autistic spectrum disorder (approximately three-fold increase in risk), childhood autism (approximately five-fold increase in risk) and delays in early development. There is evidence that children exposed to valproate *in utero* will go on to have a lower IQ than children exposed to other antiepileptic drugs.

- As a result of this risk, the MHRA published a Drug Safety Update (Valproate and risk of abnormal pregnancy outcomes: new communication materials) in February 2018 and the more recent Prevent - the valproate pregnancy prevention programme in May 2018, stating that:

    - Valproate should not be prescribed to women or girls of child bearing potential unless other treatments are ineffective or not tolerated.
    - Valproate should **NEVER** be prescribed to pregnant women for the indication of bipolar disorder.
    - Valproate may be initiated in women of childbearing potential only if the conditions of **prevent** (the valproate pregnancy prevention programme) are fulfilled. This is outlined in the prescriber checklist (see Section 2.1).
    - This treatment can only be started and supervised by a Consultant experienced in managing epilepsy or bipolar disorder.
    - Female patients and their carers should be counselled about the risk of taking valproate during pregnancy.
    - For females planning to become pregnant, all efforts should be made to switch to an appropriate alternative treatment prior to conception.

- The Drug Safety Update also stipulated communication materials which the MHRA have asked healthcare professionals to use when valproate is prescribed for females with childbearing potential. These communication materials have been incorporated into the protocol for valproate use set out in this document.

2 PRESCRIBING VALPROATE

2.1 Prescriber checklist

A: New female patients

- Initiation must **ONLY** be done by a Consultant Psychiatrist
- Ensure other treatments are ineffective or not tolerated before considering prescribing valproate and discuss the risks with the patient.
- Exclude pregnancy in women of childbearing potential (by serum pregnancy test) before the first prescription is issued (further details in Section 2.1.5)
- Arrange for highly effective contraception for women of childbearing potential before the first prescription is issued.
- Highly effective contraception includes methods such as the long acting reversible contraceptives (LARC), copper intrauterine device (Cu-IUD), levonorgestrel intrauterine system (LNG-IUS), progestogen-only implant (IMP) and female sterilisation, all of which have a failure rate of less than 1% with typical use.
- User dependent methods such as the condom, cap, diaphragm, combined oral contraceptive pill (COC) or progestogen-only contraceptive pill (POP) and fertility awareness based methods are not considered highly effective since the typical use incorporates user failure risks.
- Ensure patient understands the need to comply with contraception throughout treatment and undergo pregnancy testing when required- e.g. if there is any reason to suggest lack of compliance or effectiveness of contraception. Refer for contraception services as needed.
- Complete the Annual Risk Acknowledgment Form (see appendix 1) with patient, give them a copy, send a copy to the GP, upload to the patient's electronic RiO notes and send a copy to the KMPT Medicines Safety Officer (kmpt.mso@nhs.net). This risk form combines the MHRA's checklist requirements with KMPT specific requirements.
- Provide a copy of the Patient Guide to the patient. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/708849/123683_Valproate_Patient_Booklet_DR18.pdf
- Ensure that all women of child bearing potential have an annual review. This responsibility should be carried out by the Consultant Psychiatrist or other healthcare professionals as part of a Consultant led team including Non-Medical Prescribers (NMPs) or Advanced Clinical practitioners (ACPs) as long as it's in their scope of practice. In such teams NMPs and ACPs should be considered as specialists for this situation, allowing them to complete annual reviews for continuation of treatment. The Consultant should be available to support the NMP and ACP if any problems arise in completing the annual risk acknowledgment form.

B: Existing female patients on valproate

- Identify all women of childbearing potential on valproate and arrange for contraception if not already using contraception.
- Ensure patient understands the risks to the unborn child of using valproate during pregnancy and provide the Patient Guide (see link in Section A above)
- Ensure patient understands the need to comply with contraception throughout treatment and undergo pregnancy testing when required- e.g. if there is any reason to suggest lack of compliance or effectiveness of contraception.
- Tell patient to contact you immediately if she suspects there has been a problem with her contraception or she may be pregnant.
- Ensure patient has a copy of the Annual Risk of Acknowledgment Form (see appendix 1) signed by the Consultant Psychiatrist, a copy has been sent to the GP, uploaded to the

patient's electronic RiO notes and sent to the KMPT Medicines Safety Officer (kmpt.mso@nhs.net) .

