LOTHIAN PRESCRIBING BULLETIN

NHS Lothian

Supporting prescribing excellence - informing colleagues in primary and secondary care

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Safe use of oral liquid medicines in children - what's the content?

Prescribing oral liquid medicines for children comes with extra considerations. The main ones are excipient content, selection of either licensed, off-label or unlicensed medicines, concentration, and volumes for administration.

Why is excipient quantity so important in neonates and paediatrics?

Excipients are inactive ingredients that make up a medicine to improve taste, stability and shelf life. They may be present in quantities which are potentially harmful to children. Accumulation of excipients can occur in children taking a variety of oral liquid medication and in young children with immature metabolic capacity. Some children may suffer from conditions that can be exacerbated by the administration of certain excipients.

Where to find out about the excipients in oral liquid medicines

First ports of call include:

- Patient Information Leaflet (eMC)
- electronic Medicines Compendium (eMC)
- Medicines and Healthcare Regulatory Agency (MHRA) for licensed products not included in the eMC
- Safety and Toxicity of Excipients for Paediatrics (STEP) database written by the European Paediatric Formulation Initiative Team
- Examples of how to calculate excipient content can be found in a Position Statement published by the Neonatal Paediatric Pharmacists Group (NPPG).

When choosing a product, consider the cumulative daily excipient intake for all medicines taken by the patient so as to ensure an accurate estimation of potential toxicity.

The formulary and safe prescribing

The LJF child recommendations include standardised concentrations of oral liquid preparations approved by NHS Lothian with the following aims:

- minimising errors
- ensuring continuity of care
- encouraging cost-effective prescribing.

In some cases, formulary products may be off-label or unlicensed. These have gone through strict medicine governance processes and have been approved for use on the formulary. The NPPG recommend a dose volume between 0.2mL and 10mL to ensure safe administration and minimise harm. If these volumes cannot be met, then the dose volume should be greater than 0.1mL but no more than 20mL.

Utmost care should be taken to ensure the correct concentration and dose is prescribed, dispensed and administered in order to prevent patient harm.
Take extra care if a non-formulary option is selected for an individual patient.

References

Medicines for Children. Excipients in Children's Medicine. London. 2018

Neonatal and Paediatric Pharmacists Group. Position Statement 2020-21 Choosing an Oral Liquid Medicine for Children. London. 2020

European Paediatric Formulation Initiative. The STEP Database. London. 2015

Thanks to Amirah Irshad, Rotational Pharmacist.

Don't just say stop, look it up!

Medicines and breastfeeding guidance

The UK Drugs in Lactation Advisory Service (UKDILAS) has published some new guidance to supplement their medicines specific advice during breastfeeding. The new pages include why breastfeeding is important and how pharmacy can help. Advice is provided on medicines regimens during breastfeeding, and useful information sources.

UKDILAS are part of the recently launched Safer Medicines in Breastfeeding and Pregnancy Consortium, which brings together 16 leading organisations under a common pledge, to meet the information needs of pregnant and breastfeeding women and healthcare professionals through accessible, clear and consistent advice.

Remember, don't just say stop, look it up. It's important to get accurate, evidence-based information about medicines and breastfeeding, as recommended by NICE.

Thanks to Louise Summers, Senior Medicines Information Pharmacist.

Do not prescribe probiotics

As stated in the September 2020 formulary update, the probiotic VSL#3 is no longer included in the formulary. It is not included in the Drug Tariff and can no longer be prescribed under the Advisory Committee on Borderline Substances (ACBS) criteria. Limited evidence, as highlighted in the British Society of Gastroenterology guidelines[1] suggested probiotics could cause a modest benefit in ulcerative colitis, most notably in the maintenance of ileoanal pouchitis remission.

Following review, the ACBS deemed the evidence insufficient to continue considering VSL#3 suitable for prescribing.

Significant clinical efficacy has not yet been demonstrated by any alternative probiotics and none are included in the Drug Tariff. Probiotics should also not be prescribed through Pay and Report.

As such, patients can be advised to purchase probiotics if they wish to continue their use, after consideration of the lack of evidence and possible variations in quality as non-medicinal products.

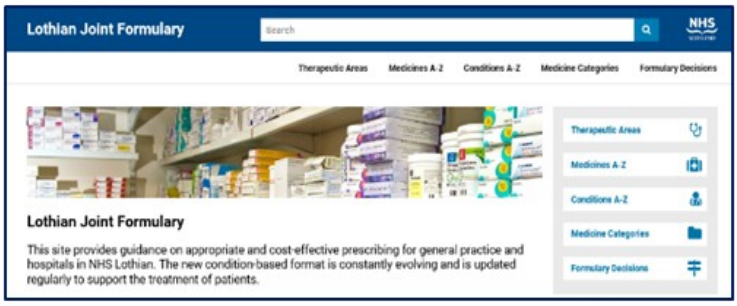
Reference

1. dx.doi.org/10.1136/gutjnl-2019-318484

Thanks to Rania Husain, Primary Care Pharmacist, for her contribution.

Medicines governance and our local procedures

Medicines governance in NHS Lothian is supported by an advisory committee structure headed by the Area Drug and Therapeutics Committee, which oversees a range of policies, procedures and guidelines. The Lothian Joint Formulary provides guidance on appropriate and cost-effective prescribing for general practice and hospitals in NHS Lothian.



