LONG-ACTING REVERSIBLE CONTRACEPTIVES: What is all this LARC-ing about?

There has been a drive in recent years to improve the sexual health of Scotland's population. One aspect is reducing the number of unplanned pregnancies. Drs Alison Bigrigg, Audrey Brown and Kay McAllister from the Sandyford Initiative discuss here the impact of long-acting reversible contraceptives.

PostScRxipt
from the
NHSGGC Area Drug & Therapeutics Committee
Issue 52 July 2009

In this issue . . .

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

What is a LARC?
A LARC is a long-acting reversible contraceptive. This encompasses any method which requires administration less than once per cycle or month, and includes all intra-uterine devices, progesterone-only injectables and implants and combined hormonal vaginal rings. All methods are currently licensed and available within the UK.

The NHSGGC *Formulary* contains the following LARC methods:
• Progestogen-only depot (Depo-Provera®; given every 12 weeks)
• Progestogen-only implant (Implanon®; lasts three years)
• Progestogen-only intra-uterine system (Mirena®; lasts five years)
• Copper intra-uterine device (TT380 Slimline®; lasts ten years, Nova-T 380®; lasts five years)

Why should we use LARCs?
It is believed that an increased use of LARC methods will help to reduce the incidence of unplanned or unintended pregnancies. With typical use, LARC methods have a lower failure rate than the commonly used reversible methods such as contraceptive pills and condoms. All LARC methods available within the UK have also been shown to be more cost effective than the combined oral contraceptive pill even at one year of use.

Since 2000, the number of female sterilisations has reduced by more than 60%. This decline is thought to be secondary to a steady increase in the uptake of LARC methods, which offer reversibility and comparable effectiveness without the need for surgical intervention.

The Scottish Sexual Health Strategy – Respect and Responsibility
In response to this document, NHS Quality Improvement Scotland (NHS QIS) has developed clinical standards for sexual health services. Standard 8 states that all women should have access to intra-uterine and implantable methods of contraception. The target is for at least 60 females per 1,000 of reproductive age per year to be prescribed one of these methods.

The contraceptive consultation is also an ideal opportunity to promote safer sex. An assessment of sexually transmitted infection risk should follow the SIGN chlamydia guidelines. This includes opportunistic screening in sexually active women less than 25 years of age and those over 25 years of age with more than one partner or a change in partner in the past year. Referral to local sexual and reproductive health care services should be facilitated if necessary.

LARC uptake within Scotland
Since 2004/05, the national uptake of very long-acting LARCs (Implanon®, IUD, Mirena®) has risen to an overall total in 2006/07 of 34 per 1,000 women. The greatest rise is in Mirena®, with copper IUD showing the smallest rise. These figures are almost half of the target NHS QIS hopes to achieve by 2011.

Which LARC?
Informed choice is central to all decision making. When agreeing on a contraceptive, the clinician should be aware of any medical restrictions to individual methods and refer to the UK Medical Eligibility Criteria for advice if required. The majority of women place as much emphasis on risks, side-effects and non-contraceptive benefits as they do on overall contraceptive efficacy.

Copper intra-uterine devices: These act principally by inhibiting ovulation via the toxic effects of copper on both sperm and ova. All devices with a copper content greater than 380 mm^2 are licensed for at least 5 years, with some having a 10-year licence. Failure rates are low for these devices; 1-2% with 5 years of use. A device inserted after a woman reaches 40 years of age can remain in place until after the menopause. This is defined as one year after the last menses if the woman is over 50 years, and two years after the last menses if she is younger than 50 years.

Progesterone-only intra-uterine systems: The progestogenic effect of levonorgestrel induces endometrial atrophy and inhibits implantation. It is currently licensed for five years as a contraceptive. If inserted at age 45 years or over, it may remain in place until after the menopause provided the woman remains amenorrhoeic.

