FOCUS ON . . . Opiate substitution therapy

PostScRxipt
from the
NHSGGC Area Drug & Therapeutics Committee
Issue 65 September 2011

Opiate Substitute Therapy (OST) has a strong evidence-base for effectiveness in individuals with heroin dependency. The evidence shows that one of the significant benefits is a much reduced mortality rate for patients in treatment. However, methadone, the most widely used OST, does itself carry a risk of overdose, especially in combination with other opiates, benzodiazepines and alcohol. Over the last decade, there has been an increase in the number of methadone-related deaths.

In NHSGGC, the majority of these deaths occur in individuals with a known history of drug misuse who are currently not in treatment but may have obtained and consumed methadone diverted from prescriptions. A number of strategies are in place to reduce the risks of illicit diversion of methadone.

Primary care

Supervised dispensing of methadone in community pharmacies is recommended for at least a three month stabilisation period by 'Drug Misuse and Dependence: UK Guidelines on Clinical Management' (2007). Supervision ensures compliance and regular contact with a service. It minimises the leakage and diversion of prescribed methadone so reducing methadone-related mortality. In NHSGGC, supervised doses are recommended beyond the stabilisation period.

In an effort to minimise methadone-related mortality, all prescribers are reminded of their responsibility to reduce the risk of diversion of methadone through ensuring appropriate levels of supervised dispensing at pharmacies. Supervised consumption should not be viewed as punitive and offers an opportunity for pharmacists where "therapeutic relationships can be built with patients" (UK Guidelines, 2007:51). Prescribing guidelines and practice standards can be found at **www.staffnet.ggc.scot.nhs.uk/Partnerships/Addictions/Pages/GGLK19052008.aspx**

Acute care

The guidelines for treatment of substance misusers in hospital have recently been updated. Admission to an acute hospital can be an ideal opportunity for engagement and retention in treatment for substance misusers. Acute Addiction Liaison Nurses are available in all acute hospitals in Glasgow while drug services in Renfrewshire and Inverclyde are able to provide information, advice and appropriate assessment for those areas. The guidance also covers benzodiazepine misuse and looks at principles of treatment, assessment, history taking, investigations and pain management. The section on managing discharge is particularly important to ensure continuity of care while minimising the risk of duplicate supply and potential overdose. The guideline on management of drug misusers in hospital is available at **www.staffnet.ggc.scot.nhs.uk/Clinical%20Info/Clinical%20Guidelines/Pages/default.aspx**

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Website
http://www.ggcformulary.scot.nhs.uk

Case study

Accidental overdose from prescription error

A patient on methadone was in an acute hospital for reasons unrelated to his substance misuse. The medicines prescription chart was written up as shown at the top of page 3.

For the first three days of his admission he received 40ml methadone 1mg/ml (the intended dose). However, on the fourth day he received 40ml of methadone 10mg/ml, developed respiratory depression and had to be treated with naloxone. The two members of staff who administered the product were unfamiliar with methadone. A number of factors contributed to this incident.

Learning points

- There was no dose included on the medicines prescription chart. Doses must always be written in terms of milligrams, not in terms of volume of liquid.
- The formulation and strength of drug should be included where possible.
- Those administering drugs must ensure dosage instructions are clear and unambiguous before administering to patients, especially if they are not familiar with the product.
- Where different strengths of a product are kept, care should be taken to choose the correct product. Is the label the colour you expect it to be? Is the pack the size you expect? Is the liquid/tablet/capsule the colour you expect it to be? Methadone 1mg/ml is green; the 10mg/ml concentrate is blue.
- The methadone concentrate in this case had been in the ward unused for several months. Where products are no longer used, contact pharmacy to discuss the options of destruction or return.

Latest ADTC decisions

Go to www.ggcformulary.scot.nhs.uk/Latest news/formulary update bulletin.pdf for full details of all ADTC decisions and links to SMC recommendations.

Added to the *Formulary*

Ⓢ **Darunavir (Prezista®)** HIV-1 infection in treatment experienced adults. Total *Formulary*. Restricted to HIV specialists.

Ⓢ **Degarelix (Firmagon®)** Advanced hormone-dependent prostate cancer. Total *Formulary*. Restricted to specialist initiation in accordance with regional protocol.

Ⓢ **Histrelin acetate implant (Vantas®)** Palliative treatment of advanced prostate cancer. Total *Formulary*. Restricted to specialist use in accordance with the clinical management guideline.

Ⓢ **Lenalidomide (Revlimid®)** Multiple myeloma in combination with dexamethasone. Total *Formulary*. Restricted to specialist use in accordance with regional protocol.

