LOTHIAN PRESCRIBING BULLETIN

Supporting prescribing excellence - informing colleagues in primary and secondary care

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NHS Lothian

In this issue …

Never mind the biologicals here are the biosimilars

A biological medicine is any drug product extracted from, or semi synthesised from a biological source. They include vaccines, blood products, gene therapies, cell therapies (e.g. stem cell therapy) and recombinant DNA products. It is the latter that are more commonly referred to as 'biologics'. Recombinant DNA medicines include relatively simple molecules that are nearly identical to the body's proteins (human and analogue insulin, erythropoietin and growth hormone) and more complex molecules such as fusion proteins and monoclonal antibodies.

Fusion proteins are created through joining two or more genes that originally coded for separate proteins. The resulting fusion gene is then used to produce a protein with the combined functions of the originators. Etanercept is a fusion protein used in the treatment of autoimmune diseases. It inhibits the activity of tumour necrosis factor (TNF), which is the master regulator of the immune response. It results from fusion between a TNF receptor and an IgG1 antibody. The antibody transports the medicine to the site of overactive immune response and the TNF receptor binds the tumour necrosis factor.

Currently the mention of biological medicines is most likely to refer to **monoclonal antibodies**. In simple terms these are manufactured by cloning a single B-lymphocyte that produces a specific antibody to a specific antigen. Originally they were manufactured using mouse B-lymphocytes, but the resulting murine monoclonal antibodies had unreliable effects and a short plasma half life. Making the antibodies more human has improved both safety and efficacy. For example, chimeric monoclonal antibodies (e.g. infliximab) are produced by fusing the mouse-derived with human antibody. Infliximab is an antibody to TNF-alpha. There is logic behind the naming of monoclonal antibodies. For infliximab the 'li' refers to it being an immunomodulator, the 'xi' refers to it being chimeric and the 'mab' refers to it being a monoclonal antibody.

Both etanercept and infliximab inhibit TNF-alpha, and are classed as **cytokine modulators**. All cytokine modulators must be used under specialist supervision. For the patient there is a predisposition to infection for up to 5 months after treatment. Of particular importance is the need to exclude or treat tuberculosis before initiating cytokine modulator therapy. Patients are at increased risk of blood disorders, presenting with fever, sore throat, bruising or bleeding. Infliximab is given as an intravenous infusion and must be administered where resuscitation equipment is available, due to potentially severe hypersensitivity reactions.

The marketing authorisation for a number of biological medicines has expired, and this has allowed competing companies to produce new biological products that are similar to the reference product. These **biosimilars** can be used for the same clinical indications as the reference product and are likely to be available at lower cost to the NHS. Biological medicines display small variations in structure and effect, even between batches of the same product. This principle also applies to the reference products. It is estimated that 50% of the current UK market for biological medicines will be subject to biosimilar competition by 2019.

The LJF includes several biological medicines. In general, the complex ones such as monoclonal antibodies are recommended for specialist prescribing only.

Further information:

- Biosimilar medicines. Policy statement. Scottish Medicines Consortium. May 2015
- Biosimilar medicines: A national prescribing framework. Healthcare Improvement Scotland. May 2015.

Injecting safety into vaccine prescribing

The majority of vaccines ordered, issued and administered in primary care are supported by either national or local procurement and with public health involvement. Ensuring the correct vaccine for the correct patient requires careful product selection and cross referencing with the appropriate schedule before administration.

Less commonly a vaccine needs to be prescribed, and this additional step also requires extra vigilance. To improve safety some authorities recommend prescribing by product name as a means of ensuring the correct vaccine is supplied and administered. Others, however, recommend approved (generic) name prescribing, and to include the phrase *'for an adult'* or *'for a child'* within the dosing instruction to reduce the risk of wrong product selection. For example there are a number of hepatitis A vaccine products with different dosing volumes for different age groups.

The table helps demonstrate how the use of brand name prescribing can reduce ambiguity when prescribing hepatitis A vaccine. Prescribing Epaxal® is perhaps the safest option, as it is the only product with the same licensed dose for age 1-17 years and adults. However there is a risk of creating supply issues and Epaxal® is contraindicated in egg hypersensitivity.

There have been a number of recent adverse events due to ambiguous prescribing of vaccines. An important system factor was the use of approved name prescribing of hepatitis A vaccine in InPS Vision. The drug directory only includes the 0.5mL approved name form, which resulted in the supply of Avaxim®, even though the prescription was for a young child. This demonstrates the importance of being explicit about the age of the patient, in the dosing instruction.

