LOTHIAN PRESCRIBING BULLETIN

Supporting prescribing excellence - informing colleagues in primary and secondary care

Happy New Year

NHS Lothian

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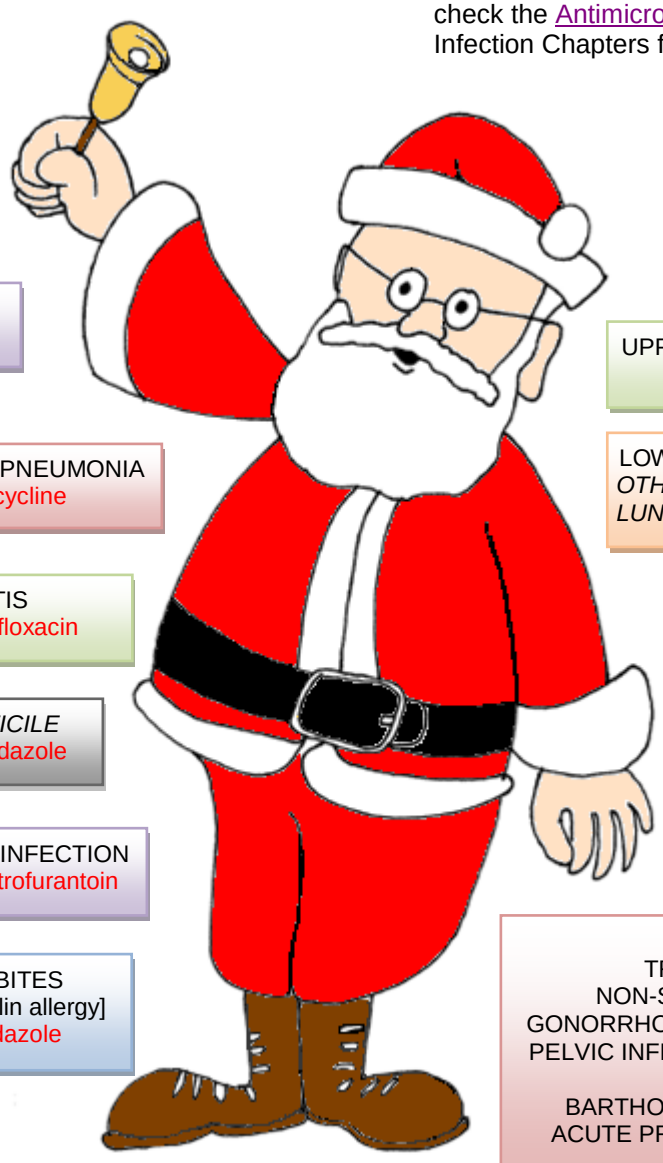
Even Santa sometimes needs an antibiotic ...

4C antibiotic (cephalosporins, co-amoxiclav, clindamycin and ciprofloxacin) use in primary and secondary care puts patients at increased risk of Clostridium difficile infection, and drives antibiotic resistance far more than narrow spectrum agents. Of particular note in primary care, there has been a significant increase in urinary tract infections caused by extended spectrum beta lactamase (ESBL) producing bacteria, which are resistant to most antibiotics.

Repeated courses of antibiotics are deleterious to frail older people and increase the risk of *Clostridium difficile* infection.

For virtually all quality prescribing areas NHS Lothian performs well. However, NHS Lothian currently has the highest use of co-amoxiclav of all Scottish Boards, despite its very limited number of indications recommended in the LJF. For further information please check the Antimicrobial Guidelines and the LJF Infection Chapters for Adults and Children.



IMPETIGO
flucloxacillin

COMMUNITY ACQUIRED PNEUMONIA
amoxicillin or doxycycline

PYELONEPHRITIS
co-amoxiclav or ciprofloxacin

CLOSTRIDIUM DIFFICILE DIARRHOEA metronidazole

URINARY TRACT INFECTION
trimethoprim or nitrofurantoin

ANIMAL and HUMAN BITES
co-amoxiclav or [for penicillin allergy]
doxycycline + metronidazole

UPPER RESPIRATORY TRACT INFECTION
NO ANTIBIOTICS

LOWER RESPIRATORY TRACT INFECTION:
OTHERWISE HEALTHY **NO ANTIBIOTICS**
LUNG DISEASE amoxicillin or doxycycline

CELLULITIS flucloxacillin

EPISIOTOMY INFECTION
co-amoxiclav

CHLAMYDIA azithromycin
TRICHOMONIASIS metronidazole
NON-SPECIFIC URETHRITIS azithromycin
GONORRHOEA refer to Chalmers Sexual Health Centre
PELVIC INFLAMMATORY DISEASE metronidazole and ofloxacin
BARTHOLINS GLAND INFECTION co-amoxiclav
ACUTE PROSTATITIS ciprofloxacin or trimethoprim

New: A policy for shared care of medicines

Shared care arrangements aim to facilitate the seamless transfer of prescribing of certain medicines from secondary care to general practice.