Ⓢ **Pazopanib (Votrient®)** Advanced renal cell carcinoma. Total *Formulary*. Restricted to first line use only by specialists in accordance with regional protocol.

Ⓢ **Retigabine (Trobalt®)** Adjunctive treatment of partial onset seizures with or without secondary generalisation in adults aged 18 years and above with epilepsy. Total *Formulary*. Restricted to patients with refractory disease and initiation by physicians who have appropriate experience in the treatment of epilepsy.

Ⓢ **Rituximab (MabThera®)** Maintenance treatment of follicular lymphoma in previously untreated patients responding to induction therapy. Total *Formulary*. Restricted to specialist use in accordance with regional protocol.

Ⓢ **Sunitinib (Sutent®)** Unresectable or metastatic, well-differentiated pancreatic neuroendocrine tumours with disease progression in adults. Total *Formulary*. Restricted to specialist use in accordance with regional protocol.

Ⓢ **Triptorelin 22.5mg injection (Decapeptyl SR®)** Locally advanced non-metastatic or metastatic prostate cancer. Total *Formulary*. Restricted to specialist initiation in accordance with regional protocol. As there are several strengths to be administered at different dosing intervals, extra care is required to ensure the correct product is selected.

New medicines, indications and formulations not added to the *Formulary*

- **Bilastine (Ilaxten®)** for symptomatic treatment of allergic rhino-conjunctivitis and urticaria.
- **Collagenase clostridium histolyticum (Xiapex®)** for treatment of Dupuytren's contracture in adults with a palpable cord.
- **Glucosamine sulphate (Glusartel®, Dolenio®)** for the relief of symptoms in mild to moderate osteoarthritis of the knee.
- **Paliperidone injection (Xeplion®)** for maintenance treatment of schizophrenia in adults.
- **Prucalopride (Resolor®)** for chronic constipation in women.
- **Ranibizumab (Lucentis®)** for the treatment of visual impairment due to diabetic macular oedema in adults.
- **Trabectedin (Yondelis®)** for the treatment of advanced soft tissue sarcoma.

Other *Formulary* decisions

- **Methotrexate injection (Metoject®)** was added to the forthcoming NHSGGC Paediatric *Formulary*, restricted to use under specialist supervision for polyarthritic forms of severe active juvenile idiopathic arthritis, when the response to NSAIDs has been inadequate.
- NICE reviewed the role of **cilostazol, naftidrofuryl oxalate, pentoxifylline** and **inositol nicotinate** in the treatment of intermittent claudication in people with peripheral arterial disease. Only naftidrofuryl is accepted for use and this is in line with the NHSGGC *Formulary*.
- **Dabigatran** is now licensed for stroke prevention in patients with AF. Advice from SMC is expected in September and will be reported in the next edition. As with all medicines, it remains non-*Formulary* until a formal decision on *Formulary* status has been made.

