Levomepromazine: patient safety in palliative care

Levomepromazine is a phenothiazine used in palliative care as a second or third line antiemetic for intractable nausea and vomiting, or to manage severe delirium and agitation at the end of a patient’s life when other measures have failed.

The oral product most commonly used is an unlicensed preparation, levomepromazine 6mg tablets. There is a 25mg tablet licensed in the UK, but this is not used in palliative care. The oral antiemetic starting dose is 3mg once or twice daily. Initially, doses may be given at night to reduce daytime side-effects. Parenteral doses usually start at 2.5-5mg SC as required 12 hourly, or 5-10mg/24 hours SC via a syringe pump.

Significant medication incidents have occurred due to the inadvertent prescription of 25mg rather than 6mg tablets, leading to serious side effects including hospital admission.

Case Study

A 90 year old, frail gentleman living at home was receiving palliative care with input from the local hospice team for symptom control. The clinical nurse specialist recommended that his GP prescribe levomepromazine 6mg tablets for intractable nausea, commencing with a dose of 3mg once daily. The community pharmacy knew that this unlicensed medicine could take a few days to obtain, so discussed the potential delay with the GP.

The prescription was changed to 25mg tablets, at an initial dose of 12.5mg, because it was thought too difficult to quarter the tablets. The patient had been advised to lie down after the first dose, but did not.

He became dizzy and hypotensive, and this contributed to a hospital admission.

What could have been done to avoid this incident?

A patient information leaflet with advice for prescribers and pharmacists has been supplied to all specialist teams. Neither the patient nor the GP was given a copy.

The community pharmacist and GP made efforts to promptly supply the required drug, but the dose was inappropriate. Referring to the palliative care guidelines would have confirmed an appropriate starting dose. Another network pharmacy may have held stock of the correct product.

Where can the required information be found?

Hard copies of the palliative care guidelines have been widely distributed; further copies are still available – contact your local palliative care team. These can be accessed on www.palliativecareguidelines.scot.nhs.uk

What’s the bottom line?

When prescribing, dispensing or administering levomepromazine for a palliative care patient, check that the dose is appropriate, seeking advice from a specialist if required. Further information can be found in the palliative care guidelines http://www.palliativecareguidelines.scot.nhs.uk/documents/Levomepromazine.pdf.

Antibiotics and other medicines for hospital use

Clinicians are reminded that a number of infection management medicines are included for use in hospital only, eg voriconazole. GPs should not be asked to prescribe these medicines.

PostScript Extra: New oral anticoagulants

A new PostScript Extra bulletin on new oral anticoagulants is available on the GGC Prescribing website. There is a summary bulletin and a fully referenced version available for those who wish more detail.
Ticagrelor update
The implementation of SMC advice on ticagrelor is incomplete in NHSGGC and final Formulary status of the medicine has not been concluded within the usual timescale. The decision has been delayed pending a consensus at regional level on the optimal place in therapy.

Ticagrelor has been added to the Formulary for patients who are intolerant to clopidogrel or have a stent thrombosis on clopidogrel. Use in other patient groups remains non-Formulary while regional guidance is being developed. That advice is expected shortly and the Formulary position will then be reviewed for the other patient groups.

New drug: Colecalciferol 800 unit capsules (Fultium D3®)
Fultium-D3® is the first oral vitamin D monotherapy preparation to be licensed in the UK. It has been added to the Total Formulary for adults, the elderly and adolescents for the prevention and treatment of vitamin D deficiency and as an adjunct to specific therapy for osteoporosis in patients with vitamin D deficiency or at risk of vitamin D insufficiency. Vitamin D is essential to maintain skeletal calcium balance by promoting intestinal calcium absorption, osteoclast-mediated bone resorption, and maintenance of serum calcium and phosphate levels. It has not been evaluated in clinical studies but was licensed on the basis of the well established use of its active constituent.

Fultium-D3 contains 800 units of colecalciferol; twice the dose of vitamin D recommended for adults who are considered to be at risk of vitamin D deficiency, as outlined in guidance issued from the Chief Medical Officer for Scotland in February 2012. Healthy Start vitamins contain 400 units of vitamin D and are available for eligible patient groups in NHSGGC. Vitamin supplement preparations containing 400 units of vitamin D are readily available for purchase by patients over the counter at pharmacies and health food stores.

Guidance on when to measure vitamin D levels and the subsequent management of vitamin D deficiency are currently in development by the NHSGGC Osteoporosis Group and Biochemistry Department. However, they note that measuring Vitamin D is not helpful in the investigation of tiredness, chronic fatigue / fibromyalgia or non-specific aches and pains (with normal bone biochemistry).