A new formulary website was launched in January which expands the traditional formulary structure, based around BNF chapters, by presenting condition-based medicine recommendations.

It doesn't have to be a FAF, just go with the flow!

The formulary website has information on Formulary Application Forms (FAFs) to request approval of medicines for prescribing. In addition, the Medicines Management Application and Forms Flowchart provides guidance to clinicians wishing to prescribe a medicine for a patient. It is an easy way to aid prescribing decisions and alert you about which forms need completed. Use the search box on the LJF to check formulary status.

The GMC guidance 'Good practice in prescribing and managing medicines and devices' advises *"you are responsible for the prescriptions that you sign. You must only prescribe drugs when you have adequate knowledge of your patient's health. And you must be satisfied that the drugs serve your patient's need."*

Examples to help familiarisation with the Medicines Management Application and Forms Flowchart:

EXAMPLE	Scenario	What do you do?
ceftazidime/ avibactam (Zavicefta)	An infectious disease specialist recommends treatment of an aerobic gram negative LRTI with ceftazidime/avibactam (Zavicefta). From the history you find that the patient was resistant to alternative treatments on the formulary.	SMC does NOT recommend the use of ceftazidime/avibactam (Zavicefta). If you consider the patient would benefit from this treatment and formulary alternatives are not appropriate then follow the PTR procedure and complete: **IPTR form**
progesterone (Utrogestan)	A doctor has asked for your advice to prescribe progesterone for luteal support in an infertile patient who cannot tolerate other vaginal preparations. She mentions she remembers SMC recently approved Utrogestan for "something".	Utrogestan is NOT recommended for use within NHS Scotland for adjunctive use with oestrogen in post-menopausal women with an intact uterus (HRT). Utrogestan Vaginal® is accepted for use within NHS Scotland in women for supplementation of the luteal phase during Assisted Reproductive Technology (ART) cycles. Utrogestan Vaginal® is also available in NHS Lothian for Specialist Use only. It CAN BE prescribed by a Specialist.
clopidogrel suspension	A paediatric patient requires clopidogrel suspension to be prescribed. The computer flashes and alerts you that this is unlicensed and has never been used in NHS Lothian before.	Clopidogrel suspension is NOT approved in NHS Lothian and is an unlicensed medicine ('Special'). If clinical and cost benefit/risk has been taken into account and you wish to prescribe, complete: **ULM form AND NON-FORMULARY REQUEST form**

Click on titles in boxes for links to Medicines and Healthcare products Regulatory Agency (MHRA) Drug Safety information

Antiepileptic drugs in pregnancy

As previously highlighted, valproate/valproic acid is only prescribed for women of childbearing age if there is a pregnancy prevention programme in place. Following a recent review of drugs used to control epilepsy, including those currently included in the Lothian Joint Formulary, the commission on Human Medicines (CHM) has confirmed that lamotrigine (Lamictal) and levetiracetam (Keppra) are the safer options for use during pregnancy.

Studies have demonstrated that, at usual maintenance doses, the two drugs were not associated with an increased risk of congenital malformations. Available data do not suggest an increased risk of neurodevelopmental disorders or delay associated with in-utero exposure to either drug, however an increased risk cannot be excluded.

Erythromycin: Problems with QT prolongation and rivaroxaban

Macrolide antibiotics are known to cause QT prolongation. A new contraindication has been added for those with risk factors for QT interval prolongation and arrhythmia, including patients with a history of QT interval prolongation or ventricular arrhythmia, and patients with electrolyte disturbances.

A reminder that erythromycin, as a CYP3A4 and P-glycoprotein inhibitor, reduces the metabolism of rivaroxaban and thereby increases the bleeding risk. This is especially important in renal impairment and doses should be adjusted accordingly. This interaction also affects other direct acting oral anticoagulants (DOACs).

Erythromycin is indicated for a number of infections in the Lothian Joint Formulary and is also included in the Microguide.

Ferric carboxymaltose (Ferinject), phosphate and fractures

Hypophosphataemia is commonly associated with Ferinject, resulting in infrequent reports of hypophosphataemic osteomalacia and fractures. Risk factors include patients requiring multiple doses of ferric carboxymaltose, long-term treatment with ferric carboxymaltose, or those with pre-existing hypophosphataemia risk (vitamin D deficiency, calcium and phosphate malabsorption, secondary hyperparathyroidism, inflammatory bowel disease and osteoporosis). Ferinject is indicated for both adults and children in the Lothian Joint Formulary for iron deficiency anaemia.

Attention to anticoagulant monitoring during COVID-19

Acute illnesses (eg. COVID-19 symptoms) can exaggerate the effect of warfarin and other vitamin K antagonists, therefore it is important that INR continues to be monitored to enable early management of a higher bleeding risk. It is also important to consider possible drug interactions between all anticoagulants and drugs used to treat acute illness (eg. antibiotics).

Healthcare professionals and members of the public should report suspected adverse reactions using the Yellow Card Scheme.

Antidepressants and small increased risk of postpartum haemorrhage

Selective serotonin reuptake inhibitors (SSRIs) and serotonin and noradrenaline reuptake inhibitors (SNRIs) carry a low but recognised, increased risk of bleeding, due to the serotonergic effect inhibiting platelet aggregation. A recent EU review has highlighted a slightly increased post-partum bleeding risk when antidepressants**,** particularly SSRIs and SNRIs, are used during the month before delivery.

Thanks to Zainab Hayat, Rotational Pharmacist.