- Remind the patient that they will need to see the Consultant Psychiatrist at least every year while taking valproate medicines for a review.
- The Royal College of Psychiatrists have provided guidance for prescribers on the withdrawal of, and alternatives to, valproate-containing medicines in girls and women of childbearing potential who have a psychiatric illness. The guidance summarises evidence for alternatives to valproate and provides advice on how women who are currently undergoing treatment with valproate medicines can be switched to alternative treatment. Available at: https://www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/position-statements/ps04_18.pdf?sfvrsn=799e58b4_2

2.1.1 Risk assessment

- Prescribers must read the Guide for Healthcare Professionals involved in the care of women and girls of childbearing potential using valproate medicines. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/708850/123683_Valproate_HCP_Booklet_DR15.pdf

- Prescribers must always carefully balance the benefits of valproate treatment against the risks. Valproate should only be used when other treatment options have been ineffective or have not been tolerated.

2.1.2 Capacity assessment

- Prescribers must ensure that the patient's capacity to consent to treatment has been assessed and has been documented in their medical notes.
- If patients are found to lack the capacity to consent to treatment, prescribers should follow the guidance in section 2.2 of this document.

2.1.3 Information provision

- It is the responsibility of the prescriber to ensure that the patient is provided with all necessary information about the risk posed by valproate use during pregnancy.

- Prescribers must ensure that the patient has been provided with a copy of the Patient Guide: What women and girls need to know about valproate. (See Section A:New Female Patients above for link)

- Prescribers must ensure that the patient has been informed about the need for effective contraception and has been given information about contraception methods.
- Prescribers must ensure that the patient has been informed to promptly contact them if she is planning a pregnancy or becomes pregnant.

2.1.4 Obtaining consent

- Prescribers should ask the patient to complete Step 3 of the Annual Risk Acknowledgment Form so that the patient understands the risks of taking valproate in pregnancy.

- The completed consent form must be uploaded to the patient's electronic RiO notes within clinical documentation and saved with the filename 'PREVENT dd/mm/yy'.

2.1.5 Risk reduction strategies

- Pregnancy testing:

  - Prescribers must ensure that a patient has had a negative pregnancy test prior to starting valproate.

  - The aim of pregnancy testing is to provide as much certainty as possible that the service user is not pregnant, *before* prescribing valproate.

  - Pregnancy testing relies on detection of human chorionic gonadotropin (hCG), which is released after a fertilised egg has implanted into the uterus wall.

  - Implantation normally occurs 6 to 12 days after ovulation. As hCG will not be released until after implantation, there is a delay between the time of fertilisation of an egg and the time at which a pregnancy is detectable.

  - In the early stages after implantation, an hCG serum assay more sensitively detects pregnancy than an hCG urine dip test.

  - Therefore, if there is any possibility that the patient has recently been sexually active, valproate should not be prescribed until:

    - 14 days have elapsed since the last possible day on which the patient could have had unprotected sex (for example, this could be 14 days from the point of admission, or 14 days from the last day on which the patient was given unescorted leave from the ward), AND FOLLOWED BY
    - A negative hCG serum assay has been obtained

  - For patients who have been admitted and who were already prescribed valproate in the community - if there is any possibility that the patient has recently had unprotected sex, valproate should be stopped. If clinically appropriate, the drug can be restarted provided that a negative serum hCG test has been obtained a minimum of 14 days after the last possible day on which the patient could have had unprotected sex.

