Essex Partnership University
NHS Foundation Trust

SECTION 3: MANAGEMENT OF BIPOLAR AFFECTIVE DISORDER

Formulary and Prescribing Guidelines

This section provides information regarding the pharmacological management of Bipolar affective disorder in secondary care. Readers should consult literature to gain a further understanding of the psychological strategies which may be employed or for further guidance relating to management in primary care (see NICE CG185).

3.1 Approved Mood stabilisers

Drug	Formulation		Comment
Aripiprazole	Tabs 5mg, 10mg, 15mg, 30mg Orodispersible tabs 15mg, 30mg Liquid 1mg/ml		Generic aripiprazole is only licensed in schizophrenia.
Asenapine (for mod/severe manic episodes associated with bipolar if alternatives unsuccessful)	S/L tablets 5mg, 10mg Consultant initiation & on-going prescribing only – consider switching once pt. stable.		Acute phase bipolar 1.
Carbamazepine	Tablets 100mg, 200mg, 400mg M/R tablets 200mg,400mg Liquid 100mg/5ml		For mood disorder use sustained release preparation.
Lamotrigine	Tablets 25mg, 50mg, 100mg 200mg Dispersible tablets: 5mg, 25mg, 100mg		
Lithium **Carbonate** (tablets)	Priadel: M/R tablets 200mg, 400mg (scored)		Bioequivalence varies widely between brands and salts
	Camcolit:400mg (scored) Tabs Essential Pharma 250mg Tabs (Bioequivalent to Camcolit - rebranded)		
Lithium **Citrate** (liquids)	Li-liquid	Yellow liq. 509mg/5ml (=200mg of Lithium tab) orange liq. 1.018g/5ml (=400mg of Lithium tab)	Bioequivalence varies widely between brands and salts
	Priadel: Liquid 520mg/5ml (=204mg of Lithium tab) NB. Exact conversion not required for Priadel.		
Olanzapine	Tabs 2.5mg, 5mg, 10mg, 15mg, 20mg Orodispersible tabs 5mg, 10mg, 15mg, 20mg		
Quetiapine	Tabs 25mg, 100mg, 150mg, 200mg, 300mg M/R tabs 50mg, 150mg, 200mg, 300mg, 400mg		Liquid not approved, immediate release tablets to be crushed.
Risperidone	Tabs 0.5mg, 1mg, 2mg, 3mg, 4mg, 6mg Orodispersible tabs 0.5mg,1mg, 2mg,3mg, 4mg Liquid 1mg/ml		
Sodium Valproate	Tablets 100mg, 200mg, 500mg M/R tablets 200mg,300mg,500mg M/R capsules 150mg, 300mg Liquid 200mg/5ml Other formulations e.g. Episenta granules, Epilim Chronosphere		Contraindicated in females of childbearing potential unless they meet the conditions of a Pregnancy Prevention Programme,
Semisodium Valproate (Depakote)	Tabs 250mg, 500mg		Contraindicated in females of childbearing potential unless they meet the conditions of a Pregnancy Prevention Programme,

Drug	Formulation	Comment
For EPUT use only, not to be initiated or continued by primary care prescribers: Omega-3 acid ethyl esters. Some evidence for improvement in bipolar disorder. Advise patient to purchase if possible. Review concordance.		