ADTC decisions summary
See the website for full details of indications and restrictions.

Some additions to the Adult Formulary:
- Colecalciferol 800 unit capsules (Fultium-D3®) for the prevention and treatment of vitamin D deficiency in adults, the elderly and adolescents and as an adjunct to specific therapy for osteoporosis in patients with, or at risk of, vitamin D deficiency.
- Collagenase clostridium histolyticum (Xiapex®) for the treatment of Dupuytren’s contracture. Restricted to specialist use according to protocol.
- Fingolimod (Gilenya®) is included in the Total Formulary for use in adults with highly active relapsing remitting multiple sclerosis (RRMS). Restricted to specialist use.
- Ivabradine (Procoralan®) for use in chronic heart failure, restricted to use in patients whose resting heart rate remains ≥75 beats per minute in sinus rhythm, despite optimal standard therapy. For initiation by prescribers in specialist heart failure teams.
- Tocilizumab (RoActemra®) as monotherapy for rheumatoid arthritis, restricted to specialist use.
- Velaglucerase (Vpriv®) for long-term enzyme replacement therapy in patients with type 1 Gaucher disease, restricted to specialist use.

The following medicines were among those not added to the Adult Formulary
- Bevacizumab (Avastin®) for advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer.
- Pasireotide (Sifnifor®) for adult patients with Cushing’s disease.
- Strontium ranelate (Protelos®) for osteoporosis in men at increased risk of fracture.
- Vemurafenib (Zelboraf®) as monotherapy for adult patients with BRAF V600 mutation-positive unresectable or metastatic melanoma.
- Zonisamide (Zonegran®) for monotherapy treatment of partial seizures (with or without secondary generalisation) in adults with newly diagnosed epilepsy.

The following medicines were among those not added to the Paediatric Formulary
- Caffeine citrate (Peyona®) for treatment of primary apnoea of premature newborns.
- Tocofersolan (Vedrop®) for vitamin E deficiency due to digestive malabsorption in paediatric patients with congenital chronic cholestasis or hereditary chronic cholestasis.

Non-Formulary pending protocol / consultation
- Tegafur/gimeracil/oteracil (Teysuno®) for advanced gastric cancer.

For all ADTC decisions see http://www.ggcprescribing.org.uk/blog/category/news/
Safety updates

1. Paracetamol overdose
The MHRA has revised guidance on the management of paracetamol overdose which simplifies patient management to a single treatment line on the new paracetamol treatment nomogram. The PDF of the Therapeutic Handbook has been updated on the GGC Prescribing website and guidance for amending the printed editions has been issued. Please ensure you are using the most up to date information.

2. Gliptins and pancreatitis
The MHRA has published reports of acute pancreatitis associated with the dipeptidylpeptidase-4 (DPP-4) inhibitor class of antidiabetic agents (gliptins). http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON185628. Patients should be informed of the characteristic symptoms of acute pancreatitis; persistent, severe abdominal pain (sometimes radiating to the back), and encouraged to report symptoms to their healthcare provider. If pancreatitis is suspected, the DPP-4 inhibitor and other potentially suspect medicinal products should be discontinued. Prescribers should note that all agents for type 2 diabetes that act on the GLP-1 pathway, ie including injectable GLP-1 analogues, have been linked with acute pancreatitis. Report suspected adverse reactions through the Yellow Card Scheme.

European Antibiotic Awareness Day (EAAD):
November 2012
The European Centre for Disease Prevention and Control (ECDC) have announced this year’s theme is decreasing inappropriate antibiotic use. Through the work of the Scottish Antimicrobial Prescribing Group (SAPG), local Antimicrobial Management Teams and Prescribing Advisers, huge inroads have been made in ensuring adherence to local prescribing guidelines (what to prescribe) and SAPG has advised the focus should now shift towards whether to prescribe (ie is an antibiotic needed at all).

The SAPG website has a page with EAAD materials http://www.scottishmedicines.org.uk/SAPG/European_Antibiotic_Awareness_Day/European_Antibiotic_Awareness_Day including:
- the primary care prescribing indicators report
- the toolkit for primary care to support improvements in antimicrobial prescribing
- the new second edition of the NHSScotland Unscheduled Care Formulary
- the revised SIGN Guideline 88 – management of bacterial urinary tract infection
- RCGP TARGET (Treat Antibiotics Responsibly; Guidance, Education, Tools) to be launched on RCGP website for EAAD.

