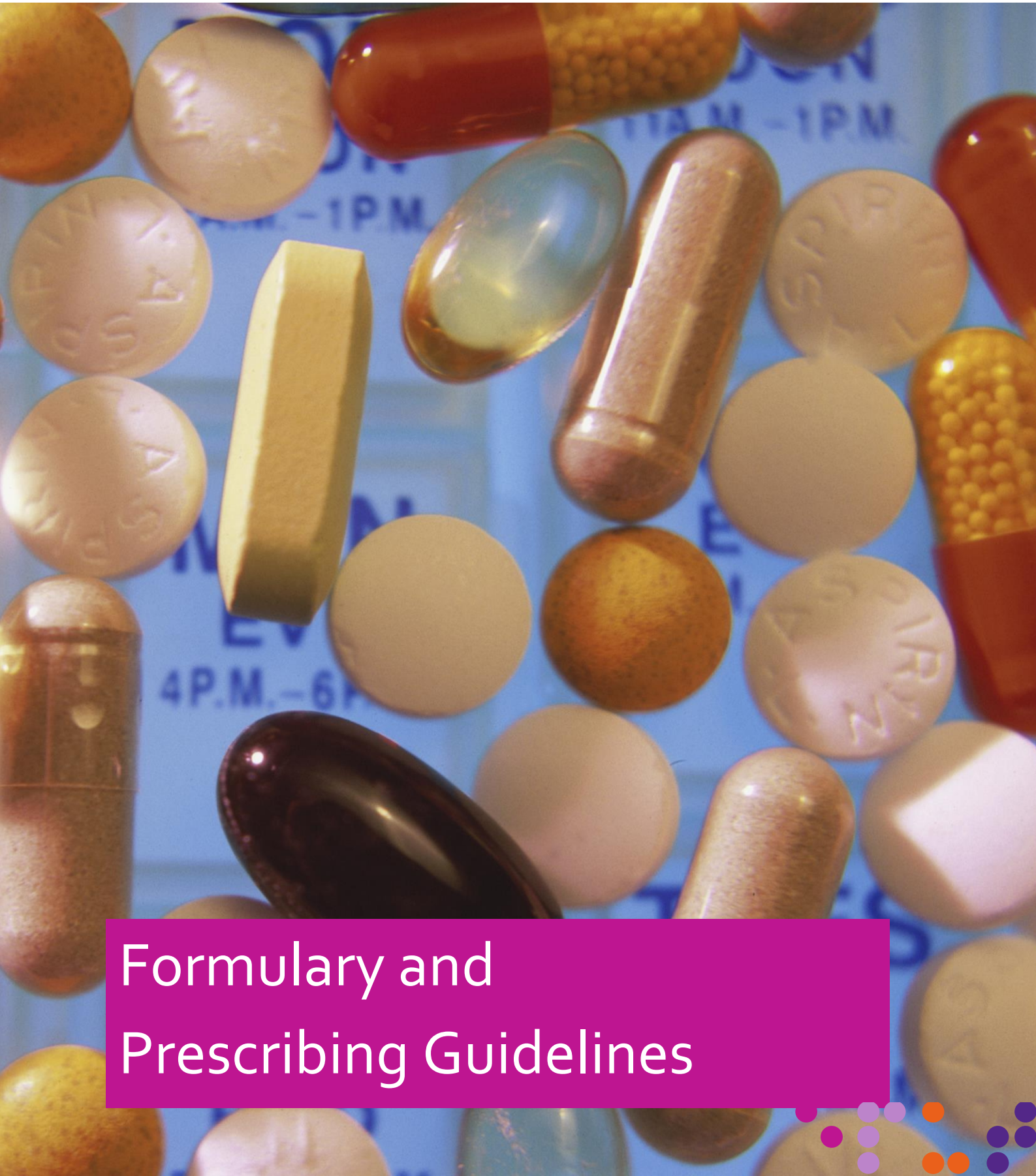
Essex Partnership University
NHS Foundation Trust

SECTION 20: ANTENATAL AND POSTNATAL PRESCRIBING



Formulary and Prescribing Guidelines

20.1 Introduction

This guidance is intended only as a quick-reference guide and must be used in conjunction with other resources when making treatment decisions. Refer to NICE CG192 Antenatal and postnatal mental health: Clinical management and service guidance[1] and other specific guidelines where appropriate, for example the UKTIS UK Teratology Information Service (www.medicinesinpregnancy.org), and the BAP consensus guidance on the use of psychotropic medication preconception, in pregnancy and postpartum[9].