Notes

- Due to variations in bioavailability between brands of lithium, products are not interchangeable. New prescriptions for tablets will be for Priadel unless clearly indicated otherwise. If a patient is already maintained on a different brand, this should be indicated on the prescription. Changing brands requires the same precautions as initiation. It is acceptable to convert someone who is taking 5ml Priadel liquid (204mg) to 200mg Priadel tablet or vice versa.
- If a patient is admitted on lithium no supply will be made (and the patient's own supply of lithium must be quarantined) until a lithium level is received. (This may mean taking an emergency blood lithium level). Baseline checks should be completed and confirmed to be satisfactory as soon as possible after admission, i.e. a 12 hour post dose lithium level has been received and is not above the therapeutic level, and kidney function tests demonstrate that prescribing lithium is still appropriate for the patient. This will prevent inadvertent administration to a patient for whom lithium is now contra-indicated and might cause harm. Any dose given without the full baseline checks being completed should not exceed 400mg.
- Valproate m/r tablets can be administered once daily to aid patient adherence.
- Valproate Semisodium ("Depakote") is licensed for the treatment of mania in bipolar disorders. Sodium Valproate may be used in bipolar mania, but these formulations are unlicensed.
- There is emerging evidence for the mood stabilising effects of atypical antipsychotic drugs. Olanzapine, Aripiprazole, Risperidone, Quetiapine as well as Semisodium Valproate, within their licensed indications, are recommended as options for control of the acute symptoms associated with the manic phase of bipolar disorder. Of the drugs available for the treatment of acute mania, the choice of which to prescribe should be made jointly between the individual patient and the clinician. In all situations where informed discussion is not possible advance directives should be taken fully into account and the individual's advocate and/or carer should be consulted.
- Generic aripiprazole is only licensed in schizophrenia.
- Valproate medicines must not be used in women or girls of childbearing potential unless a Pregnancy Prevention Programme is in place[7] and the conditions met, and only if other treatments are ineffective or not tolerated, as judged by an experienced specialist. Ensure all women and girls (and their parent, caregiver, or responsible person, if necessary) are fully informed of the risks and the need to avoid exposure to valproate medicines in pregnancy. Specialists must book in review appointments at least annually with women and girls under the Pregnancy Prevention Programme, check they are on highly effective contraception (taken without interruption), and re-evaluate treatment as necessary; explain clearly the conditions as outlined in the supporting materials (the "toolkit")[8] ;provide a "Patient Guide"[8] to girls (of any age) and women of childbearing potential (or their parent/caregiver/responsible person) who are started on or are continuing to use valproate medicines; and complete and sign the Annual Risk Acknowledgement Forms (Appendix 2)—a copy of the form must be filed in the patient's record, a copy given to the patient or patient/caregiver/responsible person, and a copy sent to their GP.
- As with all teratogenic medicines, pregnancy should be excluded before initiation on valproate medicines, with a negative plasma pregnancy test, confirmed by a healthcare professional. Women and girls of childbearing potential must use highly effective contraception if they are able to become pregnant (see guidance from Faculty of Sexual and Reproductive Health [FSRH] https://www.fsrh.org/news/fsrh-ceu-statement-on-contraception-for-women-using-known/). Methods of contraception considered 'highly effective' in this context include the long-acting reversible contraceptives (LARC): copper intrauterine device (Cu-IUD), levonorgestrel intrauterine system (LNG-IUS), and progestogen-only implant (IMP), and male and female sterilisation, all of which have a failure rate of less than 1% with typical use (see guidance from FSRH for more about user-independent methods and failure rates). If a user-independent form is not used, two complementary forms of contraception including a barrier method should be used and regular pregnancy testing considered. Individual circumstances should be, in each case, evaluated when choosing the contraception method, involving the patient in the discussion to guarantee her engagement and compliance with the chosen measures.[7]

- If the patient becomes pregnant on valproate, consideration should be given to tapering the valproate down carefully, while introducing suitable alternative drug treatment. Treatment of BPAD in children & adolescents and antenatal & postnatal services users is discussed in section 12 and section 20 respectively. Additional information regarding prescribing in older adults can also be found in section 11.

- The management of lithium in secondary care is described below and in Appendix 1. The shared management of lithium between primary and secondary care is described in the document Shared Care Protocol for the Prescribing and Monitoring of Lithium. It includes useful information on prescriber, patient and carer responsibilities, dosing and monitoring of lithium, cautions, contraindications, interactions, and advice on lithium toxicity.

3.2 Management of Mania/Hypomania

Of the drugs available for the treatment of mania, the choice of which to prescribe should be made jointly between the individual patient and the clinician. In all situations where informed discussion is not possible advance directives should be taken into account and the individual's advocate and/or carer should be consulted when appropriate.

Pre-monitoring and on-going monitoring should be undertaken in line with section 2 of the F&PG, NICE CG185 and specific SPC requirements for a named drug. Clinical judgement should also be used to determine if additional monitoring is required for the individual service user.

- If a person is taking an antidepressant as monotherapy, consider stopping the antidepressant and offering an antipsychotic – regardless of whether the antidepressant is stopped

- If the person develops mania or hypomania and is not taking an antipsychotic or mood stabiliser offer haloperidol, olanzapine, quetiapine, risperidone (or aripiprazole), taking into account advanced statements, the person preference and clinical context (including physical comorbidity, previous response to treatment and side effects)

- If the first antipsychotic is poorly tolerated or ineffective at the maximum licensed dose offer an alternative

- If the alternative is not effective at the maximum dose consider adding lithium. If lithium is ineffective or unsuitable consider valproate instead (not for women of child bearing age).

- If the person is taking an antidepressant in combination with a mood stabiliser already, consider stopping the antidepressant.

- If the person is already taking lithium, check plasma levels to optimise treatment. Consider adding an antipsychotic depending on previous response.