A new NHS Lothian Policy and Procedures for the Shared Care of Medicines was approved in June 2013 and is available on the NHS Lothian Intranet. For clinicians and patients clearly defined processes, good communication and awareness of responsibilities are essential to allow safe and effective prescribing.

Shared care arrangements will now be set out in a **shared care agreement (SCA)**. These documents have previously been known in Lothian as shared care protocols.

A medicine's SCA must be read in conjunction with its Summary of Product Characteristics (SPC). All SPCs can be found at www.medicines.org.uk. Adverse reactions, contra-indications, dosage and administration details will now only appear in the SPC and will only be detailed in the SCA where a drug is being used off-label outwith its licence. Another new feature is that a SCA may include responsibilities of patient, relatives and carers.

Shared care arrangement eligibility criteria

- ✓ prescribed for a potentially serious condition
- ✓ complex [intended use likely to be outwith the clinical experience of a GP]
- ✓ relatively high adverse effect profile
- ✓ may require specific monitoring and dose titration
- ✓ new, or rarely prescribed

Clinical Teams have been invited to review current shared care protocols in line with the eligibility criteria set out in the new policy.

Iron 1: MHRA advice on intravenous iron preparations

A Europe-wide review of intravenous (IV) iron products for iron deficiency and anaemia has recommended strengthened measures to manage and minimise the risk of hypersensitivity reactions, which are well known to occur rarely with products, and may be life-threatening or fatal.[1]

The MHRA has provided advice for healthcare professionals, including:

- An IV iron product should not be used in patients with known hypersensitivity to the active substance, the product itself, or any of its excipients; it should also not be used in patients with known serious hypersensitivity to any other parenteral iron product
- The risk of hypersensitivity is increased in patients with: known allergies (including drug allergies); immune or inflammatory conditions; or those with a history of severe asthma, eczema, or other atopic allergy. In these patients, IV iron products should only be used if the benefits are clearly judged to outweigh the potential risks
- IV iron should not be used during pregnancy unless clearly necessary. Treatment should be confined to the 2nd or 3rd trimesters, if the benefit is clearly judged to outweigh the potential risks for both mother and foetus
- Caution is needed with every dose of IV iron that is given, even if previous administrations have been well tolerated
- IV iron products should only be administered when staff trained to evaluate and manage anaphylactic or anaphylactoid reactions - as well as resuscitation facilities - are immediately available
- Patients should be closely monitored for signs of hypersensitivity during, and for at least 30 minutes after, every administration of an IV iron product
- In the event of a hypersensitivity reaction, treatment should be stopped immediately and appropriate management initiated.

Any suspected adverse reactions to IV iron products should be reported via the Yellow Card Scheme www.yellowcard.gov.uk; staff at the Yellow Card Centre (YCC) Scotland can also be contacted on 0131 242 2919 or via www.yccscotland.scot.nhs.uk

Reference

1. Drug Safety Update vol 7, issue 1 August 2013: A1. MHRA www.mhra.gov.uk

Iron 2: LJF recommendations for intravenous iron

In recent months, a number of anaphylactic reactions to Monofer® (iron isomaltoside) were reported in NHS Lothian in some clinical areas.

Therefore, following an application from a group of clinicians, the Formulary Committee has agreed to include ferric carboxymaltose (Ferinject®) on the LJF as an equal first choice drug for specialist use only, for use in GI and Haematology patients, for the treatment of iron deficiency when oral iron preparations are ineffective or cannot be used. The diagnosis must be based on laboratory tests.

Iron isomaltoside (Monofer®) remains on the LJF as a first choice drug for the Renal and Reproductive Medicine patients.

Ferinject® is advantageous over other products in that high dose infusions can be administered over a shorter period. However its use is cautioned in patients with liver dysfunction, acute or chronic infection, asthma, eczema or atopic allergies. The preparation contains sodium and aluminium therefore this should be taken into account in patients on restricted sodium intake. The dosing and administration of Ferinject® is different to that of Monofer® therefore please refer to the appropriate IV iron protocol.

Detect and treat hepatitis C infection early

Hepatitis C virus (HCV) is a blood borne virus and up to 80% of patients infected with HCV will become chronically infected. Approximately 0.8% of the Scottish population are thought to be chronically infected with HCV. Hepatitis C is usually slowly progressive over a period of many years. Five to 15 per cent of patients with chronic hepatitis may progress to liver cirrhosis over 20 years. Diagnosis of chronic HCV infection allows initiation of prompt and effective antiviral treatment if appropriate.[1]

The goal of HCV treatment is to obtain a sustained viral response (SVR), which is an undetectable viral load six months after the cessation of antiviral therapy. Treatment varies according to HCV genotype. Until recently, standard of care treatment consisted of dual therapy of pegylated interferon and ribavirin, for 24 to 48 weeks depending on genotype. A recent development has been the introduction of protease inhibitors, telaprevir and boceprevir in combination with pegylated interferon and ribavirin for treatment of HCV genotype 1. This triple therapy combination has been shown to significantly improve SVR rates for both naive and treatment experienced patients. These were approved by the Formulary Committee in Spring 2012.