Psychiatric disorders are more common in women at the reproductive age. In addition to morbidity, psychiatric illness during pregnancy is an independent risk factor for congenital malformations and perinatal mortality. Mood disorders increase the risk of pre-term delivery. The safety of psychotropic drugs in pregnancy cannot be clearly established due to lack of research and clinical trials in this specialist group. Lifestyle factors including smoking, alcohol abuse and poor eating habits can affect the outcome of a pregnancy. Concurrent use of psychotropic drugs during pregnancy can be associated with congenital malformation, long term neurodevelopmental problems and/or neonatal withdrawal symptoms depending on the agent. Most psychotropic drugs are excreted in the breast milk to some extent. It is therefore imperative, the prescriber evaluates the risks and benefits associated with all available treatments and discusses them with the service user before a treatment decision is made.

In all women of child bearing potential

- Always discuss the possibility of pregnancy. Unplanned pregnancies are more common in women with psychiatric disorders. Refer to Appendix 1
- Do not offer drugs that are contra-indicated during pregnancy in women of reproductive age (especially valproate and carbamazepine – risk of birth defect 2-3 times higher). If these drugs are prescribed, women should be made fully aware of their teratogenic properties even if not planning a pregnancy. The GP should be contacted to provide appropriate contraceptive advice and the need for using folic acid supplements when necessary.
- For valproate refer to specific guidance published by MHRA, see section 20.8 below.

20.2 General principles of prescribing in pregnancy

20.2.1 Newly diagnosed mental health condition

- Discuss changes in risk: benefit ratio of pharmacological interventions as a result of pregnancy. Try to avoid all drugs in the first trimester (when major organs are being formed) unless potential benefits outweigh perceived risks.
- Psychological interventions should be offered
- If psychological treatments prove ineffective, use an established drug at the lowest effective dose based on the most up to date information.

20.2.2 Service user using psychotropic drug(s) <u>planning</u> a pregnancy

- Consideration should be given to discontinuing treatment if the woman is well and at low risk of relapse. The risk of relapse however, always needs to be considered especially if the treatment is stopped abruptly.

- Discontinuation of treatment in women with a SMI (serious mental illness) and at a high risk of relapse is unwise. Consideration should be given to switching to a lower risk drug at the lowest effective dose. This should be carefully planned and the prescriber should be aware that switching agents may increase the risk of relapse.

20.2.3 Service user using psychotropic drug(s) has <u>unplanned</u> pregnancy

- Abrupt discontinuation of treatment post-conception for women with a SMI and at a high risk of relapse should not be recommended; relapse may ultimately be more harmful to the mother and child than established drug therapy.

- Consider remaining with current (effective) medication rather than switching, to minimise the number of drugs to which the foetus is exposed.

- Women on several medications need to have a plan to minimise the number of prescribed medications.

- Seek advice from a specialist perinatal mental health service (e.g. EPUT Perinatal Mental Health Service) or refer to the latest edition of the Maudsley Prescribing Guidelines if there is uncertainty about the risks associated with specific drugs

- All decisions should be documented.

20.3 General principles of prescribing psychotropic drugs in breast-feeding

- In each case, the benefits of breastfeeding to the mother and infant must be weighed against the risk of drug exposure in the infant
- Premature infants and infants with renal, hepatic, cardiac, or neurological impairment are at a greater risk from exposure to drugs
- Infants should be monitored more intensively for adverse effects to drugs. Feeding patterns, growth and development should also be monitored
- It is usually inappropriate to withhold treatment to allow breastfeeding where there is a high risk of relapse. Treatment of maternal illness is the highest priority
- Timing feeds to avoid peak drug levels in breast milk or expressed milk may reduce associated risks
- Women with bipolar disorder who are taking psychotropic medication and wish to breastfeed should be offered a prophylactic (antipsychotic) agent that can be used when breastfeeding
- NICE recommends that reference should be made to the UK Drugs in Lactation Advisory Service, and a specialist perinatal mental health service (e.g.