- Advising about contraception:

  - Prescribers must advise patients on the need for effective contraception. These includes methods such as the long acting reversible contraceptives (LARC), copper intrauterine device (Cu-IUD), levonorgestrel intrauterine system (LNG-IUS), progestogen-only implant (IMP) and female sterilisation, all of which have a failure rate of less than 1% with typical use. The progesterone-only injectable is reported to have a typical use failure rate of 6 pregnancies per 100 women per year of typical use compared to 0.2 pregnancies with perfect use (thought to be due to the 3 monthly requirements for re-injection and lack of compliance with this).

  - User dependent methods such as the condom, cap, diaphragm, combined oral contraceptive pill (COC) or progestogen-only contraceptive pill (POP) and fertility awareness based methods are not considered highly effective since the typical use incorporates user failure risks.

- Patients should be provided with information about the types of contraception that are available, and have the opportunity to discuss the type that would suit them best.

- Prescribing folic acid:
  - Prescribers should consider prescribing folic acid supplements to all women of childbearing potential. Folic acid supplementation may decrease the general risk of neural tube defects but there is some evidence that it does not reduce the risk of birth defects associated with in utero.

2.1.6 Confirming absence of risk of pregnancy

- Where there are compelling reasons to suggest there is absence of risk of pregnancy, this should be specified on the risk acknowledgement form. These include:
  - Patients who are post-menopausal.
    - Women over 50 years old with at least 1 year history of amenorrhoea may be considered menopausal.
    - Consider using a Follicle Stimulating Hormone (FSH) test to diagnose menopause in women aged 40 to 50 years with menopausal symptoms, including a change in their menstrual cycle
  - Patients who have had a hysterectomy
- Where the absence of risk of pregnancy is permanent the risk acknowledgement form only needs to be completed once, where the absence of risk is temporary the next review date must be documented on the risk acknowledgement form.

2.2 Patients who lack capacity

- For patients who are assessed to lack capacity to consent to treatment then prescribing of valproate should be avoided. If a decision is made to initiate valproate then it should only be done on a KMPT inpatient ward after getting a second opinion from another Consultant and this should be documented in the patient's electronic RiO notes. A best interest meeting needs to be arranged for all patients without the capacity to make an informed decision. It is important to provide the information and advice on highly effective methods of contraception and on the use of valproate during pregnancy to their responsible person and make sure they clearly understand the content.

- If, after thorough consideration of the risks, it is concluded that the patient should continue to receive valproate after being transferred out of the inpatient ward, a clear risk-minimisation plan should be put in place and clearly documented in the patient's notes.

2.3 Patients who refuse information

- Occasionally patients may not wish to receive information when valproate is prescribed, or they may not currently be receptive to such information.

- In these circumstances, serious consideration should be given to delaying valproate treatment until the patient is willing and able to accept information about the risks posed by the drug.

- However, if the initiation of valproate is considered to be absolutely necessary, then the prescriber must complete the following actions:

    - Complete as much of the Annual Risk Acknowledgment Form (see appendix 1) as possible at the current time, and add this to the patient's notes.

    - Ensure that another attempt to provide the information to the patient is made at the earliest possible opportunity.

    - Make an entry in the patient's electronic RiO notes stating why it was not possible to complete the full checklist, and why it was considered necessary to prescribe the medication despite this.

    - Put a clear risk-minimisation plan in place. This may involve putting the patient on an increased observation level and restricting their leave from the ward until the valproate prescription has been stopped, or until the patient has received the necessary risk information about the drug. The plan must be clearly documented in the patient's notes.

2.4 Sharing information

- A copy of the Annual Risk Acknowledgment Form should be forwarded to the patient's GP along with their discharge summary or clinic letter.

- The GP should be asked to remind the patient about valproate's adverse effects at every consultation in which medication is discussed.

2.5 Monitoring and follow-up

- At all routine treatment reviews, prescribers must ensure that the benefits of valproate continue to outweigh the risks.

- For inpatients, the Annual Risk Acknowledgment Form must be completed when valproate is first prescribed and for any newly admitted patients who take the medication. The risks should be reemphasised to the patient when they first go on leave, and when they are discharged.

