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**Lipid guidelines  
enclosed**

## Updated lipid guidelines

Cardiovascular disease (CVD) is the major cause of global morbidity and mortality. To provide the best advice on treatment to prevent CVD, based on evidence of clinical and cost effectiveness, and underpinned by research, guidelines for the management of CVD risk are regularly updated, the most recent being the NICE CG181 for lipid modification. The Lothian Lipid Group has published a two-page Lothian guideline updating management of adult patients with hyperlipidaemia.

The Lothian Lipid Management in Adults Guideline was launched on 4<sup>th</sup> November at the annual Edinburgh High Blood Pressure Symposium. It provides clear and concise advice on the management of cardiovascular risk. The guidelines are aimed at new patients or those requiring a management change.

The lipid guidelines are available in full on the [Clinical Guidance page of the NHS Lothian intranet](#) and on the [RIE & SJH Lipid Clinic page on RefHelp](#).

### Key areas addressed by the guideline are:

#### Identifying and assessing CVD risk

- Patients with an estimated ten-year risk of  $\geq 10\%$  should undergo full clinical assessment. As previously, the focus of this should be the investigation of underlying secondary causes, other vascular risk factors and evidence of end organ damage.
- Biochemical investigation, including that of the lipid profile, can now be undertaken on non-fasting samples.
- [ASSIGN](#) remains the cardiovascular risk calculator of choice with the caveat that it should not be used in patients with familial hypercholesterolaemia or existing cardiovascular illness.

#### Management

- Patients whose CVD risk threshold is greater than 10% should now be considered for statin therapy.
- Lifestyle modification focuses on the management of overall cardiovascular risk, improved lipid profile and the reduction of blood pressure.
- Atorvastatin is now first line treatment in both primary (20mg daily) and secondary (80mg daily) prevention (dose adjustments might be necessary depending on renal function and drug interactions).
- Treatment aims in secondary prevention remain the attainment of an LDL  $< 2$ . No specific lipid targets exist in primary prevention.

#### Monitoring statin adverse effects and intolerance

- Lower starting doses of atorvastatin should be used in patients who have potential drug interactions or high risk of adverse effects. Advice and hyperlinks are included in the guidelines.
- Further advice is included for the identification of patients with definite or possible familial hypercholesterolaemia.
- An abbreviated summary of the management of hypertriglyceridaemia guidelines is also included.

#### Key messages



**The ten-year cardiovascular risk threshold for consideration of therapy is now 10%.**

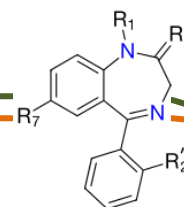


**Atorvastatin is now the first line agent for pharmacological therapy.**



**Patients established on therapy should not routinely have their statin changed.**

Thanks to Dr Emma Morrison, Clinical Research Fellow, and Professor David Webb, Christison Chair of Therapeutics and Clinical Pharmacology, Queen's Medical Research Institute, on behalf of the Lipid Working Group, for contributing this article.



## Substance misuse

The LJF advice for opiate and benzodiazepine misuse has been updated, [section 4.10](#). Throughout the section there have been changes to layout and amendments to prescribing notes and dosing information. The website should be referred to for full prescribing information.

### Some key changes are:

#### (b) opioid maintenance prescribing

- Buprenorphine is now second choice, replacing dihydrocodeine. It should be prescribed generically.
- Suboxone® (buprenorphine and naloxone) should only be prescribed for those at risk of intravenous use of buprenorphine. There is a Shared Care Agreement for Suboxone®.
- Methadone tablets should not be prescribed. The only strength of methadone oral solution to be prescribed is 1mg/mL.

#### (c) opioid detoxification

- The section has been amended to refer to [NICE guidance 52: Drug Misuse – opioid detoxification](#).

#### (e) take home naloxone

- This is a new section providing some information about the take home naloxone programme.

#### (f) benzodiazepine prescribing

- **Only the 2mg strength of diazepam tablets should be prescribed.** This is to help tackle the high street value associated with diverted diazepam tablets. The 2mg tablets also allow for easier reduction regimens.
- This change in diazepam prescribing has been made in line with most other Scottish health boards.
- Maintenance prescriptions for benzodiazepines should not be started.