Progesterone-only subdermal implants: There is currently only one implant available in the UK. Implanon® contains etonogestrel within a single subdermal rod. It has a three

contd on page 4

Alphabetical list of most recent ADTC decisions

For full details of SMC advice, visit **www.scottishmedicines.org** For NICE advice, visit **www.nice.org.uk** For previous ADTC decisions, visit **www.ggcformulary.scot.nhs.uk**

Drug	Indication under consideration (There may be other licensed indications)	NHSGGC decision	
Aripiprazole (Abilify®)	Treatment of moderate to severe manic episodes in bipolar 1 disorder and for the prevention of a new manic episode in patients who experienced predominantly manic episodes and whose manic episodes responded to aripiprazole treatment.	Non-*Formulary*.	x
Caffeine base 5mg/ml injection	Treatment of apnoea of prematurity.	(S) Total *Formulary*. Restricted to use on the advice of specialists in neonatal paediatrics. Prescribers should note that, although the SPC describes this product in terms of caffeine base (5mg/ml), the neonatal formulary and the British National Formulary for Children currently recommend prescribing the dose as caffeine citrate (equivalent to 10mg/ml).	✓R
Caspofungin (Cancidas®)	Empirical therapy for presumed fungal infections (such as Candida or Aspergillus) in febrile, neutropenic paediatric patients (12 months to 17 years).	(S) Total *Formulary*. Acknowledge new indication. Restricted to use in accordance with local guideline.	✓R
Caspofungin (Cancidas®)	Treatment of invasive candidiasis in paediatric patients (12 months to 17 years).	(S) Total *Formulary*. Acknowledge new indication. Restricted to patients with fluconazole-resistant Candida infection who do not respond to, or cannot tolerate amphotericin B therapy or who are at an increased risk of serious side effects with amphotericin, eg transplant patients, especially those receiving bone marrow transplants.	✓R
Danaparoid sodium injection (Orgaran®) (ADTC review)	Treatment of thromboembolic disorders in patients who require anticoagulation following the development of heparin-induced thrombocytopenia.	(S) Total *Formulary*. Restricted to use in accordance with local guideline.	✓R
Paclitaxel (Abraxane®)	Treatment of metastatic breast cancer in patients who have failed first-line treatment for metastatic disease and for whom standard anthracycline containing therapy is not indicated.	Non-*Formulary* for this indication.	x
Pemetrexed (Alimta®)	In combination with cisplatin for the first treatment of patients with locally advanced or metastatic non-small cell lung cancer other than predominantly squamous cell histology.	Non-*Formulary*.	x
Pregabalin (Lyrica®)	Treatment of peripheral neuropathic pain in adults.	Total *Formulary*. Acknowledge new indication. Restricted to use in patients who have not achieved adequate pain relief from, or have not tolerated, conventional first and second line treatments for peripheral neuropathic pain. Treatment should be stopped if the patient has not shown sufficient benefit within 8 weeks of reaching the maximally tolerated therapeutic dose.	✓R
Quinagolide (Norprolac®)	Hyperprolactinaemia	(S) Total *Formulary*.	✓R
Sapropterin (Kuvan®)	Treatment of hyperphenylalaninaemia (HPA) in adult and paediatric patients with phenylketonuria and for the treatment of HPA in adult and paediatric patients with tetrahydrobiopterin deficiency.	Non-*Formulary*.	x
Tadalafil tablets (Cialis®)	Regular once-daily administration in patients with erectile dysfunction responding to an on-demand regimen of tadalafil who anticipate frequent use (at least twice weekly).	Total *Formulary*. Acknowledge new indication.	✓

✓ =*Formulary* ✓R =*Formulary* (restricted) **x** =non-*Formulary* **?** = awaiting final decision (S) =specialist initiation only (S) =specialist use only

Scottish patient safety programme

Healthcare is a dangerous business. Literature suggests one in ten patients will experience an adverse event in hospital and at least half are believed to be avoidable. The Scottish Government and NHS Scotland have established the Scottish Patient Safety Programme (SPSP) to significantly reduce adverse events and improve patient safety.

SPSP has initially focused on acute hospitals. A similar safety initiative in 3,000 American hospitals resulted in the prevention of more than 122,000 avoidable deaths. The challenging aims of SPSP are, among others, by 1 January 2011 to:

- reduce mortality by 15%,
- reduce adverse events by 30%,
- reduce MRSA bacteraemias by 50%,
- reduce harm from anticoagulation by 50%.

From a medicines perspective, one of the five basic programme objectives is to reduce adverse drug events. The remaining objectives are: to reduce healthcare associated infections, to reduce adverse surgical incidents, to improve critical care outcomes and to improve organisation and leadership on safety.