Ⓢ specialist use only Ⓢ specialist initiation only

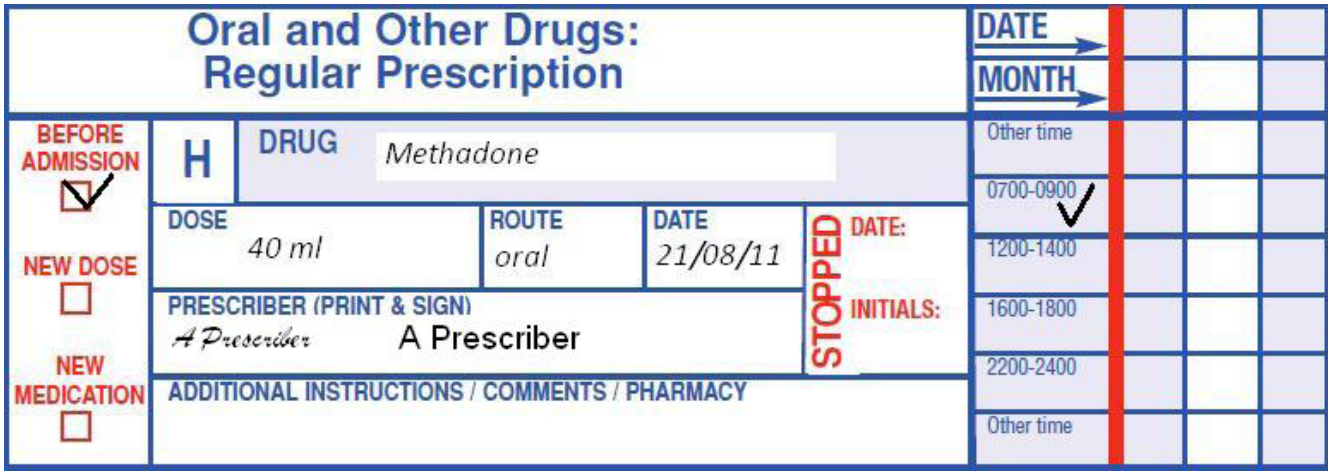
SIGN Guidelines App for iPhone®

Developed by SIGN in collaboration with Root Creative, Glasgow, the SIGN Guidelines app for the Apple iPhone®, iPod Touch® and iPad® has been launched. It contains quick reference guides (QRG) of some recently published guidelines. The QRG content is enhanced with material from the main guideline and online resources. All future QRGs will be added to the app as they are published.

This new format will be particularly useful for frontline healthcare professionals wishing to access a specific guideline. The information is stored on the device, and so is available even when the device is being used in 'airplane mode' without access to phone or wireless internet networks.

Currently the guidelines featured include:
- 113: Diagnosis and pharmacological management of Parkinson's disease
- 115: The management of obesity
- 116: The management of diabetes
- 118 & 119: The management of patients with stroke
- 120: The management of chronic venous leg ulcers
- 123: The management of early rheumatoid arthritis
- 125: Management of atopic eczema in primary care

The app features keyword search and bookmarking and access to the SIGN website (when connected to the internet). It is available at no charge from the Apple App Store.



Drug choice

NICE and SMC recommend methadone as the first choice drug and it remains the mainstay of treatment in NHSGGC. Methadone oral solution 1mg/1ml is the preferred formulation. Other formulations should only be prescribed in exceptional medical circumstances as they have been linked to increased risk of injection (sugar free solution), diversion (tablets) and errors (concentrated solutions).

Suboxone® can be considered as an alternative to methadone, in conjunction with advice from the specialist addiction services. The combination of buprenorphine (partial opiate agonist) and naloxone (opiate antagonist) makes it relatively safer than methadone if misused. Suboxone is intended for sublingual administration. If used in this way, the naloxone undergoes almost complete first pass metabolism and shows no pharmacological effects. If injected intravenously, the naloxone produces marked opioid antagonist effects and opioid withdrawal. The formulation is therefore intended to deter intravenous abuse.

For further guidance or queries, contact Glasgow Addiction Services on 0141 276 6600.

Key contacts are: Dr Saket Priyadarshi, Lead Clinician; Dr Muhammad Ali Mahmood, Senior Medical Officer; Carole Hunter, Lead Pharmacist; Dr Tony Martin, Drug Death Research Associate.

Individual patient treatment requests: An introduction

In October 2010, the non-*Formulary* processes in the acute sector were amended to reflect guidance from the Scottish Government (see footnote). What have previously been known as non-*Formulary* requests became Individual Patient Treatment Requests (IPTRs).

To comply with Scottish Government guidance, when a prescriber wishes to initiate a medicine for an indication not recommended for use in NHS Scotland by the SMC or NHS HIS, he/she has to submit a request for each individual and seek approval prior to prescribing.

Within NHSGGC, we have stratified the IPTR system into different levels, as shown in the panel on the right, to ensure the system is manageable in practice.

The Formulary and Handbook Team, based within Medicines Information, and the Specialist Oncology Clinical Effectiveness Team manage the reporting process on behalf of NHSGGC. IPTR activity is reported to the Scottish Government on a regular basis. It is imperative that all relevant documentation is completed and processed properly; including all forms being returned to the Formulary and Handbook Team in Medicines Information once the process has been completed.

To find out more about the IPTR process, the Board's policy can be found under the Medicines Policy section on the ADTC website (**www.ggcformulary.scot.nhs.uk**). Alternatively, please contact a member of the Formulary and Handbook Team at Glasgow Royal Infirmary (0141 211 4407).

- **Level 1 non-*Formulary* drugs** are historical medicines that predate SMC or medicines accepted by SMC that have not been added to the *Formulary*, eg the ACE inhibitor trandolapril. These are not anticipated to have a large use. Patterns of use are monitored but no pro-active action is taken unless there are signs that prescribing is becoming common.

- **Level 2 IPTRs**, eg buprenorphine patches or esomeprazole, have the potential for high levels of use. The prescriber or senior nurse on the ward must complete a form before pharmacy will supply the product.

- **Level 3 IPTRs**, eg infliximab for ankylosing spondylitis, gefitinib in non-small cell lung cancer or Sativex® for spasticity in MS, need a form to be completed by a consultant. The request will be considered by a panel typically consisting of the Associate Medical Director for the Directorate, the relevant General Manager, a suitable Lead Clinical Pharmacist and another suitable clinician.