## What do you know about mirabegron?

Mirabegron is a beta-3-adrenergic-receptor agonist. It works by attaching to and activating beta-3 receptors that are found in the muscle cells of the bladder. When activated, these receptors cause the bladder muscles to relax. This is thought to lead to an increase in the capacity of the bladder and changes in the way the bladder contracts, resulting in fewer bladder contractions and thus reduced frequency.<sup>1</sup>

Mirabegron is included in the prescribing notes of [LJF section 7.4.2 \(a\) urinary frequency due to bladder instability](#). It may be used in patients who have not responded to treatment with two different antimuscarinics or in whom antimuscarinics are contraindicated.

A **new prescribing note** has been added to the LJF noting that mirabegron may also be considered as a first line option where there is concern that patients have a high anticholinergic load.

#### Reference

1. [Summary of the European public assessment report \(EPAR\) for mirabegron \(Betmiga®\)](#). Updated 15.10.15.

There has been heightened awareness regarding the risks of high anticholinergic load. Anticholinergics have long been linked to impaired cognition and falls risk, and (more recently) have also been linked to increased morbidity and mortality. This may prompt some prescribers to discontinue treatment for overactive bladder. Mirabegron provides an option to treat overactive bladder without increasing the anticholinergic burden. Further information about anticholinergic load can be read in the [Scottish Government Polypharmacy Guidance, March 2015](#).

Recent [MHRA safety advice](#) noted that mirabegron must not be used in people who have hypertension that is severe and uncontrolled.

Other common side-effects are

- tachycardia seen in just over 1 person in 100
- urinary tract infection seen in just under three people in 100

Serious but uncommon side-effects include atrial fibrillation. For the full list of all side-effects reported see the [SPC](#).



# Measuring formulary prescribing across primary and secondary care

LJF adherence measures have been developed in discussion with the Medicines Utilisation Review Group (MURG), a subgroup of the Area Drug and Therapeutics Committee, who will be monitoring these over the coming months. The overall aim is to encourage improvements in the percentage adherence to each measure across both primary and secondary care. The six therapeutic areas below were selected to reflect key formulary priorities. Reports are sent out to prescribers quarterly to raise awareness and encourage peer review.

## Antidiabetes drugs

**LJF 1<sup>st</sup> choice: dipeptidyl peptidase-4 inhibitor (*sitagliptin*), incretin mimetics (*lixisenatide*), sodium-glucose co-transporter 2 (*dapagliflozin*)**

There are a number of newer antidiabetes medicines available with limited clinical difference between drugs in a similar class. The LJF recommendations are made following consideration of evidence, SMC approved indications and cost. There is limited evidence to support the need for use of non-formulary medicines in this therapeutic area.

## Hypnotics

**LJF hypnotic of choice**

The LJF recommends no pharmacological treatment as first choice and zopiclone as second choice. When 'z drugs' were first marketed, prescribing was discouraged as they were expensive with no real clinical advantages over temazepam. Zopiclone is now available as a generic and is substantially cheaper than temazepam. Significant cost savings can be achieved with no difference to clinical efficacy. Use of hypnotics should be short term.

## Antimicrobial wound dressings

**LJF 1<sup>st</sup> choice antimicrobial wound dressings**

[Support materials](#) are available to help guide decision-making when managing a wound that may require an antimicrobial dressing. Historically NHS Lothian was a high user of silver dressings, which have limited clinical evidence of efficacy. Silver dressings are not included in the wound formulary (since 2013) and use of the LJF approved antimicrobial dressings will help to ensure appropriate management of wounds.

## Inhaled corticosteroids

**LJF 1<sup>st</sup> choice inhaled combination preparations: *Fostair*® for asthma and COPD, *Relvar Ellipta*® for COPD**

The aim is to maximise the use of first choice inhaled corticosteroid combination preparations to support lower steroid doses and help reduce prescribing costs. Seretide remains the top item for cost and is 26<sup>th</sup> for volume in primary care in NHS Lothian and is more expensive than the first choice products.

## Opioid analgesics

**LJF 1<sup>st</sup> choice morphine modified release**

This measure is agreed as a proxy measure for the appropriate management of chronic pain and to encourage the use of modified release morphine first line when considering an opioid for severe chronic pain. There are significant amounts of alternative opioids being prescribed.

