SECTION 21: HIGH RISK MEDICINES

Formulary and Prescribing Guidelines
There are many medicines which can be classed as high risk due to the number of potentially harmful medication incidents that have been reported through the National Reporting and Learning Services (NRLS) and NHS Improvement. This document aims to highlight those medicines and highlight the issues involved.

21.1 **Anticoagulants**

Anticoagulants are one of the classes of medicines most frequently identified as causing preventable harm and admission to hospital. Medicines included in the category are:

<table>
<thead>
<tr>
<th>Older oral anticoagulants</th>
<th>Novel oral anticoagulants</th>
<th>Parenteral anticoagulants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>Dabigatran</td>
<td>Heparin</td>
</tr>
<tr>
<td>Phenindione</td>
<td>Apixaban</td>
<td>Enoxaparin</td>
</tr>
<tr>
<td>Acenocoumarol</td>
<td>Rivaoxaban</td>
<td>Dalteparin</td>
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<tr>
<td></td>
<td>Edoxaban</td>
<td>Tinzaparin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fondaparinux</td>
</tr>
</tbody>
</table>

For further information on the use of these medicines see Chapter 14 Anticoagulants and CG83 Clinical Guideline for the management of patients on anticoagulants in inpatient units.

**References:**


21.2 **Insulin**

Errors in the administration of insulin are common and may cause severe harm or death. In order to ensure that the correct dose is administered it is essential that where possible insulin pen devices are used. If a syringe has to be used it should be an insulin syringe marked in units and not mls. Intravenous syringes should never be used.

When prescriptions for insulin are written, prescribers should ensure that the word “unit” is used and not “U” or “IU”

Insulin preparations are available in increasingly high strengths. Where these are available in pen devices they are calibrated so that the correct dose is administered to the patient. **Insulin should never** be withdrawn from these devices using a syringe.

Many patients are competent at managing their own insulin and many use carbohydrate counting to adjust the dose that is administered. Every effort should be made to ensure that patients are allowed to continue with this wherever possible. If it is felt that this is not possible for reasons of patient safety there should be a discussion with the patient and/or their family regarding the best solution to the management of insulin administration.
All patients should carry an insulin passport. This will normally be issued by the clinic where the insulin is initiated, but they are available from pharmacy if it is discovered that the patient does not have one.

References:

21.3 Lithium

Some patients taking Lithium have been harmed because they have not had their dosage adjusted based on the results of recommended blood tests.

For information on how to initiate Lithium and monitor ongoing treatment refer to Chapter 3. Formulary and Prescribing Guidelines.

As Lithium can be extremely toxic when not used at the correct dose, no patient who is being admitted to the Trust should receive a dose until the results of a valid blood test have been received.

All patients prescribed Lithium should be issued with a Lithium Therapy pack. This contains information for patients, a booklet where blood test results can be recorded and a Lithium alert card.

If patients are admitted to the Trust already being treated with Lithium should have a Lithium Therapy pack that has been completed with details of previous blood tests. If this is not the case the current booklet should be updated by prescribers with previous results and if there is no pack a new one should be issued.

Lithium Therapy packs can be obtained from the Trust Pharmacy department.

References:

21.4 Valproate

Valproate is an effective medicine used to treat epilepsy and bipolar disorder. Unborn babies exposed to valproate during pregnancy are at very high risk of neurodevelopment disability e.g. lower intelligence and autistic spectrum disorders. In girls and women of a childbearing potential, valproate should be initiated and supervised by a specialist and only when other medicines have not been tolerated or have been proved to be ineffective.
The Medicines and Healthcare products Regulatory Agency (MHRA) has published a valproate toolkit providing sets of resources for patients, GPs, pharmacists and specialists.

Valproate medicines must not be used in women or girls of childbearing potential unless a Pregnancy Prevention Programme is in place 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”); provide a “Patient Guide” 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—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.

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 F&P section 12 and section 20 respectively. Additional information regarding prescribing in older adults can also be found in section 11.

References:

21.5 **Methotrexate**

Oral methotrexate is used in low doses (up to 25mg weekly) for the treatment of rheumatoid arthritis and psoriasis.

Prescribers will not be asked to initiate methotrexate treatment, but may be responsible for maintaining therapy and monitoring patients.

Written confirmation of the dose should be sought before prescribing, including the dosage and frequency of taking, plus the day of the week when methotrexate is normally taken. This should be done through the medicines reconciliation process. Additional information may be available in a patient held record book.

Confirmation of the frequency of monitoring should also be clarified with the original prescriber.

Prescribers should ensure that only one route of administration for methotrexate is prescribed.