- If the patient is already taking valproate or another mood stabiliser as prophylactic treatment consider increasing the dose (up to maximum level in BNF). If there is no response consider adding an antipsychotic.

- Within 4 weeks of symptom resolution, discuss with the person/carers whether to continue treatment or start long term treatment. Explain potential benefits and risks of long term, including side effects. If the person decides to continue treatment offer it for a further 3 to 6 months then review.

- Do not offer lamotrigine to treat mania.

For all patients consider adding short-term benzodiazepine (lorazepam or clonazepam).[1]

3.3 Treatment of Bipolar Depression

Not currently receiving treatment

- If a person develops moderate to severe bipolar depression and is not taking a drug to treat their bipolar depression, offer fluoxetine combined with olanzapine **or** quetiapine monotherapy, depending on the person's preference and previous response to treatment.

- If the person prefers, consider either olanzapine monotherapy or lamotrigine monotherapy

- If there is no response to fluoxetine with olanzapine or quetiapine monotherapy consider lamotrigine monotherapy.

Currently taking lithium

- If a person develops moderate to severe bipolar depression and is taking lithium check lithium plasma levels and if necessary increase dose.

- If at maximum lithium dose, add either fluoxetine with olanzapine **or** quetiapine depending on the person preference or previous response to treatment.

- If the person prefers, consider adding olanzapine (without fluoxetine) or lamotrigine to lithium therapy.

- If there is no response to adding fluoxetine combined with olanzapine or quetiapine, or adding quetiapine, stop the additional treatment and consider adding lamotrigine to lithium.

Currently taking valproate (not women of child bearing age)

- If a person develops moderate to severe bipolar depression and is taking valproate consider increasing the dose within the therapeutic range.

- If the maximum tolerated dose, or the top of the therapeutic range has been reached and there has been limited response with valproate add fluoxetine combined with olanzapine **or** add quetiapine alone.

- If the person prefers, consider adding olanzapine (without fluoxetine) or lamotrigine to valproate.

- If there is no response to adding fluoxetine with olanzapine or quetiapine alone, stop the additional treatment and consider adding lamotrigine.

- Within 4 weeks of resolution of symptoms, discuss with the person whether to continue treatment for bipolar depression or start long term treatment. Explain the benefits and risks associated with long term treatment and potential side effects. If the person decides to continue with treatment for bipolar depression offer medication for 3 to 6 months and then review.

3.4 Prophylactic Treatment of Bipolar Affective Disorder

After each episode of mania or bipolar depression, discuss with the person, and their carers if appropriate, managing their bipolar disorder in the longer term. Discussion should aim to help people understand that bipolar disorder is commonly a long-term relapsing and remitting condition that needs self-management and engagement with primary and secondary care professionals and involvement of carers.

When planning long-term pharmacological treatment to prevent relapse, take into account drugs that have been effective during episodes of mania or bipolar depression. Discuss with the person whether they prefer to continue this treatment or switch to lithium, and explain that lithium is the most effective long-term treatment for bipolar disorder.

- Offer lithium as a first line, long term treatment for bipolar disorder and if it is ineffective consider adding valproate (not in women of child bearing age).

- If lithium is poorly tolerated or is not suitable (e.g. person does not agree to blood monitoring) consider valproate or olanzapine OR if has been effective during an episode of mania or depression, consider quetiapine.

- If stopping long-term treatment discuss with the person early signs of relapse and what to do if symptoms recur. Treatment should be stopped gradually (at least 4 weeks, see BNF).

- Carbamazepine may be used under specialist supervision for the prophylaxis of bipolar disorder in patients unresponsive to a combination of other prophylactic drugs; it is used in rapid cycling manic depressive illness (4 or more episodes/year). The dose should not normally be increased if an acute episode of mania occurs[5]

3.5 Rapid Cycling disorder management

Rapid cycling disorder is usually defined as bipolar disorder where there have been 4 or more episode of mania/hypomania or depression within a 12 month period. There is relatively little evidence supporting strategies and response to treatment tends to be less pronounced compared to ‘typical’ bipolar disorder.

- Consider withdrawal of antidepressants in all patients[1]
- Consider a combination of lithium and valproate
- For patients already taking lithium consider keeping towards top end of therapeutic level.
- For the management of depressive symptoms, avoid the use of an antidepressant. Instead, consider increasing the dose of the antimanic agent or the addition of a second antimanic agent (including lamotrigine). On occasions, and on advice from a specialist in bipolar disorder, antidepressants can be considered. When a patient is in remission from depressive symptoms (or symptoms have been significantly less severe for 8 weeks), stopping the antidepressant medication should be considered, to minimise the risks of switching to mania and increased rapid cycling
- Consider combinations of lithium or valproate with lamotrigine, especially in bipolar II disorder

3.6 Monitoring Physical Health

See Appendix 1~~Appendix 1~~ *for monitoring required for Lithium, Carbamazepine and Valproate. See Section 2 appendices for physical health monitoring relating to antipsychotics*

There is growing concern about the physical health of service users with bipolar disorder.