EPUT Perinatal Mental Health Service) for information on the use of specific drugs in breastfeeding.

20.4 Rapid tranquillisation

When choosing an agent for rapid tranquillisation in a pregnant woman, an antipsychotic or a benzodiazepine with a short half-life should be considered if non pharmacological, de-escalation techniques fail. If an antipsychotic is used, it should be at the minimum effective dose because of extrapyramidal symptoms. If a benzodiazepine is used, the risks of floppy baby syndrome should be taken into account.

20.5 Antipsychotics

20.5.1 Risks to consider

- Placental passage of antipsychotics is incomplete but varies between drugs. Four antipsychotics have been studied[5]: higher rates were found for Olanzapine, then Haloperidol, then Risperidone and the least was Quetiapine.

- Raised prolactin levels with some antipsychotics (amisulpride, risperidone, sulpiride, phenothiazines and butyrophenones). Consider a prolactin sparing antipsychotic e.g. Aripiprazole

- Gestational diabetes and weight gain with all atypical antipsychotics especially olanzapine. Offer advice about diet and monitor for excessive weight gain.

- Agranulocytosis in the foetus (theoretical) and breastfed infant with clozapine

- A recent Europe-wide review[3] has concluded there is a risk of EPSE or withdrawal symptoms (or both) in newborns after maternal use of antipsychotics during the 3rd trimester.

20.5.2 Actions to take

- Offer information leaflets on use of the specific drug in pregnancy, from the UK Teratology Information Service, available at www.medicinesinpregnancy.org, and from the Choice and Medication website www.choiceandmedication.org/eput

- Older, first-generation antipsychotics are generally considered to have minimal risk of teratogenicity

- Advise women taking antipsychotics who are planning a pregnancy that raised prolactin levels reduce the chances of conception. If there are side effects and levels are raised consider an alternative drug

- Doses prescribed should be kept as low as possible whilst still achieving a clinical response

- Do not offer depot antipsychotics to a woman who is planning a pregnancy, pregnant or considering breast feeding unless responding well to a depot and has a previous history of non-adherence of oral medication.

- If pregnant women develop mania while taking prophylactic medication, prescribers should:

    - Check the dose and adherence

    - Increase the dose of the antipsychotic (switch to, if she is not taking one)

    - If there is no response to changes in dose or drug and the patient has severe mania, consider the use of ECT

- If prescribing olanzapine, consider risk factors for gestational diabetes and weight gain, including family history, existing weight and ethnicity.

- Close monitoring of the baby in the neonatal period may be needed as antipsychotic discontinuation symptoms/EPSE can occur in the neonate (e.g. crying, agitation, hypertonia, hypotonia, tremor, somnolence, and respiratory distress). Refer to advice from UKTIS on the risk for specific drugs.

- Certain drugs like chlorpromazine increase the risk of cholestasis and pruritus in pregnancy. If patient has had cholestasis/pruritus in previous pregnancies, be cautious whilst prescribing such drugs.

- **Do not** routinely prescribe:

    - Clozapine to women who are pregnant or breastfeeding. NICE recommends that pregnant women should be switched from clozapine to another antipsychotic

    - Anticholinergic drugs for extrapyramidal side effects of antipsychotics, except for short-term use. Instead adjust dose and timing of the antipsychotic or switch to another drug to avoid side effects

20.6 Antidepressants

20.6.1 Risks to consider

- More than 1 in 10 women experience depression at some point during pregnancy[4].

- Relapse rates are higher in those with a history of depression who discontinue medication.