New guidelines:
These guidelines are all available on the Staffnet guidelines repository (Info Centre, Policies Procedures and Guidelines Documents, NHS GG&C Clinical Guideline Electronic Resource Directory).

1. Antiplatelet therapy in secondary prevention of stroke and TIA
This guideline is aimed at prescribers working within both the acute setting and primary care to guide antiplatelet therapy in patients who have had an ischaemic stroke or transient ischaemic attack (TIA).

Key recommendations:
- For patients in sinus rhythm who have had an ischaemic stroke or transient ischaemic attack (TIA), the standard long-term antithrombotic treatment should be clopidogrel 75mg once daily.
- Patients who cannot tolerate clopidogrel should receive aspirin dispersible 75mg once daily and dipyridamole modified-release (MR) 200mg twice daily.
- Aspirin dispersible 75mg once daily should be used if both clopidogrel and dipyridamole MR are contraindicated or not tolerated.
- If both clopidogrel and aspirin are contraindicated or not tolerated, then dipyridamole MR 200mg twice daily should be used.
- All patients with a diagnosis of stroke or TIA should receive life-long antiplatelet therapy as above.
- The combination of aspirin and clopidogrel is not recommended for long-term prevention following a stroke or TIA stroke unless there is another indication to consider, such as acute coronary syndrome or recent coronary stent procedure.

Cautions and supporting information:
- Ideally, blood pressure should be controlled prior to the commencement of any antiplatelet agent
- When consideration is being given to prescribing antiplatelets, a GI risk assessment should be undertaken

2. Diagnosis, prevention and management of delirium.
Although largely aimed mainly at acute settings, this will also be of relevance for clinicians working within care homes. The next edition of PostScript Acute will include more details.
3. Thromboprophylaxis for orthopaedic patients.

Many operations carried out in orthopaedic fall into the general “high risk” category (lower limb arthroplasty, osteotomy, etc). Others such as knee arthroscopy, foot surgery, upper limb surgery are in a general “low risk” group. Orthopaedic thromboprophylaxis policies need to differentiate between patients with a standard level of risk for the operation and patients who have other factors making their surgery significantly higher risk for venous thromboembolism (VTE).

Assessment of VTE and bleeding risk

All patients must have their risk of VTE assessed at pre-assessment and/or admission using the appropriate risk assessment tool. The risk of bleeding and VTE should be reassessed within 24 hours of admission and regularly thereafter during their stay in hospital. A record of these assessments must be made and documented in the thromboprophylaxis section of the kardex.

Do not offer pharmacological prophylaxis to patients with risk factors for bleeding unless the risk of VTE outweighs the risk of bleeding. Patients already receiving therapeutic anticoagulation do not need additional thromboprophylaxis.

Indicators of patients at increased risk of VTE

It is recognised that most orthopaedic patients are at risk of VTE. It is important to stratify risk to tailor thromboprophylaxis to minimise adverse effects on other aspects of patient overall care. Patients presenting at least one of these risk factors should be regarded at increased risk of VTE compared to standard orthopaedic risk:

- critical care admission
- obesity (BMI > 30kg/m²)
- active cancer or cancer treatment
- thrombophilia
- personal history or 1st degree relative with a history of VTE
- pregnancy or ≤ 6 weeks post partum (seek specialist advice)
- hormone replacement therapy, tamoxifen, oestrogen containing contraceptive
- varicose veins with phlebitis
- current significant medical condition, eg serious infection, heart failure, respiratory failure, inflammatory disease

Indicators of patients at high risk of bleeding

Regard patients at high risk of bleeding if they have any of the following risk factors:

- surgery expected within the next 12 hours
- surgery expected within the next 48 hours and/or risk of clinically important bleeding
- active bleeding or risk of bleeding including new-onset stroke, platelet count <75 x 10⁹/L, acute liver failure, active duodenal or gastric ulcer, concurrent use of therapeutic anticoagulant, acute bacterial endocarditis
- spinal surgery (seek specialist advice) or any spinal intervention
- persistent uncontrolled hypertension (BP ≥ 230/120 mmHg)
- untreated inherited bleeding disorder
- proliferative diabetic retinopathy

Recommendations for thromboprophylaxis

The policy lists the different therapeutic regimens taking into account the procedure and the risk stratification. Details are provided for treatment during hospital stay and at discharge.

It is the responsibility of the consultant in charge to decide on appropriate VTE prophylaxis.