- For outpatients, the checklist must be completed when valproate is first prescribed by the Responsible Consultant and reviewed at least annually for all women receiving long-term valproate. This is to ensure that their understanding of the risks and benefits is updated appropriately as their life plans change.

- If the patient's care is transferred back to the GP then there should be a plan agreed for the Responsible Consultant to continue with the annual reviews. A copy of the completed Annual Risk Acknowledgment Form should be forwarded to the patient's GP along with their discharge summary or clinic letter.

- The consultant needs to email the form to the medicine safety officer at kmpt.mso@nhs.net for every woman who is prescribed valproate and is of child bearing age in order for the Trust to keep a database of these details.

- Suspected side effects to valproate should be reported via the Yellow Card reporting scheme (https://yellowcard.mhra.gov.uk/) and recorded on the Trust DATIX system.

3 ACTION FOR PHARMACISTS

- When valproate is dispensed for a woman of childbearing potential on an inpatient ward, it is the responsibility of the pharmacist to ensure she is provided with a Patient card, unless she confirms that she already has one. For community patients who are prescribed valproate a patient card can be obtained from the locality KMPT pharmacy team.

  KMPT Pharmacy team- Canterbury - 01227 812193
  KMPT Pharmacy team- Dartford - 01322 622070
  KMPT Pharmacy team- Maidstone - 01622 723219
  KMPT Pharmacy team- Medway - 01634 968472 ext 22472

- The pharmacist must encourage the patient to read the card and enter her name and current date in the spaces provided.
- Pharmacist should remind patients of the risks in pregnancy and the need for highly effective contraception
- Remind patients of the need for annual specialists review
- Ensure the patients has received the Patient Guide (See link in Section A:new female patients)

4 FURTHER INFORMATION

- Further information can be accessed via Pregnancy Prevention Programme materials online. Available at:
  https://www.gov.uk/drug-safety-update/valproate-medicines-epilim-depakote-pregnancy-prevention-programme-materials-online

