NHS Forth Valley

Prescriberfile

From the Primary Care Prescribing Group

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Please circulate to all relevant Staff

Prescribing Safety Advice

Prescribing of Melatonin Oral Solution in Children Under 6 years old (Off-Label)

Following a recent review of the available formulations of melatonin, the NHS Forth Valley formulary choices for melatonin have been updated. Of key importance is the updated advice relating to the off-label use of melatonin oral solutions in children **under 6 years old**. In recent years, new licensed melatonin oral solutions have come to market. However, there are no licensed melatonin oral solutions which are indicated for regular use in children under 6 years old - **any use in this age group would be considered off-label**.

Of the marketed oral solutions available, there is significant variability in their excipient profiles, with some manufacturer's products containing excipients which make them unsuitable for use in young children under 6 years old. Specifically, some brands may contain:

⇒ Propylene Glycol

Propylene glycol is a substrate of alcohol dehydrogenase, and so there is the potential for accumulation when ingested repeatedly or concurrently with ethanol, especially in young children with low or immature metabolic capacity. Potential effects of propylene glycol include CNS depression, especially in neonates and young children, hyperosmolality, metabolic acidosis and renal impairment. For more information, see here.

⇒ Benzyl Alcohol

Has been linked with the risk of severe side effects including breathing problems (called “gasping syndrome”) in young children. See European Medicines Agency (EMA) information for further details.

A recent review by the Neonatal & Paediatric Pharmacy Group (NPPG) identified that **if melatonin oral solution is to be prescribed to children under 6 years old (off-label), that the preferred option would be the Consilient Health brand of Melatonin 1mg/1ml oral solution sugar free.** The Forth Valley formulary page has been updated to reflect this advice.

Prescribing of NSAIDs in Cirrhosis

Managing pain in patients with cirrhosis requires care as **NSAIDs are considered contra-indicated in patients with cirrhosis**. Cirrhosis is considered a risk factor for renal impairment in patients administered NSAIDs [1]. NSAIDs are largely metabolised by the hepatic cytochrome P450 enzyme and heavily protein bound, meaning that serum levels can be increased in cirrhotic patients. Moreover, in patients with portal hypertension, prostaglandins have a reno-protective effect and NSAIDs may exacerbate fluid retention and can precipitate acute kidney injury [2]. NSAIDs are also associated with a two-fold increased risk of variceal and non-variceal upper gastro-intestinal bleeding amongst cirrhotic patients [3].

This contra-indication is easily missed because of the way SPCs are worded. For example, Atnahs Pharma’s SPC states that naproxen is contraindicated in hepatic failure. However, the European Association for the Study of the Liver highlights that NSAIDs are contraindicated in patients with ascites and the current opinion is that oral NSAIDs should be avoided in all patients with cirrhosis [4,5].

Options for managing pain in cirrhotic patients include **oral paracetamol at a dose of up to 1g three times daily**. Topical NSAIDs can be considered. **Weak opioids should be avoided where possible** as cirrhosis can alter the pharmacokinetics of many drugs, and weak opioids can be prone to unpredictable therapeutic effects. If monotherapy with paracetamol is insufficient, a strong opioid like morphine oral solution can be used at a low dose. Immediate release morphine formulations are preferable to modified release. Importantly, all opiates including codeine may precipitate hepatic encephalopathy and particular caution is advised in patients already known to have this complication.

For further information or queries, please contact fv.hepatology@nhs.scot

References:

1. MARTINDALE, 2017. *Nonsteroidal Anti-inflammatory Drugs*. [online]. Available from: https://www.medicinescomplete.com/#/content/martindale/2600-p?hspl=nsaids [Accessed 2024].
2. Claria J, Kent JD, Lopez-Parra M et al. Effects of Celecoxib and Naproxen on Renal Function in Nonazotemic Patients with Cirrhosis and Ascites. Hepatology 2005; 579-587.
3. Lee YC, Chang CH, Lin JW, et al. Non-steroidal anti-inflammatory drugs use and risk of upper gastrointestinal adverse events in cirrhotic patients. Liver Int 2012;32 (5):859066.
4. EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. J Hepatol 2010;53:397-417.
5. Rakowski M, Goyal P, Spencer-Safier M, et al. Pain management in patients with cirrhosis. Clin Liver Dis 2018;11(6):135-140.

Prescribing Safety Advice

Topical Corticosteroids - Use in Pregnancy

Appropriate use of topical corticosteroids should, in general, not lead to high systemic levels and is therefore unlikely to pose significant risks during pregnancy. However, a number of factors can lead to increased exposure levels, such as use of higher potency preparations, use on broken skin or large areas of skin, use for prolonged periods, and use outside of the manufacturer's instructions (particularly regarding frequency and quantity of application). This should be borne in mind when carrying out risk assessments.

Systemic exposure to corticosteroids in pregnancy has been associated in some, but not all studies, with increased rates of orofacial clefts in the infant. Overall, the available data do not demonstrate that use of topical corticosteroids in pregnancy increases the risk of congenital malformation, including orofacial clefts, although information on some specific malformations is limited.

Prescribers should be aware of multi-ingredient products that may contain a steroid – a recent example of this is Scheriproct® Ointment (contains prednisolone and cinchocaine) which has recently added a warning about a possible increased risk of oral clefts among newborns of women who were treated with glucocorticoids during the first trimester of pregnancy.