Only the 2.5mg tablets will be issued by the pharmacy department. If folic acid is prescribed alongside methotrexate, it is not usually given on the same day as methotrexate.

Monitoring of methotrexate therapy is to specifically look for adverse toxic effects. Blood tests for renal and liver function in addition to full blood counts are monitored at baseline, then 1-2 weekly until stable, at the clinic, then every 2-3 months.

Liver and renal function tests and FBCs should be done on admission for all patients. If they are abnormal the information should be shared with the initiating clinic.

If the patient is on the ward-unit for longer than 3 months the tests should be repeated. Patients on methotrexate are considered to be immunosuppressed and should not receive live vaccines.

Methotrexate interacts with some commonly prescribed medicines including non-steroidal anti-inflammatories (NSAIDs) such as ibuprofen and aspirin, as well as antibiotics such as trimethoprim which can be fatal if prescribed together.

Healthcare professionals must be aware of potentially toxic adverse effects of methotrexate including blood dyscrasias – often found through symptoms of infection or unexplained bruising or bleeding, liver cirrhosis - picked up through blood tests or symptoms of jaundice, and also pulmonary toxicity – manifested as shortness of breath or dry persistent cough.

Persistent nausea and vomiting poses additional risks for patients on methotrexate as the risk of toxicity increases if dehydration occurs. These symptoms could also be indicative of intolerance to oral methotrexate.

**References:**


21.6 Midazolam

Buccal midazolam can be prescribed to treat prolonged epileptic seizures in adults and children. It is available as pre-filled oral syringes and a multidose bottle. Care must be taken to ensure that only the oral syringes provided by the manufacturer should be used and never a syringe that is designed to administer injectable preparations.

The solution should be administered into the buccal cavity (the space between the gum and the cheek). If necessary, half should be given on the left and half on the right side of the mouth. The full contents of the syringe should be given. The dose should only be repeated in accordance with the patient’s careplan.

These preparations are intended for oromucosal use only, and must never be injected.

Intravenous midazolam for conscious sedation should only be used during electro-convulsive therapy (ECT) under the direct supervision of an anaesthetist experienced in this area. Only the high strength midazolam (10mg in 2mL) ampoules are kept in the Trust, and only on the ECT suite.

Subcutaneous midazolam may be prescribed and supplied for named patients for subcutaneous use.

References:


21.7 Oral Bowel Cleansing Preparations

Oral bowel cleansing preparations are used before certain investigational or medical procedures. These preparations have been highlighted as hazardous due to electrolyte imbalances, dehydration or other problems associated with their use, particularly in vulnerable patient groups such as elderly, frail and children. Service users may need to use these preparations before undergoing surgery or investigations for physical health problems, and therefore staff must understand how and when they are to be used.

It is usual procedure that a clinician at the acute hospital will advise use of an oral bowel cleansing preparation, and they usually supply it directly.

It is the responsibility of the clinician authorising the surgery or investigative procedure to ensure that there is no contraindication (e.g. clinical condition such as diverticulitis) or risks (e.g. concurrent medication such as diuretics) from the use of a bowel cleansing solution. The same clinician authorising the use of the oral bowel cleansing preparation must also ensure that adequate information is given to the patient and/or carer. For inpatients, staff must ensure that the preparation is prescribed on the patient’s Prescription and Administration chart, and that the information on when to take it and how much fluid to drink is strictly adhered to.

Staff must contact the authorising clinician if there are any questions or concerns around the use of an oral bowel cleansing preparation.

References:
21.8 **Paraffin Based Skin Products**

Paraffin based skin products may be a fire hazard when in contact with dressings, clothing and bedding (11).

Pharmacy will apply a “fire hazard” label to any preparation containing white soft paraffin, white soft paraffin plus 50% liquid paraffin and emulsifying ointment.

Ward staff should be aware of the potential risk of fire if any open flames (including cigarettes) are used near the paraffin product, or any sites where it has been applied to.

A check should be made that the patient understands these risks.
If, against advice, a hospitalised patient intends to leave the ward to smoke, they should be informed of the risk and advised to wear a thick outer covering that has not been contaminated with paraffin based products.

