LOTHIAN PRESCRIBING BULLETIN

Supporting prescribing excellence - informing colleagues in primary and secondary care

NHS Lothian

In this issue …

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What's in a (drug) name?

How are drugs named?
The Drugs and Therapeutics Bulletin recently published an article about the derivation of drug names.[1] There are three main types of name for pharmaceutical substances:

1. The **chemical name**. This follows rules issued by the International Union of Pure and Applied Chemistry.
2. The **International Nonproprietary Name (INN)** is globally recognised, is public property and has been co-ordinated by WHO since 1953. It is the approved or generic name. In the early 20th century, generic names were created by shortening the chemical name into fewer syllables, e.g. 1-(5-nitrofurfurylideneamino) hydantoin became nitrofurantoin. This, however, resulted in inconsistencies. Since the 1960s, standard word fragments 'stems' have been used for all drugs in the same therapeutic class.
3. **Proprietary (brand) names** are created by pharmaceutical companies. This is defined at a national level and the MHRA regulates applications in the UK. The brand name must be significantly different from the generic name and INN stems. Names should not convey misleading claims for efficacy or safety, e.g. Reallygoodaform or Fabumab. Promotional connotations should be avoided, e.g. Forte, strong.

How are drug names pronounced?
The abundance of new pharmaceuticals has created a challenge in pronunciation for clinicians. Having a uniform pronunciation is beneficial for communication without embarrassment and also for patient safety. The United States Adopted Names (USAN) council has produced a pronunciation guide.[2]
Some examples:

- The suffix 'umab' in human monoclonal antibodies, e.g. adalimumab is pronounced 'you mab'.
- The thrombin inhibitors of the argatroban type, e.g. dabigatran, use the suffix 'gatran'. The pronounciation is *da bye gat'ran* with an emphasis on the GAT.
- The SGLT2 inhibitor *empagliflozin* is spelt phonetically as *em pa gli floe'zin* by USAN. The sugar flows in to the urine to treat diabetes and the drug name ends in 'flows in'.

Confusion over drug names
Recently the MHRA issued a safety alert for confusing drug names.[3] Errors can be made with look-a-like or sound-a-like drug names. Some examples of drugs which have been confused include:

- atenolol/amlodipine
- carbamazepine/carbimazole
- clobazam/clonazepam
- clotrimazole/co-trimoxazole
- mercaptamine/mercaptopurine
- olanzapine/omeprazole
- propranolol/prednisolone
- risperidone/ropinirole

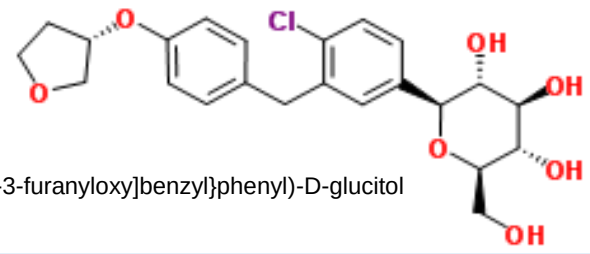
Care should be taken when prescribing and/or dispensing these medicines.

Think ***right drug*** for the ***right patient*** in the ***right dose*** by the ***right route*** and at the ***right time***.

1. Drugs and their names. DTB 2018;56(3):33-36. http://dtb.bmj.com/content/dtb/56/3/33.full.pdf
2. American Medical Association. United States Adopted Names Council: Pronunciation Guide. www.ama-assn.org/pronunciation-guide *Accessed 30.04.18*
3. MHRA Drug Safety Update volume 11 issue 6; January 2018:3. www.gov.uk/drug-safety-update/drug-name-confusion-reminder-to-be-vigilant-for-potential-errors
4. empagliflozin. Royal Society of Chemistry. www.chemspider.com/Chemical-Structure.10123957.html *Accessed 30.04.18*

empagliflozin[4]

Structure:



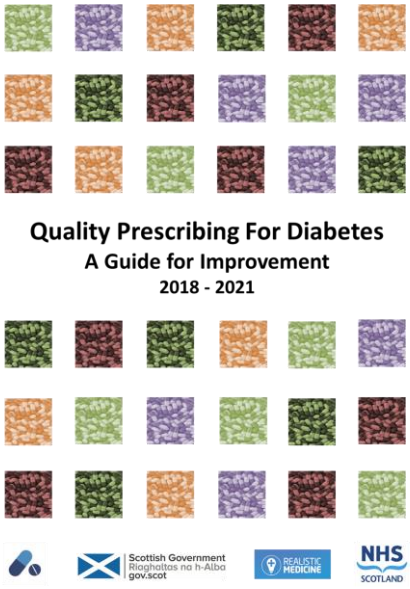
Chemical Name: $C_{23}H_{27}ClO_7$

INN: (1S)-1,5-Anhydro-1-(4-chlor-3-{4-[(3S)-tetrahydro-3-furanyloxy]benzyl}phenyl)-D-glucitol

~~Standardised~~ Personalised sugar control strategy

Quality Prescribing for Diabetes – A Guide for Improvement 2018-2021, published in March 2018, provides a strategic framework for the management of people with type 2 diabetes within the context of updated guidance from SIGN 154, long-term follow-up evidence from key diabetes population studies, and alignment with the principles of the Chief Medical Officer's report, *Realistic Medicine*.

The Qualities Outcome Framework contract recommended a standardised approach to managing type 2 diabetes by treating all people with diabetes to the same glycaemic control target. However, current thinking now stresses the importance of a **personalised** goal for each individual as there are different evidence- based priorities between groups of patients. The fine balance of benefits and risks of different intensities of glycaemic control are affected by many factors. Agreement of the individual's glycaemic target should consider the potential for reduction of microvascular and macrovascular complications with the risks of hypoglycaemia, weight gain and other adverse drug events.



The time to derive clinical benefit from pharmacological intervention to improve glycaemic control is an important concept in the management of people with type 2 diabetes. Trial evidence shows that ten years of treatment is necessary to derive benefits, so the patient's age and life expectancy are important considerations. The presence of comorbidities, functional and cognitive impairment, falls risk, ability to adhere, medication burden and cost are also factors to consider.

For patients who are relatively healthy, with long life expectancy and who will live long enough to derive benefits, such as reduced microvascular events, then tight glycaemic control (HbA_{1c} <53 mmol/mol) may be appropriate. Long-term follow up of patients from UKPDS showed that those receiving tight glycaemic control (with sulphonylureas and/or insulin) derived clinical benefit of up to 17 years, despite the trial only lasting ten years. This sustained clinical benefit suggests that personalised care for patients who have a long life expectancy (>15 years) may include more stringent targets for glycaemic control particularly for those patients motivated to adopt this approach and with a clear understanding of the risks of hypoglycaemia.

Conversely this approach will need to change for people who are older and frailer, and particularly when they have co-morbidities. Reduced life expectancy means that it is unlikely the individual patient will actually derive any clinical benefit from tight glycaemic control. In turn there is an increased risk of hypoglycaemia which is associated with poor outcomes such as increased mortality, cardiovascular disease, falls and accidents. There is likely to be a time for each individual when the harm caused by managing glycaemic control starts to outweigh any potential benefits. The challenge is to identify when this happens. The strategy helps identify an important subgroup of patients for prioritised review, namely over 75 year olds prescribed a sulphonylurea. Regardless of the individual's glycaemic control consider stopping the sulphonylurea. An alternative antidiabetic is only required if the patient develops any hyperglycaemia symptoms.