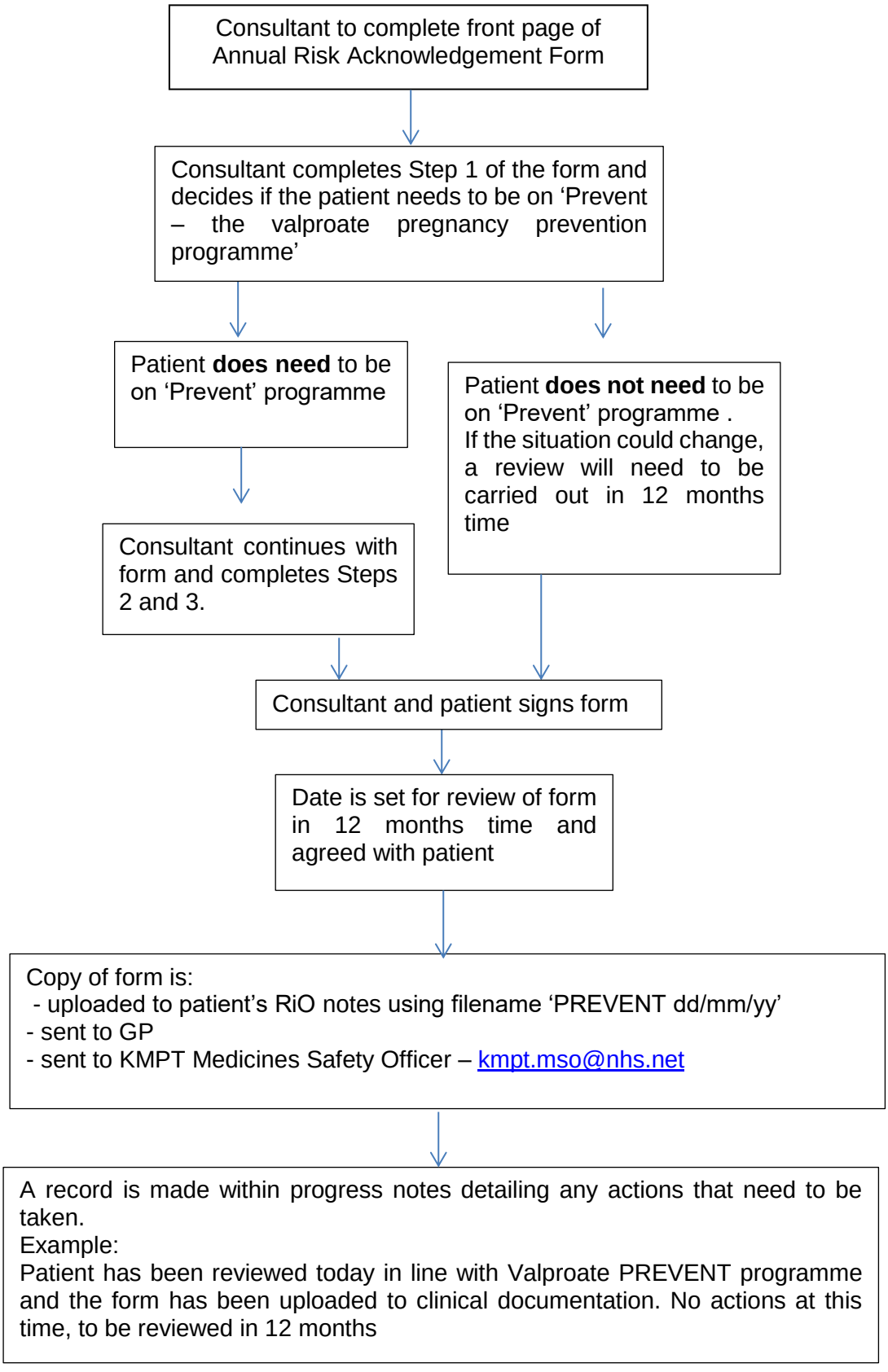
- The link above provides printable versions of the communication materials mentioned in this document:
  - Patient Card – to be given by pharmacists to all female patients who are dispensed valproate medicines to inform them of the risks
  - Patient Guide – to be provided to girls (of any age) and women of childbearing potential (or their parent/caregiver/responsible person) taking any medicine containing valproate
  - Guide for Healthcare Professionals – for all prescribers, pharmacists, and other healthcare providers involved in the care of women and girls of childbearing potential using valproate medicines
  - Risk Acknowledgement Form – for the specialist and patient (or their parent/caregiver/responsible person) to sign at initiation and at treatment reviews at least every year. The patient should receive a copy of the form; one copy should be filed in the specialist notes, and one copy sent to the patient's GP

- Hard copies of these materials can be ordered by contacting the Sanofi Medical Information Department on 0845 372 7101, or via e-mail UK-Medicalinformation@sanofi.com

- More detailed information about valproate can be obtained by consulting the most recent Summary of Product Characteristics (SPC), available online through the eMC website (www.medicines.org.uk)

- Pregnancy testing information obtained from: Bastian LA and Brown HL. *Clinical manifestations and diagnosis of early pregnancy.* From “UpToDate®” clinical resource (Wolters Kluwer), Topic 440, Version 32.0. Topic last updated: 4th January 2016.

Annual Risk Acknowledgment Form



Annual Risk Acknowledgement Form
VALPROATE HAS RISKS IN PREGNANCY

Name of valproate user: _____ **Date of Birth:** _____

Identification (NHS or hospital) number: _____

Name and role of specialist: _____

Signature of specialist and date: _____

Name of valproate user's GP: _____

Children exposed to valproate in utero have a very high risk for congenital malformations and neurodevelopmental disorders. Valproate is therefore contraindicated in women of childbearing potential unless the conditions of 'prevent', the pregnancy prevention programme are fulfilled.

The specialist must provide this form to girls and women of childbearing potential treated with valproate (Epilim, Depakote, Convulex, Episenta, Epival, Kentlim, Orlept, Syonell, Valpal, Belvo) – or to their "responsible person": a parent/legal guardian or person capable of giving consent on behalf of patients who are minors or without the capacity to make an informed decision or person acknowledging that the treatment is in the best interests of the patient.