If a person gains weight during treatment their medication should be reviewed, and the following considered:

- Dietary advice and support from primary care and mental health services
- Advising regular aerobic exercise
- Referral to relevant health services for specific programmes to manage weight gain
- Refer to a dietician if the person has complex co-morbidities (e.g. coeliac disease).
- Drug treatments such as sibutramine are not recommended to promote weight loss.

A physical health review is needed to ensure that the following are assessed at least each year

- Fasting lipid levels, including cholesterol in all patients over 40 even if there is no other indication of risk.
- Fasting plasma glucose levels
- Blood pressure
- Weight
- Smoking status and alcohol use

References

1. South London & Maudsley NHS Foundation Trust Prescribing Guidelines 12th edition, Wiley Blackwell, 2015
2. Psychotropic Drug Directory 2016, Bazire S., Page Bros Ltd
3. Summary of Product Characteristics for Individual Drugs [accessed May 2017], sodium valproate (Epilim) accessed 23/5/2018.
4. BNF on-line, Current edition, Accessed 23/5/2018.
5. NICE Clinical guideline [CG185]. Bipolar disorder: assessment and management. Published date: September 2014 Last updated: April 2018. Accessed 23/5/2018.
6. Guidance for Mental Health Professionals on the management of Acute Kidney Injury
7. Drug Safety Update. Valproate medicines (Epilim▼, Depakote▼): contraindicated in women and girls of childbearing potential unless conditions of Pregnancy Prevention Programme are met. Medicines and Healthcare products Regulatory Agency. Published 24 April 2018. Accessed 23/5/2018. https://www.gov.uk/drug-safety-update/valproate-medicines-epilim-depakote-contraindicated-in-women-and-girls-of-childbearing-potential-unless-conditions-of-pregnancy-prevention-programme-are-met
8. Guidance. Valproate use by women and girls. Information about the risks of taking valproate medicines during pregnancy. Toolkit. Medicines and Healthcare products Regulatory Agency. Last updated 9 April 2019. Accessed 23/5/2019.https://www.gov.uk/guidance/valproate-use-by-women-and-girls

Appendix 1

Physical Health monitoring for mood stabilisers

Clear (unshaded boxes) indicate monitoring required - See section 2 for physical health monitoring relating to antipsychotics.

Lithium

Parameter	Baseline	1 month	3 months	6 months	9 months	12 months	Then…
Weight/BMI							6 monthly
TFTs							6 monthly
U&Es							6 monthly
eGFR							6 monthly
Calcium							Annually
FBC							Annually
BP and pulse							Annually

Perform **full physical examination** and **ECG (risk factors)** before starting lithium and issue NPSA lithium therapy booklet. Check **plasma lithium 12(±2) hours post-dose** every 5-7 days until level is 0.4 –1.0 mmol/l, then 3 monthly or more frequently whenever toxicity, reduced renal function is suspected, other medication is changed and 1 week after dose changes. Target range will be dependent on indication and individual. Annual physical check should also be performed. See 3.5 for more details. There is an increased risk of Acute Kidney Injury (AKI) [6]This can be investigated by measuring Serum Creatinine.

Carbamazepine

Parameter	Baseline	1 month	3 months	6 months	9 months	12 months	Then…
Weight/BMI							6 monthly
LFTs							6 monthly
U&Es							6 monthly
FBC							6 monthly

Perform **full physical examination** before starting carbamazepine. Perform **ECG** in elderly/risk factors. **Plasma levels** are not useful when carbamazepine is used for mood stabilisation, and only needed if toxicity suspected. Therapeutic and toxic levels are close. Annual physical check should also be performed. See 3.5 for more details

Valproate (sodium, e.g. “Epilim” and semisodium “Depakote”) – Lamotrigine (baseline parameters)

Parameter	Baseline	1 month	3 months	6 months	9 months	12 months	Then…
Weight/BMI							6 monthly
LFTs							6 monthly
U&Es							6 monthly
FBC							6 monthly

Perform **full physical examination** before starting valproate. **Plasma levels** are not useful when valproate is used for mood stabilisation, & only needed if toxicity suspected. ? Pregnancy test. Annual physical check should also be performed. See 3.5 for more details

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) - 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.

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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.

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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.

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