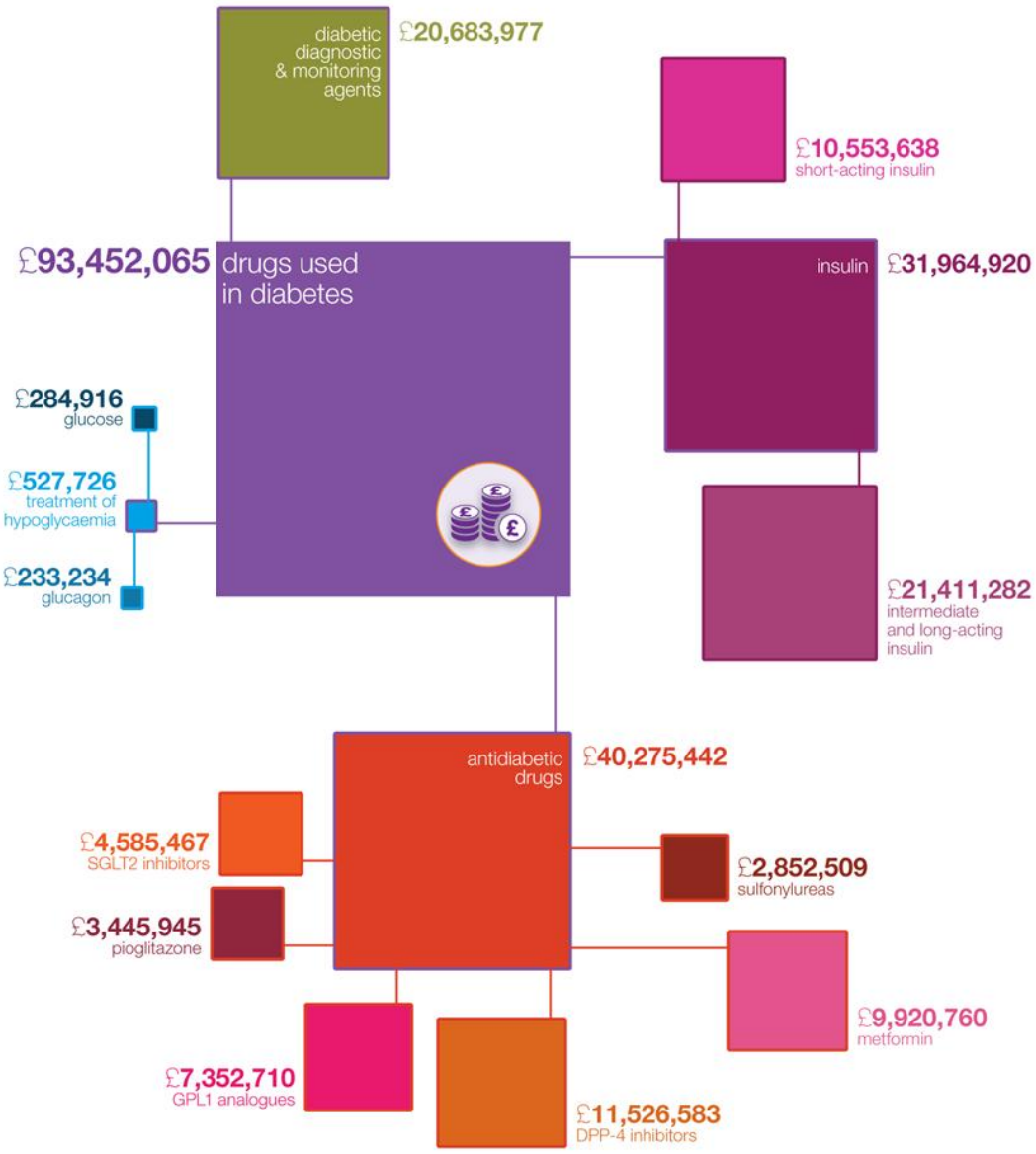
For all patients with type 2 diabetes clinicians should provide counselling and emphasise the importance of lifestyle interventions, including exercise, dietary changes, and weight loss, to achieve good glycaemic control. Smoking cessation, adequate blood pressure control, and lipid management are also indicated in patients with type 2 diabetes and, for many patients, may take priority over achieving glycaemic control, especially for preventing macrovascular complications.

There remains clear evidence of the benefit from tight glycaemic control in younger people (<55 years) with type 2 diabetes. The clinical benefits take ten years to be realised, but once established are shown to last a further seven years, even if the tight glycaemic control is not maintained, which is termed the 'Legacy Effect'. Each individual will reach a tipping point when tight glycaemic control does more harm than good, and it is these patients that should be targeted for review.

Key messages:

- Review patients >75 years of age who are taking a sulphonylurea, and consider stopping it.
- Tight glycaemic control in patients <55 years is appropriate. Evidence shows that there are 17 years of benefit for 10 years of treatment. This extra 7 years is known as the legacy effect.

This graphic illustrates the prescribing spend in NHS Scotland in relation to management of diabetes.



