LOTHIAN PRESCRIBING BULLETIN

NHS Lothian

Supporting prescribing excellence - informing colleagues in primary and secondary care

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Severe respiratory depression with pregabalin and gabapentin

Gabapentin and pregabalin are *'gabapentinoid'* medicines, with similar structure and mechanism of action. Both are subject to misuse. The gabapentinoids can cause central nervous system depression resulting in drowsiness, sedation, respiratory depression and at the extreme, death. These effects are additive when used with other centrally acting drugs, particularly opioids. The pharmacokinetic properties of pregabalin make this medicine relatively more dangerous than gabapentin in high doses.[1]

Gabapentin and pregabalin are included in the formulary for a range of indications. Please refer to the formulary pathways for epilepsy and pain and the formulary decisions for more details.

A recent MHRA safety update advised that **pregabalin** has been associated with infrequent reports of severe respiratory depression, including cases without the presence of concomitant opioid medicines.[2]

There are also case reports of respiratory depression, sedation, and death associated with **gabapentin** when co-administered with CNS depressants, including opioids[3] and like pregabalin, it has also been associated with severe respiratory depression, even without concomitant opioid medicines.[3,4]

In some of these reports, the authors considered the combination of **gabapentin** with opioids to be a particular concern in frail patients, in the elderly, in patients with serious underlying respiratory disease, with polypharmacy, and in those with substance abuse disorders. Therefore, patients who require concomitant treatment with opioids should be carefully observed for signs of CNS depression, such as somnolence, sedation and respiratory depression, and the dose of gabapentin or opioid should be reduced appropriately.[3]

KEY MESSAGES

- For **both pregabalin and gabapentin**, consider whether adjustments in dose or dosing regimen are necessary for patients at higher risk of respiratory depression, this includes those with compromised respiratory function, respiratory or neurological disease, or renal impairment; those taking other CNS depressants (including opioid-containing medicines); people aged 65 years or older.[2,4]
- Advise patients to report new or increased trouble breathing or shallow breathing after taking **pregabalin**; a noticeable change in breathing might be associated with sleepiness.[2]
- Advise patients to avoid alcohol during **pregabalin** treatment.[2]
- Healthcare professionals and members of the public should report suspected adverse reactions using the Yellow Card Scheme.

References

1. Public Health England. 2014
2. MHRA. Drug Safety Update. Feb 2021
3. Neurontin (gabapentin) tablets. Revised SPCs. June 2021
4. MHRA. Drug Safety Update. Oct 2017

Thanks to Zainab Hayat, Rotational Pharmacist.

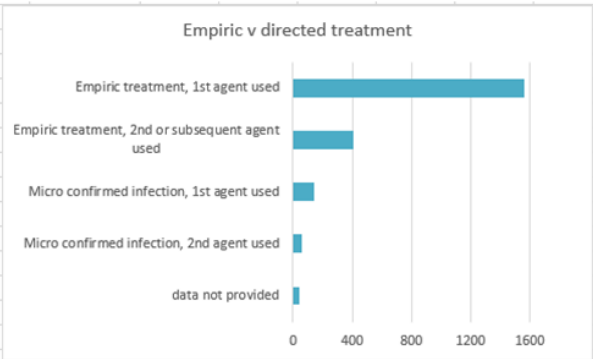
Co-amoxiclav - we 4C change

Primary care has made significant progress in reducing unnecessary antibiotic prescribing while increasing use of narrower spectrum antibiotics. However, prescribing of co-amoxiclav had recently increased in NHS Lothian. An audit of co-amoxiclav prescribing was undertaken to understand the reasons for this increased use.

Co-amoxiclav is a broad spectrum antibiotic, being overly broad for many primary care indications and with causal association to Clostridioides difficile. It has very limited indications in the formulary.

Snapshot audit

GP practices were asked to review co-amoxiclav prescriptions issued in an eight-week period between August and November 2020. 113 practices across Lothian provided results from review of 2,210 prescriptions. See table below.