CEL(2010)17: Introduction and availability of newly licensed medicines in the NHS in Scotland. Available for download at **www.sehd.scot.nhs.uk/mels/CEL2010_17.pdf**

Smoking cessation and effects on drug metabolism

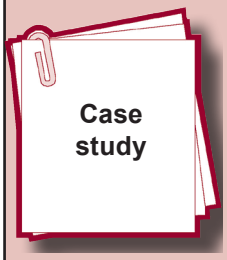
Key messages

- Metabolism of certain drugs can be affected by smoking status.
- Patients who are prescribed drugs which have a clinically significant interaction with smoking should be advised to discuss quit attempts with their GP.
- Specialist services should be involved in quit attempts for patients on drugs not initiated by GPs, eg clozapine.
- SmokeFree Services will provide advice and support to the professional involved in smoking cessation and will provide behavioural support to patients who do not want to take medication.

The metabolism of some drugs can be affected by smoking. The polycyclic aromatic hydrocarbons found in tobacco smoke induce the cytochrome P450 system in the liver. This can increase the metabolism of certain drugs so that a higher dose is required to achieve the same clinical effect. When a patient stops smoking, the dose may need to be reduced to prevent side effects and/or toxicity. A resource of interactions between medicines and smoking is available on our website. Drugs with established evidence of interaction with smoking include:

- **Cardiovascular:** beta blockers, flecainide, warfarin
- **Respiratory:** theophylline
- **Mental health:** clozapine, olanzapine, rivastigmine
- **Pain:** duloxetine
- **Gastro-intestinal:** cimetidine, ranitidine

A lady with a history of schizophrenia who was taking clozapine attempted to quit smoking using NRT patches. Within two weeks she developed drowsiness/sedation and dizziness and discussed this with the pharmacist supporting her quit attempt and her GP. The GP advised her to stop using the patches and she returned to smoking.



Smoking induces the metabolism of clozapine, with maximum effect seen at 7-12 cigarettes per day. When the patient stops smoking, the dose of clozapine needs to be reduced to prevent the plasma concentrations rising to toxic levels. All clozapine patients should be advised to inform the mental health team caring for them if they intend to stop smoking.

This lady has recently returned for another quit attempt. The patient was reassured that her medication would be reviewed and told to inform her CPN and psychiatrist whenever there is a major change to her smoking. Her psychiatrist was given details of the previous history and he agreed to monitor her medication from the start of this new quit attempt.

Contact SmokeFree Services on 0800 389 3210, or call 0141 211 6564 to speak to a mental health practitioner.

SPC Zaponex **www.medicines.org.uk**
Stockley's Interactions **www.medicinescomplete.com**

Webwatch

Knowledge network updated subscriptions
The NHS Scotland e-library is now found at **www.knowledge.scot.nhs.uk** The list of books and journals which can be accessed through your Athens password on this site is updated regularly.

Useful resources for frontline clinical staff include Stockley's Drug Interactions. This database is an invaluable tool to find information on drug interactions and their clinical significance. For example, try a search for clozapine and smoking to get details on the clinical evidence, a description of the mechanism plus commentary on the importance and management of such an interaction.

You will also find the *Drug and Therapeutics Bulletin* which provides evaluations of, and practical advice on, individual treatments and the overall management of disease for doctors, pharmacists and other healthcare professionals. Recent editions include articles covering adults with ADHD, an update of systemic lupus erythematosus, management of acute infective conjunctivitis and reviews of new drugs such as ticagrelor. A future edition will consider the role of dabigatran in stroke.

Addictions Services Resources
The Glasgow Addictions Services pages on Staffnet can be found at www.staffnet.ggc.scot.nhs.uk/Partnerships/Addictions/Pages/GAS%20Home.aspx There are pages detailing all the services available including Community Alcohol Support, Community Rehabilitation, Addiction Services to Offenders and Pharmacy Services such as needle exchange and the take home naloxone pilot. This is another way to try to minimise harm from opiates and comprises overdose awareness, practical basic life support training for family and friends plus supply of the antagonist naloxone.

A link under policies and procedures takes readers to a variety of national and local guidelines used by the service, eg UK Guidelines on Clinical Management of Drug Misuse and Dependence, joint policies on management of alcohol and drug addiction from Glasgow City Council and the Glasgow Addictions Service and the guidelines for prescribers and dispensers in primary care.

NHS Greater Glasgow and Clyde

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