LJF Summary of Amendments January 2018

The cardiovascular chapter has been updated to reflect current practice and ensure consistency with the NHS Lothian Hypertension and Lipid Guidance.

Choice of antimuscarinic inhalers in the respiratory chapter has now been revised and the triple therapy inhaler Trimbow® is now included. Prescribers are reminded that best practice is to prescribe all inhalers by brand name (except salbutamol) and device type.

The smoking cessation section now contains flowcharts summarising patient pathways and choice of product. These reflect that NRT and varenicline are joint first choice for symptom control of nicotine withdrawal after a 'quit date' has been set.

Warnings from the MHRA on headlice eradication products and Esmya® (ulipristal acetate) have been added to the LJF:

- During treatment with dimeticone 4% lotion (Hedrin®) keep away from fire, especially naked flames and burning cigarettes as hair can burn readily if ignited.
- Esmya® (ulipristal acetate) should not be initiated or re-started in patients following reports of serious liver injury in women treated for uterine fibroids. This is a temporary safety measure whilst EU reviews are ongoing.

Methotrexate toxicity with co-prescribing

A frequently asked question relates to the interaction of NSAIDs with methotrexate. This is especially so as the GP and pharmacy IT systems raise caution when prescribing this combination.

Review of the drug interactions sources indicate that while some studies show a significant reduction in the clearance of methotrexate when ibuprofen is taken concomitantly, other studies show that ibuprofen has no effect on the pharmacokinetics of methotrexate.

The consensus of opinion seems to be that the risks are greatest with high dose methotrexate (150mg or more daily to treat neoplastic disease) and in patients with impaired renal function, but less in those given low doses (5-25mg weekly) with normal renal function. However, the use of an NSAID with methotrexate at any dose is a recognised additional risk factor for toxicity and patients on this combination should be monitored carefully.

The following advice from the NHS Lothian rheumatology service has been incorporated within the Shared Care Agreements for methotrexate (oral and subcutaneous) for the treatment of inflammatory rheumatic diseases:

> *'NSAIDs and aspirin (not including low dose aspirin 75mg) can reduce the excretion of methotrexate, increasing the risk of toxicity. NSAIDs are commonly used in conjunction with methotrexate in inflammatory diseases, therefore, increased monitoring is essential in patients who are newly started on NSAIDs until they are stable on both treatments. Please revert to initial monitoring schedule when NSAID newly initiated.'*

In summary, for patients taking methotrexate, NSAIDs should be avoided where possible with paracetamol being considered a safer alternative. However, if an NSAID is needed, regular use is preferred and appropriate monitoring should be in place according to the relevant shared care agreement.

Patient on methotrexate should be advised not to purchase NSAIDs without consulting with a pharmacist or their doctor. Pharmacists should discuss the risks and ensure that their doctor is informed that they are using an NSAID so they can be appropriately monitored and followed up.

Another interaction that can be overlooked is PPIs with methotrexate. Information is limited, but it has been shown that PPIs can reduce the clearance of methotrexate, leading to methotrexate toxicity in some cases. The potential for increased toxicity should be considered when initiating PPIs in patients already established on methotrexate and increased monitoring is recommended until stable on both treatments. Ranitidine may be a suitable alternative.

Prescribing Indicators 2018/19

The NHS Lothian Prescribing Indicators (PIs) for 2018/19 have been agreed by the General Practice Prescribing Committee (GPPC). A full list of the PIs is available from the LJF website in 'Prescribing Bulletins' as a downloadable supplement. The main points to note are:

- 1 indicator has been updated - the high strength inhaled corticosteroid measure, the 9 other indicators are unchanged from 2017/18
- 7 of the 10 indicators follow the National Therapeutic Indicators developed by the Scottish Government Therapeutics Branch.

Warfarin 2-page ready reckoner

In issue 88 of the Lothian Prescribing Bulletin we highlighted to readers the updated warfarin guidelines. This guideline has been updated slightly, and you should now be using the guideline dated February 2018. In addition many GPs have commented that a short 2-page summary document would be very useful. This has now been produced and is available from this link - Home > Directory > Lothian Unscheduled Care Service > Clinical Information

Please take care when searching on the intranet for these guidelines, the search results sometimes still return old versions. Every effort has been made to get these removed.

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