Product	Dose (initial)	Age
Avaxim®	0.5mL	16-17 years and adult
Epaxal®	0.5mL	1-17 years and adult
Havrix Junior Monodose®	0.5mL	1-15 years
Havrix Monodose®	1mL	16-17 years and adult
Vaqta® Paediatric	0.5mL	1-17 years
Vaqta® Adult	1mL	adult

Click here for Public Health England guidance: Complete immunisation schedule.

Risk of serious birth defects with mycophenolate

Mycophenolate mofetil and its active metabolite mycophenolic acid are immunosuppressive agents used in combination with other immunosuppressants for the prevention of acute rejection in patients who have received kidney, heart or liver transplants. **They are associated with a high rate of serious birth defects and increased risk of spontaneous abortion**.[1]

Mycophenolate mofetil is the first choice antiproliferative immunosuppressant in LJF section 8.2.1 for renal, combined pancreas/renal and islet transplant. The local shared care agreement is currently under review. It may also be used in other therapeutic areas such as dermatology.

Suspected adverse reactions, including adverse pregnancy outcomes, should be reported. You can submit a Yellow Card online, by post or via the app. Information at the Yellow Card Centre (YCC) Scotland website.

New pregnancy-prevention advice for women and men[1] - mycophenolate mofetil and mycophenolic acid:

- Should not be used in pregnancy unless there is no suitable alternative treatment
- Physicians should ensure that women and men taking these medicines understand the risk of harm to a baby, the need to plan for pregnancy and change treatment as necessary
- Patients must immediately consult a physician if there is a possibility of pregnancy
- Treatment should only be initiated in women of child bearing potential when there is a negative pregnancy test result
- Women should use two forms of effective contraception during treatment and for six weeks after stopping treatment
- Men (including those who have had a vasectomy) should use condoms during treatment and for at least 90 days after stopping treatment
- Female partners of male patients treated with these drugs should use highly effective contraception during treatment and for 90 days after the last dose.

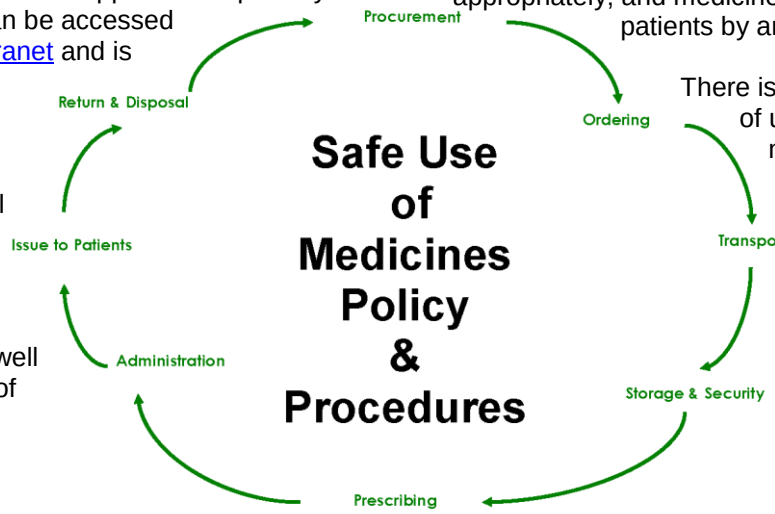
References

1. Drug Safety Update volume 9 issue 4 December 2015: 2. Medicines and Healthcare products Regulatory Agency. www.gov.uk/government/uploads/system/uploads/attachment_data/file/485099/Drug_Safety_Update_Dec_2015.pdf

Safe use of medicines - refreshed policy and procedure

The Safe Use of Medicines Policy and Procedures for NHS Lothian has been reviewed in line with current regulations and guidance to ensure these are reflected in local practice. It is applicable in primary and secondary care, can be accessed on the NHS Lothian intranet and is now easier to navigate with hyperlinked, numbered sections.

The policy underpins all aspects of the safe use of medicines, from procurement and ordering to prescribing and administration, as well as return and disposal of medicines.



It details that all medicines should be ordered through pharmacy and that an accurate audit trail is maintained; medicines are stored and stocked appropriately; and medicines are prescribed to patients by an authorised prescriber.

There is also guidance on the use of unlicensed medicines and medicines used as part of clinical trials, for which the appropriate documentation must be completed.

Key points

Medicine samples *(Section 1.2.1)*
NHS Lothian staff must not accept any product, including medicines or dressings, from medical representatives.

Medication Administration Records (MAR charts) *(Section 3.11.4)*
The procedure for supplying MAR charts from NHS Lothian hospitals, including which patients are considered eligible for MAR charts.