- Antidepressants should be considered for women with mild depression during pregnancy if they have a history of severe depression and they decline, or their symptoms do not respond to psychological treatments. [4]

- SSRI with lowest known risk during pregnancy is Fluoxetine. However, if the patient is prescribed another SSRI, it is often prudent to continue the same

SSRI (except paroxetine) to avoid risk of relapse. The risk of intrauterine growth retardation (although low) is greater in untreated major depression than with drugs like fluoxetine, hence it is advisable to continue the antidepressant in major depression.

- Foetal heart defects are noted when paroxetine taken in the first trimester.
- Persistent pulmonary hypertension in the neonate is noted when SSRIs are taken after 20 weeks' gestation.
- High blood pressure with venlafaxine at high doses noted, together with higher toxicity in overdose compared to SSRIs and some TCAs.
- There is emerging data about the relationship between SSRIs and Autistic Spectrum Disorder [6], but further research is needed to specifically assess the risk associated with antidepressant types and dosages during pregnancy.
- Withdrawal or toxicity in the neonate with all antidepressants, in particular paroxetine and venlafaxine (usually mild and self-limiting).
- There is no evidence to suggest that ECT causes harm to either the mother or foetus during pregnancy although general anesthesia is not without risks
- Highest levels in breast milk are noted with citalopram and fluoxetine
- Lower levels in breast milk are noted with imipramine, nortriptyline and sertraline
- A cohort study[4] found women exposed to SSRIs at delivery had a higher risk of postpartum haemorrhage, RR=1.47. The risk of postpartum haemorrhage at delivery was also raised in women who had recently been exposed to SSRIs (RR=1.19)
- The MHRA [13] has published reports of a small increased risk of postpartum haemorrhage with SSRI/SNRI antidepressant medicines, when used in the month before delivery. Advice for healthcare professionals:
    - SSRIs and SNRIs are known to increase the bleeding risk; observational data suggest that the use of some antidepressants in the last month before delivery may increase the risk of postpartum haemorrhage
    - continue to consider the benefits and risks for use of antidepressants during pregnancy, and the risks of untreated depression in pregnancy
    - healthcare professionals, including midwives, should continue to enquire about the use of antidepressant medicines, particularly in women in the later stages of pregnancy
    - consider the findings of the review in the context of individual patient risk factors for bleeding or thrombotic events

- do not stop anticoagulant medication in women at high risk of thrombotic events in reaction to these data but be aware of the risk identified

- report any suspected adverse reactions associated with medicines taken during pregnancy via the Yellow Card Scheme

20.6.2 Actions to take

- Offer information leaflets on use of the specific drug in pregnancy, from the UK Teratology Information Service, available at www.medicinesinpregnancy.org , and from the Choice and Medication website www.choiceandmedication.org/eput

- Patients who are already receiving antidepressants and are at high risk of relapse are best maintained on antidepressants during and after pregnancy

- Advise a woman taking paroxetine who is planning a pregnancy or has an unplanned pregnancy to stop the drug (due to the risk of cardiovascular malformations of the foetus)

- If a woman planning a pregnancy becomes depressed after stopping prophylactic medication, psychological therapies (CBT) should be considered in preference to an antidepressant drug

- Women who are prescribed an antidepressant during pregnancy should be advised of the potential adverse effects on the neonate

20.7 Lithium

20.7.1 Risks to consider

- Foetal heart defects (risk raised from 8 in 1000 to around 60 in 1000)

- Ebstein's anomaly (risk raised from 1 in 20 000 to around 10 in 20 000)

- In the third trimester, the use of lithium may be problematic because of changing pharmacokinetics (total body water increases). An increasing dose of lithium is required to maintain the drug level during pregnancy, however the requirements return abruptly to pre-pregnancy levels immediately after delivery

- Neonatal goitre, hypotonia, lethargy, and cardiac arrhythmia can occur

- High levels in breast milk

20.7.2 Actions to take

- Offer information leaflets on use of the specific drug in pregnancy, from the UK Teratology Information Service, available at

www.medicinesinpregnancy.org , and from the Choice and Medication website www.choiceandmedication.org/eput

- Do not offer lithium to women who are planning a pregnancy or are pregnant unless antipsychotic medication has not been effective.