For more information - see here.

Fluconazole - Use in Women of Childbearing potential & Pregnancy

The Summary of Product Characteristics (SPC) for fluconazole states that:

⇒ Fluconazole in standard doses and short-term treatments **should not be used in pregnancy** unless clearly necessary.

⇒ Fluconazole in high dose and/or in prolonged regimens **should not be used during pregnancy** except for potentially life-threatening infections.

⇒ Before initiating treatment, the patient should be informed of the potential risk to the fetus.

Observational studies suggest an increased risk of spontaneous abortion in women treated with fluconazole during the first and/or second trimester compared to women not treated with fluconazole or treated with topical azoles during the same period.

For women of childbearing potential, the SPC recommends that:

⇒ After single dose treatment, a **washout period of 1 week (corresponding to 5-6 half-lives) is recommended before becoming pregnant.**

This advice has now been further updated to say that:

⇒ For longer courses of treatment, **contraception may be considered, as appropriate, in women of childbearing potential throughout the treatment period and for 1 week after the final dose**.

Forth Valley Formulary Updates

Addition - Tavneos® (Avacopan) Capsules (Secondary Care Only)

Tavneos® has been accepted onto the Forth Valley formulary for use in combination with a rituximab or cyclophosphamide regimen, for the treatment of adult patients with severe, active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA). Please note that this should **NOT** be prescribed in Primary Care and its prescribing is limited to Acute/Specialist services only.

Other Formulary Amendments

⇒ **Ovestin® branded vaginal cream has been discontinued.** Generic equivalents for estriol 1mg/g remain available and should be prescribed instead. The formulary page has been updated to remove mention of the Ovestin® brand.

⇒ The formulary page has been updated to remove mention of Dovobet® branded gel and ointments. Calcipotriol 0.005% / Betamethasone dipropionate 0.05% gel and ointment are available as generic products. **Patients needing treated with Dovobet® should instead be prescribed the generic equivalent as this is more cost-effective.**

⇒ **The Forth Valley preferred brand of acetylcysteine effervescent tablet has change from NACSYS® to Acepiro®.** Acepiro® is now the 1st line mucolytic for patients aged 18 years and above. The main difference with Acepiro® is that it should be taken after food. Acepiro® is more cost-effective to prescribe than NACSYS®.

Prescribing Improvement Initiative (PII) Update

2023/24 Respiratory PII - Outcomes

The 2023/24 respiratory PII concluded on the 30th April 2024. A total of 43 practices undertook the project. Of the 11,367 patients that were reviewed as part of the project, a total of 10,038 patients were switched (88.31%) in accordance with the project guidance. It is estimated that the project will save NHS Forth Valley ~£500,000 annually.

Useful Resources

Sleepio (digital CBT for insomnia)

Sleepio is recommended first line over hypnotics for the treatment of insomnia and insomnia symptoms. NICE recommends Sleepio as a cost-saving option for insomnia in patients who cannot access Cognitive Behavioural Therapy for Insomnia (CBT-I). It offers an evidence based, NHS recommended treatment that is free for all adults in Scotland. Patients can access it free through www.sleepio.com/nhs. Sleepio can be accessed through a web browser or through the Sleepio app for iOS and Android devices. Further information can also be found on NICE and through the Sleepio website.

Daylight (digital CBT for generalised anxiety)

Daylight is an evidence based, NHS recommended treatment for worry and anxiety. When prescribing Propranolol or SSRIs for anxiety, consider offering Daylight to help patients with their symptoms. It offers an evidence based, NHS recommended treatment that is free for all adults in Scotland. Patients can access it free through www.trydaylight.com/nhs. Daylight can be accessed through a web browser or through the Daylight app for iOS and Android devices.

MHRA Drug Safety Update (Click here for full alerts)

Finasteride - risk of psychiatric and sexual side effects

Finasteride has been associated with depression, suicidal thoughts and sexual dysfunction. Patients have reported that sexual dysfunction (including decreased libido and erectile dysfunction) has persisted even after treatment was stopped. Patients prescribed finasteride for benign prostatic hyperplasia should be advised to contact their GP as soon as possible if they develop depression or suicidal thoughts. For patients on finasteride for male pattern hair loss, they should be advised to stop finasteride immediately if they develop depression or suicidal thoughts and to contact their GP as soon as possible. A patient alert card will be introduced in all finasteride packs to raise patient and prescriber awareness of the risk of sexual and psychiatric side effects. See here for more information.

Montelukast - risk of neuropsychiatric reactions

Neuropsychiatric reactions have been reported in child, adolescent, and adult patients taking montelukast. Some patients taking montelukast may experience new or worsening changes in mood, sleep or behaviour such as nightmares, aggression, anxiety, or thoughts about self-injury. Healthcare professionals should remain alert for reactions in all patients. Montelukast should be discontinued if patients experience new or worsening symptoms of neuropsychiatric reactions. Patients should be encouraged to read the Patient Information Leaflet (PIL) which contains a list of the neuropsychiatric reactions, and they should be advised to seek medical advice as soon as possible if neuropsychiatric reactions occur. See here for more information.