Delivery of medicines by NHS Lothian staff or couriers to patients' homes *(Section 5.4)*
The process to be followed when delivering medication to patients: risk assessment which should be undertaken prior to delivery, terms and conditions the courier must agree to before handing over medication and confirmation of receipt.

Requests for non-formulary medicines in secondary care *(Section 7.19)*
The procedure to be followed and where to find the appropriate forms which should be completed when medication not included in the LJF is prescribed.

Individual Patient Treatment Requests *(Section 7.21)*
The process for prescribing medicines which have not been approved for use by the SMC and when the prescriber intends to use the medication within the licensed indication. The policy includes guidance on completing IPTR requests, with a link to the correct documentation.

Administration of medicines outwith prescribed times *(Section 9.3)*
Guidance for nursing staff on managing patients who have not been administered regularly prescribed medication at the correct time. The policy states who to contact and how to clearly document what medication has been administered and when.

Procedure for suspicious substances within hospitals *(Section 27.3.16)*
Links to the appropriate forms regarding potential illicit substances.

Supply of Controlled Drugs (CDs) to external organisations or other health and social care bodies in exceptional circumstances *(Section 27.4.16)*
The current guidance has changed and the policy has been updated to reflect these changes. Supplying external organisations with CDs is only permitted under a named patient basis and should not be routine practice.

Thanks to Joanna Main and Zoe McGroarty, Pharmacy Pre-Registration Pharmacist Trainees, and Sheena Kerr, Lead Pharmacist at Western General Hospital, for contributing this article.

Instalment prescriptions for controlled drugs: new wording

Prescriptions for Controlled Drugs (CD) which are supplied in instalments must contain specific wording to allow supply in advance of public holidays or where the patient has failed to collect part of an instalment.

In response to concerns, the Home Office has recently published updated sets of wording which are more concise and aim to improve patient safety, reduce workload for GPs and pharmacists and reduce difficulties for the patient.

One or more of the new sets of wording can be used to ensure the prescriber's intentions are clear:

- Please dispense instalments due on pharmacy closed days on a prior suitable day
- If an instalment's collection day has been missed, please still dispense the amount due for any remaining day(s) of that instalment
- Consult the prescriber if 3 or more consecutive days of a prescription have been missed
- Supervise consumption on collection days
- Dispense daily doses in separate containers

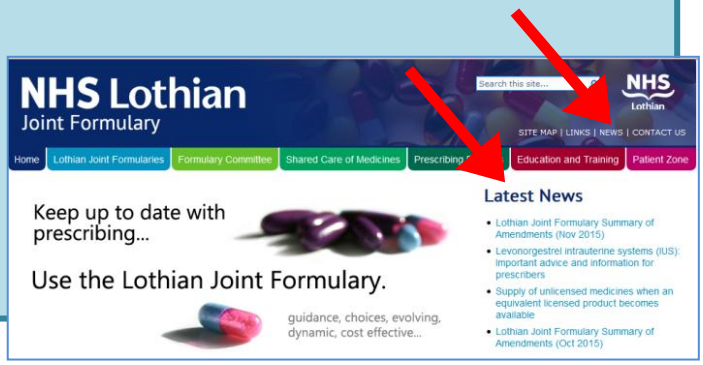
Note:

- The previous wording can still be used as long as the prescriber's intentions are clear.
- Prescriptions with the previous wording should be dispensed as usual where legally compliant and there are no other concerns about supply.
- The expectation is that prescribers will take steps to move from using the old approved wording to the new set of approved wording in the coming months. The Home Office will review the position in three to six months.
- Instalments can now be supplied on a **suitable day** prior to closure; not specifically the day **immediately** prior to closure e.g. on a Monday Public Holiday closure, a patient who normally receives a three day supply on a Friday can now be supplied with the Monday supply on the Friday, if suitable and the appropriate wording appears on the script. Previous approved wording would have required the patient to return on the Saturday to collect the Monday supply.
- This new wording is not intended for use to cover normal weekend closing.

Thanks to Judie Gajree, Lead Pharmacist, Controlled Drugs Governance Team, for contributing this article.

LJF summary of amendments available online

All amendments made to the content of the Lothian Joint Formulary are summarised in an easy-to-read document on the LJF website. These can be found in the News section and date back to January 2015.
As the amendments remain on the website please note that previous advice might have been superseded.
Documents are dated as per Formulary Committee meeting at which changes were approved.



Supplement: Recent SMC and Lothian Formulary Committee Recommendations

The supplements can be accessed via the LJF website www.ljf.scot.nhs.uk in 'Prescribing Bulletins'.

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