96% of co-amoxiclav prescriptions were issued as 'acute', with the remaining 4% as 'repeats'.

Results showed that 89% of co-amoxiclav prescriptions related to empirical use (where the pathogen is not known). 13% of prescriptions were on advice of a hospital specialist.

The audit found co-amoxiclav to be prescribed across all age groups, of whom 32% were aged over 60. With advancing age and frailty the risk of *C.difficile* infection increases, and co-amoxiclav is not recommended for these patients unless there is no appropriate alternative.

The LJF gives alternatives to the 4C antibiotics (co-amoxiclav, ciprofloxacin and other quinolones, clindamycin and cephalosporins) for frail/elderly wherever there are empiric choices.

RECOMMENDATIONS

⇒ Alternatives should be used over the 4C antibiotics for empiric treatment in the frail or elderly.

⇒ Co-amoxiclav should be avoided for prophylaxis for long term treatment where possible.

⇒ Antibiotics should not be used for self-limiting infections such as cough. The RCGP TARGET resources can support patient conversations and education.

⇒ Antibiotics should be prescribed for the shortest possible duration, as advised in the formulary.

⇒ Antibiotics should be the last resort for recurrent UTIs. Use RefHelp prior to Urology referral.

Thanks to Carol Philip, Lead AMT Pharmacist / Primary Care Pharmacist for contributing.

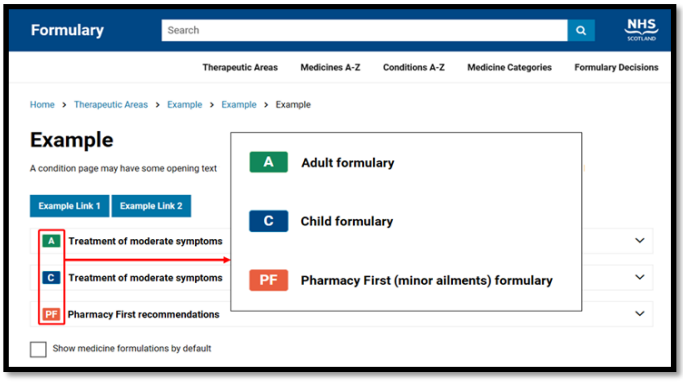
Regional formulary - next steps

The migration of the LJF was the first step in establishing a new regional formulary for the East of Scotland. The regional team are now working closely with the formulary teams in NHS Lothian, NHS Borders and NHS Fife, to scope and establish a regional formulary.

We are working on the following aspects:

- comparisons of the three board formularies, looking at differences in advice and in medicine usage. This will be used to aid review of formulary sections.
- developing a robust governance structure to support the development, review and maintenance of a regional formulary.
- developing and agreeing solutions to operational issues.
- agreeing a workplan for review and development of formulary chapters. We will be forming regional chapter expert working groups soon.

The website has been operational since December 2020. Use of the website has steadily risen and in the last 30 days there have been 5.4k users. Feedback to date has been positive, with users liking the new pathway approach to medicine recommendations. One common query received has been users being unable to find the paediatric formulary content. Paediatric pathways have a BLUE 'C', Adult pathways have a GREEN 'A' and Pharmacy First (Minor Ailments) pathways have an ORANGE 'PF'. Further website functionality is described in the user videos.



The project team are keeping an eye on questions from users to identify any areas for improvement. Very few questions could not have been answered by viewing the short user videos developed for the website and app to help answer common queries. They are available on the website here, to provide guidance on navigating the formulary, and understanding some of the functionality.

An app has been developed to complement the website. The new app provides users with a fast and focused approach to finding formulary recommendations. The app is able to operate offline, so a loss of signal won't stop the user from checking the formulary.

The app is available via Apple and Google stores. Search for 'NHS Scotland Formulary' and download it to your smartphone and have easy access to formulary recommendations. The new 'NHS Scotland Formulary' mobile app has been designed to be used by multiple Health Boards, with NHS Lothian being the first to adopt the new platform.