**References:**


21.9 **Antimicrobials**

Antimicrobial resistance (AMR) is a major global threat to public health and has risen alarmingly over the last 40 years. Very few novel antimicrobials have been developed meaning that existing antibiotics are under extreme pressure and inappropriate use of these antibiotics has increased the risk to patients of colonisation with resistant organisms, which can subsequently be transmitted to other patients. Antibiotics selected for prescribing should therefore be the narrowest spectrum for the identified condition and broad spectrum antibiotics such as co-amoxiclav, fluoroquinolones and cephalosporins should be avoided unless indicated. Prescribers should use the following principles to guide antibiotic selection, thereby promoting safe, effective and economic use and minimising the emergence of antibacterial resistance:

- Ensure you document all your decisions
- Use local guidance based on clinical evidence in conjunction with professional judgement and taking patients’ wishes/clinical condition into account
- Take a thorough allergy history
- Initiate treatment within one hour of diagnosis in life threatening infection and severe sepsis
- Ensure the presence of viral infection has been excluded before prescribing
- Do not prescribe during a telephone consultation except in exceptional circumstances
- Ensure the indication, dose and route are recorded on both the drug chart and in the patients’ record
- Prescribe the shortest appropriate duration (broad spectrum antibiotics taken for protracted periods can promote resistance) and ensure a review/stop date is documented
- Avoid topical antibiotics unless indicated (this can promote resistance)
• Take cultures prior to commencing treatment (where appropriate) but do not delay initiation in the absence of cultures
• Contact your local microbiologist for advice in cases of recurrent or resistant infection

Patients and their carers should be advised that if an antibiotic is prescribed, it should be taken exactly as directed even if the patient is feeling better. There are numerous pieces of legislation, guidance and reviews, both national and local, to guide clinicians and provide background information.

References:


21.10 Injectable Phenytoin

Injectable phenytoin is used to slow and stabilise erratic electrical brain activity in for example, status epilepticus, which is a life threatening medical emergency. Phenytoin is a particularly complicated drug to use. It is unlikely that injectable phenytoin will be used in this Trust, but if prescribing is considered the pharmacy department should be contacted for advice.

References:
Annex 1

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, Convulox, Epigenta, Epival, Kentim, Orept, Syonell, Valpar) – 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.

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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 fulfill 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-menarche), the date for the next annual discussion of the risks must be documented and the patient or the patient’s family/caregivers 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

<table>
<thead>
<tr>
<th>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):</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ 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):</td>
</tr>
<tr>
<td>□ the absence of pregnancy risk is permanent for the following reason (insert reason):</td>
</tr>
<tr>
<td>□ I consider that sexual activity that could lead to pregnancy will not occur before the next annual review because (insert reason):</td>
</tr>
<tr>
<td>□ I have given the patient or responsible person a copy of the Patient Guide</td>
</tr>
</tbody>
</table>

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’.

<table>
<thead>
<tr>
<th>To be completed and initialed by the specialist</th>
<th>Initials</th>
</tr>
</thead>
<tbody>
<tr>
<td>I confirm that the patient needs valproate because:</td>
<td></td>
</tr>
<tr>
<td>• her condition does not respond adequately to other treatments, or</td>
<td></td>
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<tr>
<td>• she does not tolerate other treatments, or</td>
<td></td>
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<tr>
<td>• she is undergoing a treatment change from valproate</td>
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</tr>
</tbody>
</table>

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 “Risks 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.

<table>
<thead>
<tr>
<th>To be completed and signed by the patient or their responsible person</th>
<th>Initials</th>
</tr>
</thead>
<tbody>
<tr>
<td>I have discussed the following with my specialist and I understand:</td>
<td></td>
</tr>
<tr>
<td>□ Why I need valproate rather than another medicine</td>
<td></td>
</tr>
<tr>
<td>□ That I should visit a specialist regularly (at least once a year) to review whether valproate remains the best option for me</td>
<td></td>
</tr>
<tr>
<td>□ The risks in children whose mothers took valproate during pregnancy are:</td>
<td></td>
</tr>
<tr>
<td>■ 1 out of 10 children will have physical birth defects</td>
<td></td>
</tr>
<tr>
<td>■ 3 to 4 out of 10 children will have early developmental problems that can lead to significant learning disabilities</td>
<td></td>
</tr>
<tr>
<td>□ That I have had a pregnancy test (if advised by my doctor/specialist)</td>
<td></td>
</tr>
<tr>
<td>□ Why I must use effective contraception, without stopping or interruption, at all times while taking valproate</td>
<td></td>
</tr>
<tr>
<td>□ The options for effective long-term contraception (or a consultation has been planned with a professional who can give me advice)</td>
<td></td>
</tr>
<tr>
<td>□ 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</td>
<td></td>
</tr>
<tr>
<td>□ That I should request an urgent GP appointment if I think I am pregnant</td>
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</tr>
<tr>
<td>□ I have been given a copy of the Valproate Patient Guide and know where to find more information</td>
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</tr>
</tbody>
</table>

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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