## GI / mesalazine

**LJF 1<sup>st</sup> choice mesalazine**

Overall use of the LJF first choice mesalazine preparation (*Pentasa*®) remains low and has not significantly increased over the past few years. It is anticipated that this measure will encourage its use for all new patients. *Pentasa*® should be prescribed by brand name.

## Apixaban - LJF 1<sup>st</sup> choice for DVT and PE

Apixaban was recently added to the LJF as first choice for the treatment of acute DVT or acute pulmonary embolism and prevention of recurrent DVT and pulmonary embolism in adults. It is also in the LJF as second choice for prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation (NVAF.)

Apixaban is a 'factor Xa inhibitor'. It blocks factor Xa, an enzyme involved in the production of thrombin. Thrombin is central to the process of blood clotting. By blocking factor Xa, the levels of thrombin reduce in the blood, which reduces the risk of blood clots.

Care should be taken to ensure the patient receives the correct dose for the stage of their treatment as there is a decreasing dosing regimen over time. Refer to the LJF and BNF for further information.

The dosing regimen of apixaban varies depending on the indication being treated.

Protocols for treatment of DVT and PE are being developed by clinicians and pharmacists in secondary care. Patients may require treatment for six months, 12 months or longer.



# Taking medicines with food – are we making a meal of it?

There are six main reasons why medicines may need to be taken with or just after food, or a meal:

- 1. Medicines that may cause nausea or vomiting.** These should *preferably* be taken *with or after a meal* to minimise this side effect. Examples include: allopurinol and co-beneldopa (e.g. Madopar®).
- 2. Irritant medicines.** These may cause gastrointestinal disturbances, so it is preferable to take these medicines with a meal to minimise this. A small amount of food such as some biscuits, a sandwich or a glass of milk is usually sufficient. Examples include: aspirin, non-steroidal anti-inflammatory drugs and steroids.
- 3. Medicines to treat conditions in the mouth and/or throat.** These should be used *after meals* to maximise retention of the medicine in the mouth. Examples include nystatin, miconazole oral gel and treatments for mouth ulcers.
- 4. Medicines that are better absorbed with food.** Some medicines need food in the stomach to be absorbed into the bloodstream. There are very few medicines where this is clinically important, however one such example is saquinavir (HIV medicine), where food greatly increases its absorption.
- 5. Antidiabetic medicines.** These are taken before, with or after meals, depending on drug, and are timed to reduce blood glucose after meals, and reduce the risk of hypoglycaemia.
- 6. Antacids in patients with meal-time symptoms.** Taking antacids immediately after a meal may relieve these symptoms.

This information can be found in the patient information leaflet (PIL) or summary of product characteristics (SPC), both of which can be accessed online via the [electronic Medicines Compendium](#) (eMC). The [British National Formulary](#) (BNF) also gives advice on this subject in Appendix 3.

*Adapted from UKMI Q&A 336.3: Why must some medicines be taken with or just after food, or a meal? Date prepared: 20 April 2015.*

Conversely, some medicines must be taken when the stomach is empty, or before food. The main reasons are:

- 1. Reduced absorption in the presence of food/acid.** These medicines should be taken an hour before food, or two hours after food to allow them to be absorbed when the stomach is empty. Examples include flucloxacillin, azithromycin and oxytetracycline. Bisphosphonates are significantly affected by the presence of even a small amount of food, and are generally taken first thing in the morning (when fasted).
- 2. Medicines which act directly on the gut.** The time these are taken in relation to food affects their action. Examples are sucralfate (taken at least an hour before food to prevent food interfering with 'coating' action) and mebeverine (taken 20 minutes before meals so onset of action is timed in relation to ingestion of food).

*Adapted from UKMI Q&A 337.4: Why must some medicines be taken when the stomach is empty? Date prepared: 28 April 2015 (partial revision 16 June 2015).*

## Key messages



**Some medicines must be taken with or just after food. Failing to do this may cause gastrointestinal upset or reduce the effectiveness of the medicine.**



**Some medicines require an empty stomach for absorption, and some need to be taken just before meals in order to work properly. Failing to do this for the occasional dose is unlikely to be a problem, but repeated failure to do this could reduce efficacy.**



## Supplement: Recent SMC and Lothian Formulary Committee Recommendations, Lothian Lipid Guidelines 2015

The supplements can be accessed via the LJF website [www.ljf.scot.nhs.uk](http://www.ljf.scot.nhs.uk) in 'Prescribing Bulletins'.

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