Thanks to Jane Browning, Regional Formulary Team.

LJF Update… LJF Update… LJF Update…

A summary of the information relating to LJF amendments can be found on the LJF website.

Central Nervous System

Adult Epilepsy: Prolonged Seizures and Status Epilepticus Management

- The treatment pathway has been updated to reflect the revisions on off-label levetiracetam and off-label dosing of sodium valproate.

Adult Opioid Overdose: Treatment with nasal naloxone

- Nyxoid is now available for patients (or their carers/ representatives) who are unable or unwilling to use the injection.

LJF Update… Cont.

Endocrine

Growth Hormone Deficiency Treatment Options

- Humatrope, Norditropin, Omnitrope are included on the formulary as first choice options for growth hormone deficiency. Genotropin, Zomacton, Saizen and NutropinAq are included for consideration for patients with specific needs.

Allergic emergencies

- Due to ongoing supply issues with adrenaline auto-injectors, Jext and Epipen devices are added as alternatives to Emerade. If an alternative to the usual brand needs to be prescribed ensure training is provided for the new pen issued.

Adult Blood Glucose Monitoring

- Freestyle Libre is replaced on the formulary by Freestyle Libre 2.

Infections

Child Bacterial Conjunctivitis

- Pharmacy First infected eye pathway has been updated to advise referral to GP for patients under the age of two years.
- There have been concerns regarding the use of boron-containing chloramphenicol eye drops in children under two. Chloramphenicol 1% ointment is considered a suitable alternative for under two year olds for bacterial conjunctivitis by local specialists; depending on the circumstances, the drops may be recommended by specialists. Refer to the formulary for more information.

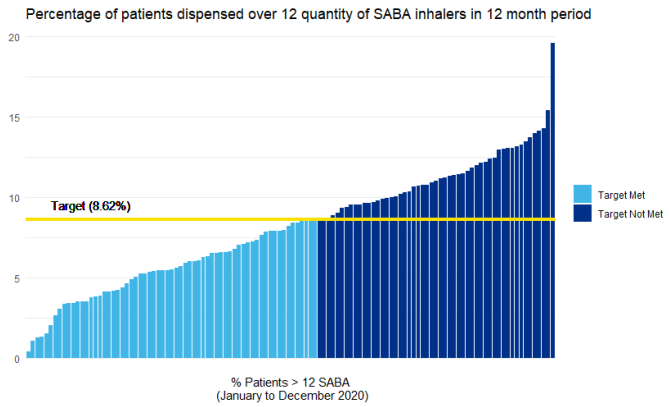
Thanks to Zainab Hayat, Rotational Pharmacist.

Avoid over-reliance on short-acting beta-agonists in asthma

Over-reliance of short-acting beta-agonists (SABA) often indicates poor asthma control and is a predictor for future risk of asthma attack and death. The National Review of Asthma Deaths (2014) recommended that patients prescribed over 12 SABAs per year are reviewed to assess their asthma control.

In NHS Lothian, the percentage of patients prescribed more than 12 SABA per year, compared to the total number of people prescribed SABAs, has fallen since 2016 (from 10.6% to 8.8%). However, current analyses show wide variation in SABA prescribing between GP practices (see graph below).

As we seek to improve SABA over-reliance further and reduce variation between practices in NHS Lothian, a number of initiatives are being implemented. To learn more contact Dr Luke Daines, or Katie Johnston, Primary Care Pharmacist. General resources can be found on prcs-uk.org/resource/arc.



KEY MESSAGES

- If asthma is well controlled there should be little or no need for SABA.
- Three or more doses of SABA per week may indicate poor asthma control and a need to move up maintenance treatment.
- Most salbutamol inhalers contain 200 doses, in theory one SABA inhaler should be sufficient for one year in an individual with well controlled asthma. In practice, individuals often request extra inhalers to keep at school or work.

Thanks to Katie Johnston, Primary Care Pharmacist for contributing.