SPSP in practice

In January 2009, the following system was identified in the Mansionhouse Unit's Cathkin View. In an effort to improve care delivery and safety, a system has been put in place whereby drug kardexes are double checked. The nursing staff split the ward in two at the drug round, then swap kardexes to check that all patients have received medicines and every item has been signed for. Where errors are identified such as a drug not given, not signed for or codes are unacceptable, these are addressed immediately. The system works well on ward and literally takes minutes.

This simple example of how changes can be made in practice dovetails with the recent 'No Interruptions' policy for the preparation and administration of medicines. Although the causes of medication errors are multifactorial, frequent interruptions and distractions during preparation and administration of medicines is highlighted as being a common factor. Within NHSGGC, audit demonstrates that there are frequent interruptions to medicines rounds which cause delay and increase the risk of error.

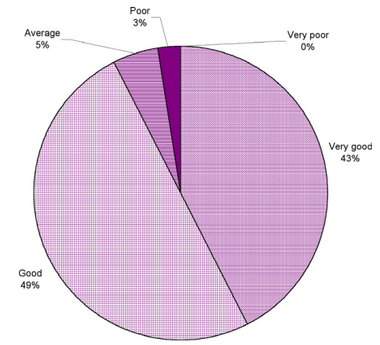
The policy identifies a number of strategies that can be adopted to promote a culture of 'No Interruptions'. Teams should adopt an approach or combination of approaches which best suits the area of care. Methods for consideration include:

- **Disposable purple plastic apron:** A member of the ward Health Care team wearing a disposable plastic apron is a common sight. A person wearing a purple apron is engaged on medicines duties and should only be interrupted by an emergency.
- **Signage:** This can be used on closed doors, eg to a six-bedded bay or treatment room or on trolleys.
- **Protected times:** Some areas can allocate protected times when medicines rounds are taking place. Staff and visitors are discouraged from attending the ward at these times. Where this practice has been adopted, it has proven to be successful in reducing the number of interruptions.

PostScript reader survey

Thank you to all our readers who took part in our user survey. Half of the respondents see a paper copy of the bulletin, but 93% access *PostScript* electronically. Most people would prefer to receive the bulletin electronically in the future with only eight people expressing a wish for a paper copy sent directly to them. No respondent was interested in paper copies being left in communal areas.

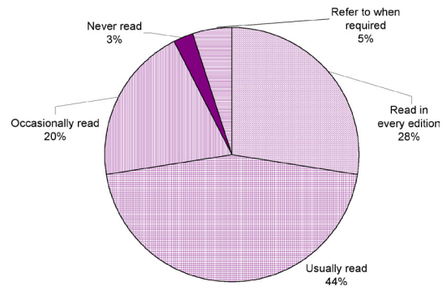
We are pleased to see that *PostScript* is rated as 'good' or 'very good' for relevance by 93% of respondents and for reliability by 98%. 77% of you found the quality of content 'good' or 'very good'.



The following aspects were usually read or read in every edition:

ADTC decisions	73%
New drug reviews	83%
Case studies	76%
Therapeutics based articles	93%
Non-therapeutic articles	69%

How often do you read ADTC decisions?



Actions

- We will stop printing paper copies after the current edition.
  - Distribution will be carried out electronically through directorates/CHCPs and by our mailing list. Sign up at **www.ggcformulary.scot.nhs.uk**
- Most readers were aware of the ADTC website with 66% having accessed copies of *PostScript* this way.
  - We will continue to maintain the site, and in response to requests will develop a webpage format for the latest edition to allow easier on-screen reading.
  - For those who prefer not to read from the screen, we will continue with the PDF format for printing.
- We will focus our content on therapeutics and new drug reviews as these are the most frequently read.

Pregabalin added to *Formulary*

Following a restricted acceptance by the SMC, pregabalin has been added to the NHSGGC Total *Formulary* for the treatment of peripheral neuropathic pain in adults. It is restricted to use in patients who have not achieved adequate pain relief from, or have not tolerated, conventional first and second line treatments for peripheral neuropathic pain. Treatment should be stopped if the patient has not shown sufficient benefit within eight weeks of reaching the maximally tolerated therapeutic dose.

The NHSGGC Guidelines for the treatment of neuropathic pain are to be resubmitted to ADTC following the *Formulary* addition of pregabalin to ensure it has an appropriate place in the guidelines. These state that simple analgesics and NSAIDs are seldom effective for neuropathic pain.