- A woman planning a pregnancy taking lithium who is well and not at risk of relapse, should be advised to stop the drug. The risk of developing fetal heart malformations when lithium is taken in the first trimester should be explained along with an explanation that there may be high levels of lithium in breast milk with a risk of toxicity for the baby.

- Women taking lithium should deliver in hospital and be monitored during labour by the obstetric team. Monitoring should include fluid balance because of the increased risk of dehydration and the subsequent risk of lithium toxicity (in prolonged labour it may be appropriate to check serum lithium levels)

- If a woman maintained on lithium is at high risk of manic relapse in the immediate postnatal period, augmenting treatment with an antipsychotic should be considered

- If a woman taking lithium becomes pregnant:

    - If the pregnancy is confirmed in the first trimester, and the woman is well and not at high risk of relapse, stop the drug gradually over four weeks. Explain that this may not remove the risk of cardiac defects in the foetus and that there is a risk of relapse especially in the postnatal period, if she has bipolar disorder.

- If she is not well or is at high risk of relapse, consider:

    - Switching gradually to an antipsychotic, or

    - Stopping lithium and restarting it in the second trimester if the woman is not planning to breastfeed and her symptoms have responded better to lithium than to other drugs in the past, or

    - Continuing with lithium if she is at high risk of relapse and an antipsychotic is unlikely to be effective.

- If a woman continues taking lithium during pregnancy:

    - High-resolution ultrasound and echocardiography should be performed at 6 and 18 weeks of gestation

    - Check serum levels every four weeks, then weekly from the 36th week, and less than 24 hours after childbirth. Adjust the dose to keep serum levels towards the lower end of the therapeutic range

    - Ensure adequate fluid intake is maintained

- Lithium should be stopped during labour and plasma levels checked 12 hours after the last dose.

20.8 Valproate[12]

20.8.1 Risks to consider

- Valproate should not be prescribed for women of child bearing potential or in pregnancy.
- Neural tube defects (spina bifida and anencephaly; risk raised from around 6 in 10000 to 100-200 in 10000)
- Delay on the child's intellectual development
- Polycystic ovary syndrome in women younger than 18 years
- Publications on association between foetal valproate exposure and neurodevelopment delay of autistic spectrum disorder have promoted a re-evaluation of the benefits and risks. See latest MHRA drug safety updates and BNF.

20.8.2 Actions to take

- Valproate medicines must not be used in women or girls of childbearing potential unless a Pregnancy Prevention Programme is in place[10] 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")[11] ;provide a "Patient Guide"[11] 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 Form (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.[10]

- In particular, do not prescribe to women younger than 18 years (increased risk of unplanned pregnancy in this group).

- If the patient becomes pregnant on valproate, consideration should be given to tapering the valproate down carefully, while introducing suitable alternative drug treatment.

- If there is no alternative to valproate, a second opinion should be sought by another consultant employed by the Trust. If both agree that valproate should be prescribed; the lowest possible dose limited to a maximum of 1 gram per day, in divided doses and in the slow-release form should be used. In addition prescribe folic acid 5mg daily. Specialist prenatal monitoring should be instigated to detect possible occurrence of neural tube defects or other malformations when valproate has been used.

20.9 Carbamazepine

20.9.1 Risks to consider

- Neural tube defects (risk raised from 6 in 10000 to around 20-50 in 10000) and other major foetal malformations including gastrointestinal tract problems and cardiac abnormalities

20.9.2 Actions to take

- Advise a woman taking carbamazepine that is planning a pregnancy or has an unplanned pregnancy to stop taking the drug. Consider an alternative drug such as an antipsychotic

- Folic acid should be prescribed before and during pregnancy[7]

- Offer information leaflets on use of the specific drug in pregnancy, from the UK Teratology Information Service, available at www.medicinesinpregnancy.org, and from the Choice and Medication website www.choiceandmedication.org/eput

- Do not routinely prescribe carbamazepine for pregnant women

- Use of carbamazepine in the third trimester may necessitate maternal Vitamin K.