There are three steps needed to complete this form:

Step 1 – Decide if the patient needs to be on 'prevent' – the valproate pregnancy prevention programme

Step 2 – 'prevent' applies to this patient- she is of childbearing potential and at risk of pregnancy

Step 3 – Your patient needs to complete this section to confirm they understand the risks of valproate in pregnancy

WARNING: Prescribing valproate to a woman of childbearing potential without the pregnancy prevention programme conditions being fulfilled is contraindicated and represents an unlicensed use of the drug. Use of valproate during pregnancy for bipolar disorder, and during pregnancy for epilepsy (unless there is no suitable alternative treatment), are both unlicensed. This is the case even when treatment is based on an informed choice made by the patient.

Prescribers are expected to follow the General Medical Council's guidance in *"Good practice in prescribing and managing medicines and devices".* You must document in the patient's clinical record your reason for unlicensed use, that you have informed the patient of the unlicensed use and its associated risk.

This form expires on_____(12 months after completion).

Complete a new form at each annual review.

More information can also be found online at www.medicines.org.uk by entering "valproate" in the search box and then clicking on "Risk Materials" next to any of the medicines that appear.

Annual Risk Acknowledgement Form
VALPROATE HAS RISKS IN PREGNANCY

Step 1 – Decide if the patient needs to be on 'prevent' – the valproate pregnancy prevention programme

- Women of childbearing potential (from menarche to menopause) who are taking any medicine containing valproate, regardless of the indication, should fulfil all the requirements of **'prevent'**.
- The only exception is when you (the specialist) consider that there are compelling reasons to indicate that there is no risk of pregnancy.
- The absence of risk of pregnancy may be permanent (e.g., post-menopausal patients or those after hysterectomy) and in this case the risk does not need to be discussed in the next annual review and the requirements of **'prevent'** do not apply.
- If the absence of risk is subject to change (e.g., the patient is pre-menarchal), the date for the next annual discussion of the risks must be documented and the patient or the patient's family/carers asked to contact you rapidly if the situation changes before the next annual review in order to bring this review forward.
- Girls who have not yet reached menarche **DO NOT** need to be on **'prevent'**, but they and their responsible person need to be aware of the risks for the future. You should provide a copy of the Patient Guide, and remind the responsible person to contact the specialist or GP to arrange for review of treatment as soon as menarche occurs.

If you consider there is a compelling reason that indicates there is no risk of pregnancy, record this here. **If appropriate, you and your patient should still complete the rest of the form** so that your patient and/or their responsible person is aware of the risks if their situation were to change in the future.

To be completed by the specialist when they consider a Pregnancy Prevention Programme (PPP) is not needed
The requirements of **'prevent'**, the valproate pregnancy prevention programme, are not necessary because there are compelling reasons to indicate that there is no risk of pregnancy, because (*tick* which applies):
☐ the patient has not yet reached menarche. I have informed the patient and family to inform me if this changes before the next annual review which is due on *(insert date)*:
☐ the absence of pregnancy risk is permanent for the following reason *(insert reason)*:
☐ I consider that sexual activity that could lead to pregnancy will not occur before the next annual review because *(insert reason)*:
☐ I have given the patient or responsible person a copy of the Patient Guide
Signature of patient or responsible person to confirm:

More information can also be found online at www.medicines.org.uk by entering "valproate" in the search box and then clicking on "Risk Materials" next to any of the medicines that appear.

Annual Risk Acknowledgement Form
VALPROATE HAS RISKS IN PREGNANCY

Step 2 – 'prevent' applies to this patient- she is of childbearing potential and at risk of pregnancy

This form confirms that you have discussed the risks with girls, women of childbearing potential and their responsible person (if applicable), and you are acting in compliance with the pregnancy prevention programme.