Boceprevir and telaprevir are substrates and inhibitors of the cytochrome p450 isoenzyme 3A4. This enzyme is involved in the metabolism of many medicines and there is great potential for **drug interactions**. As part of their assessment for HCV treatment, patients are asked to give a drug history and are screened for potential interactions. Prescribers should be vigilant if commencing new medicines for patients receiving antiviral medication. Commonly used medicines affected include simvastatin, methadone, benzodiazepines and anti depressants. The protease inhibitors affect the efficacy of hormonal contraceptives and due to the teratogenicity of HCV treatment, two non-hormonal methods of contraception should be used for the duration of therapy. The QT interval can be prolonged by use of the protease inhibitors and patients may require ECG monitoring. This can be a particular issue if patients are co-prescribed other medicines that also prolong the QT interval.

The most common **side-effects** of telaprevir are rash, pruritus, and anaemia. There is a very small but significant risk of serious **skin rashes** including Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) and Stevens-Johnson syndrome. It is vital that patients monitor their skin for any changes. Patients are encouraged to use emollients and the majority of cases are mild and can be managed with corticosteroids. Referral to dermatology is essential for significant rashes and all telaprevir patients will have a rash management plan. For boceprevir, taste disturbance and anaemia are the most commonly reported side-effects. In the next few years, further treatments will be licensed for all genotypes.

Key messages:

- **New treatments for HCV have shown increased rates of cure.**
- **Be vigilant for drug interactions in patients receiving treatment with protease inhibitors.**
- **Patients and healthcare professionals should monitor skin closely during telaprevir therapy.**

Reference

1. Management of hepatitis C. SIGN 133. Scottish Intercollegiate Guidelines Network. Healthcare Improvement Scotland. July 2013. www.sign.ac.uk

Thanks to Katherine Davidson, Clinical Pharmacist.

Safe use of anti-arrhythmic drugs

Anti-arrhythmic drugs are divided into four classes based on mode of action. Class I: membrane stabilising drugs (e.g. lidocaine, flecainide); Class II: beta-blockers; Class III: amiodarone; sotalol (also Class II); Class IV: calcium-channel blockers (includes verapamil but not dihydropyridines). The safe use of Class I and III anti-arrhythmics is discussed in this article.

Class I anti-arrhythmic drugs block sodium channels in the atrial and ventricular myocardium in a similar way to the action of local anaesthetics. Flecainide and propafenone are the commonest ones in use, and flecainide is the preferred choice in Lothian. Class I agents are used exclusively in the management of atrial fibrillation, when there is no structural heart disease. Both heart failure and ischaemic heart disease are contraindications to their use. As negative ionotropes they worsen heart failure. In patients with ischaemic heart disease they increase the risk of potentially fatal ventricular arrhythmias.

Class III anti-arrhythmic drugs block potassium channels in the atrial and ventricular myocardium, thereby prolonging the ventricular action potential and QT interval. Sotalol is both a beta-blocker and potassium channel blocker. It has a great potential to cause the ventricular tachycardia Torsades des Pointes, especially in bradycardic patients. Both dronedarone and amiodarone are less likely to cause ventricular arrhythmias. Dronedarone has been known to cause potentially fatal hepatotoxicity. Amiodarone has a long list of serious and surprisingly common side-effects. Most patients will get photosensitivity and corneal microdeposits. Both thyroid and liver dysfunction are common. And pulmonary fibrosis is not uncommon.

The risk of QT prolongation is increased when co-prescribing class III agents and other drugs with this effect, such as antibiotics, antipsychotics, antiepileptics and antidepressants. Low potassium enhances this risk, so diuretics should be co-prescribed with caution.

Class I and III anti-arrhythmics should only be initiated on the recommendation of a cardiologist after cardiovascular examination, echocardiogram and ECG.

Patients taking these agents should be advised to report immediately very rapid palpitations, dizzy spells or blackouts, as this may indicate potentially life-threatening pro-arrhythmic effects. If any of these symptoms occur an immediate ECG is required and admission if the QT interval is longer than 500 milliseconds.

Flecainide, dronedarone and amiodarone are useful in the management of atrial fibrillation in patients without structural heart disease. Sotalol should be avoided wherever possible due to the increased risk of ventricular arrhythmias. Patients and healthcare providers should be vigilant for symptoms that may indicate a serious side-effect.

Key messages:

- **Only initiate class I and III anti-arrhythmics on cardiologist advice.**
- **Remind patients to report palpitations, dizziness or blackouts.**
- **Immediate ECG is required for concerning cardiac symptoms.**
- **Be alert to drug interactions.**

Thanks to Dr Chris Lang, Consultant Cardiologist.

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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