20.10 Lamotrigine

20.10.1 Risks to consider

- Cleft lip (risk estimated at nearly 9 in 1000)

- Dermatological problems (notably Stevens-Johnson syndrome) in the infant if taken while breastfeeding.

- There is emerging data about cardiac anomalies associated with Lamotrigine, which requires further research. [8]

20.10.2 Actions to take

- Advise a woman taking lamotrigine that is planning a pregnancy or has an unplanned pregnancy to stop taking the drug. Consider an alternative drug such as an antipsychotic.

- Offer information leaflets on use of the specific drug in pregnancy, from the UK Teratology Information Service, available at www.medicinesinpregnancy.org, and from the Choice and Medication website www.choiceandmedication.org/eput

- Do not routinely prescribe lamotrigine for pregnant women

- Do not routinely prescribe lamotrigine for women who are breastfeeding

20.11 Benzodiazepines

20.11.1 Risks to consider

- Cleft palate and other foetal malformations.

- Floppy baby syndrome in the neonate.

20.11.2 Actions to take

- Do not routinely offer to pregnant women, except for short-term treatment of severe anxiety and agitation.

- Consider gradually stopping in women who are planning a pregnancy, pregnant or considering breastfeeding.

- **Promethazine** has been used in hyperemesis gravidarum and appears not to be teratogenic,

- NICE recommends the use of low-dose chlorpromazine or amitriptyline for sedation and anxiety

- Offer information leaflets on use of the specific drug in pregnancy, from the UK Teratology Information Service, available at www.medicinesinpregnancy.org, and from the Choice and Medication website www.choiceandmedication.org/eput

20.12 Methadone

- Methadone at a stable dose can be used in pregnancy without any additional risk to the development of the foetus. Abrupt withdrawal can be dangerous.
- Information relating to the usage of methadone should be shared with the maternity team and the possibility of neonatal withdrawal syndrome explained to the mother.
- See Formulary and Prescribing Guideline Section 10 for further information

- Offer information leaflets on use of the specific drug in pregnancy, from the Choice and Medication website www.choiceandmedication.org/eput

20.13 Electroconvulsive therapy

- In resistant depression, NICE recommend that ECT is used before/instead of drug combinations
- For acute mania in pregnancy use an antipsychotic and if ineffective consider ECT

20.13 Summary

Class of Drug	Recommended during Pregnancy	Recommended during Breastfeeding	Other options
Antipsychotics	Quetiapine is first choice. Experience with Chlorpromazine, Haloperidol, Trifluoperazine	Sulpiride, Olanzapine	
Antidepressants	Sertraline is first choice. Nortriptyline, Amitriptyline Imipramine.	Paroxetine, Sertraline	CBT for moderate depression, ECT for resistant depression
Mood Stabilisers	Mood stabilising antipsychotics	Mood Stabilising antipsychotics	ECT for resistant /acute mania
Sedatives	Quetiapine, Promethazine	Lorazepam for anxiety and Zolpidem for sleep	

References

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Aide Memoire to assist in accurate record keeping – Things to consider when treating women of Childbearing age

1. Has the possibility of an unplanned pregnancy been discussed?

2. Already taking carbamazepine or in exceptional circumstances valproate: have the risks of birth defects been discussed even if not pregnant? Use the Patient Guide in the valproate toolkit.

3. If the service user becomes pregnant has a risk/benefit assessment of prescribed medicines been carried out and documented?

4. If Paroxetine is prescribed: has the risk of foetal withdrawal/ cardiac defects been discussed even if the service user is not pregnant?

5. If Lithium is prescribed: has the risk of foetal cardiac defects been discussed?

6. If Valproate is prescribed: Have the risks of neural tube defects/ delayed intellectual development been discussed? Use the Patient Guide in the valproate toolkit.

7. If carbamazepine is prescribed: Have the risks of neural tube defects / GI problems been discussed?

8. If Lamotrigine is prescribed: Have the risks of cleft lip/ dermatological problems been discussed?

9. If a benzodiazepine is prescribed: have the risks of cleft palate and floppy baby syndrome been discussed

10. Have all decisions been documented?

Appendix 2

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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