You need to:

- Explain the risks of valproate in pregnancy and ensure these are understood.
- Give your patient (or their responsible person) a copy of the Patient Guide.
- Complete all parts of this form, keep the original in the patient record and provide a copy to the patient, her responsible person (if appropriate), and to her GP.
- Arrange a follow-up appointment at least every year to review the need for continued treatment with valproate and compliance with **'prevent'**.

To be completed and initialled by the specialist	Initials
I confirm that the patient needs valproate because: • her condition does not respond adequately to other treatments, or • she does not tolerate other treatments, or • she is undergoing a treatment change from valproate **I confirm I have discussed the following with the patient:**	
Valproate must not be used during pregnancy (except in rare situations in epilepsy for patients who are resistant or intolerant to other treatments)	
The overall risks in children exposed to valproate during pregnancy are: • an approximately 10% chance of birth defects • a 30% to 40% chance of a wide range of early developmental problems that can lead to learning disabilities.	
The conditions of the pregnancy prevention programme must be fulfilled	
The need for regular (at least annual) review of the need to continue valproate treatment by a specialist	
The need for effective contraception, without interruption, throughout treatment with valproate	
The need to arrange an appointment with her specialist as soon as she is planning pregnancy to ensure timely discussion, and a timely switch to an alternative treatment before stopping contraception and conception occurring.	
The need to contact her GP immediately for an urgent review of her treatment in case of suspected or inadvertent pregnancy.	
The need for a negative (ideally serum) pregnancy test result at start and if needed thereafter	
I confirm I have given the patient or responsible person a copy of the Patient Guide	
In case of pregnancy, I confirm that:	
• We have discussed options for switching treatment	
• She is fully aware of the risks of pregnancy, and has had the opportunity for counselling about the risks	
• I have given the patient or responsible person a copy of the Patient Guide	

More information can also be found online at www.medicines.org.uk by entering "valproate" in the search box and then clicking on "Risk Materials" next to any of the medicines that appear.

Annual Risk Acknowledgement Form
VALPROATE HAS RISKS IN PREGNANCY

Step 3 – Your patient needs to complete this section to confirm they understand the risks of valproate in pregnancy

If you use valproate while you are pregnant, your future child has significant risk of serious harm.

Completing this form confirms that you (or your responsible person) understand the risks of using valproate during pregnancy, and what method of contraception you will use to prevent becoming pregnant during treatment.

To be completed and signed by the patient or their responsible person	Initials
I have discussed the following with my specialist and I understand:	
√ Why I need valproate rather than another medicine	
√ That I should visit a specialist regularly (at least once a year) to review whether valproate remains the best option for me	
√ The risks in children whose mothers took valproate during pregnancy are: • 1 out of 10 children will have physical birth defects • 3 to 4 out of 10 children will have early developmental problems that can lead to significant learning disabilities	
√ That I have had a pregnancy test (if advised by my doctor/specialist)	
√ Why I must use effective contraception, without stopping or interruption, at all times while taking valproate	
√ The options for effective long-term contraception (or a consultation has been planned with a professional who can give me advice)	
√ The need to consult my specialist or GP as soon as I start thinking about becoming pregnant. This is to make sure I have time to switch to another treatment before I come off contraception	
√ That I should request an urgent GP appointment if I think I am pregnant	
√ I have been given a copy of the Valproate Patient Guide and know where to find more information	
In case of pregnancy, I confirm that: √ Options for switching treatment have been considered √ I am fully aware of the risks and have had the opportunity to have counselling about the risks	

Name of patient: _____

Name of responsible person (if applicable): _____

Signature of patient (or responsible person) and date: _____

Effective contraception is essential while taking valproate.

At least one highly effective method of contraception (preferably a user independent form such as an intrauterine device or implant) or two complementary forms of contraception including a barrier method should be used. Individual circumstances should be evaluated in each case. When choosing the contraception method involve the patient in the discussion to guarantee her engagement and compliance with the chosen measures. Even if she has amenorrhoea she must follow all the advice on highly effective contraception.

More information can also be found online at www.medicines.org.uk by entering "valproate" in the search box and then clicking on "Risk Materials" next to any of the medicines that appear.