The total daily quantity of pregabalin can be split over two or three doses and there is no evidence of clinical or safety differences in these regimens. Due to the pricing structure, twice daily dosing will result in lower costs than three times daily and should be used where possible.

Clopidogrel and Proton Pump Inhibitors

Following recent advice about the concomitant use of clopidogrel and Proton Pump Inhibitors (PPIs), the NHS Greater Glasgow and Clyde Heart Disease Managed Clinical Network has issued the following consensus statement.

The EU Committee for Medicinal Products for Human Use (CHMP) and its Pharmacovigilance Working Party have concluded that concomitant use of PPIs and clopidogrel should be discouraged since PPIs may reduce the efficacy of clopidogrel in reducing thrombotic events. Large studies (observational data), however, have shown no difference in mortality between those on clopidogrel + PPI and those on clopidogrel and no PPI.

Please note that PPIs are used widely and reduce the likelihood of gastric bleeding with both aspirin and clopidogrel (a side effect of their use and with a significant adverse outcome, especially in the acute coronary event).

There are several scenarios.

Some cardiologists will recommend switching from a PPI to an H2 antagonist (ranitidine) when commencing clopidogrel, or indeed when reviewing a patient already on clopidogrel and a PPI. Many will not. The variation is because there is as yet such a poor evidence base for risk. Advice is to follow the recommendation of the individual consultant. However, for all patients with a drug eluting stent or on limited term clopidogrel following an acute coronary episode, it is generally agreed that if ranitidine does not control upper GI symptoms satisfactorily, it is better to re-commence a PPI than to stop the clopidogrel before the recommended time period, on the balance of risks and benefits.

For those on clopidogrel because of true intolerance to aspirin, the same applies. It is better to continue the clopidogrel with a PPI than stop clopidogrel if ranitidine does not control upper GI symptoms.

There is no reason to consider a formal switching programme in general practice, for those on clopidogrel, from PPI to ranitidine.

The EMEA statement indicates that no individual PPI is more or less likely to interact with clopidogrel than any other.

- **Prescribers should continue to follow the local antiplatelet guideline for patients with indications for the combination of aspirin and clopidogrel.**
- **Prescribers should avoid the use of a PPI with clopidogrel if possible.**

Long-acting reversible contraceptives *contd from page 1*

year licence with a low failure rate of less than 1 per 1,000 at three years.

Progesterone-only injections: The most commonly used preparation in the UK is Depo-Provera®, which contains medroxyprogesterone acetate. Its primary mode of action is in prevention of ovulation. Pregnancy rates are low at 0-1 per 100 women years of use. Current practice is to repeat the intra-muscular injection at 12-weekly intervals. The association with reduced bone mineral density may increase the risk of osteoporosis in later life. As this effect may be more marked in adolescents, the MHRA recommends it should not be prescribed as a first-line choice in this group unless other methods are unsuitable or unacceptable. Prescribing by GP practices has fallen by almost 20% over the past five years to just under 20,000 injections annually in NHSGGC.

Recommendations and implications for providers

As with many aspects of health care, a woman requesting contraception should be given both verbal and written information detailing all methods including LARCs. It is accepted that not all providers will be able to offer LARCs within their own practice, as the healthcare professionals delivering these treatments require specific training to develop and maintain the relevant skills. However, NHS QIS standards stress that there should be a clear pathway for onward referral to an appropriate service. In primary care, practices that do not supply LARCs can refer suitable patients for this treatment option through a locally enhanced scheme.

NHS Greater Glasgow and Clyde

Area Drug & Therapeutics Committee
Chair: Dr J Fox

Communications Sub-group
Chair: Mrs A Thompson

Published by the Communications Sub-group to reflect the views of the Area Drug & Therapeutics Committee but not necessarily those of NHS Greater Glasgow and Clyde.

PostScRipt

PostScript Editor: Mrs A Thompson
Prescribing Team, NHS Greater Glasgow & Clyde
Pharmacy & Prescribing Support Unit
Queen's Park House, Victoria Infirmary, Langside Road
Glasgow G42 9TY Tel: 0141 201 5214 Fax: 0141 201 5338
E-mail: audrey.thompson@nhs.net

PostScript Web editor: Dr A Power

Design, layout and production control:
Strathcashel Publications Project Management (01505 850 344)
Printed by: Mackay & Inglis, Glasgow

PostScript 52 references

Clopidogrel PPIs:

1. http://www.emea.europa.eu/humandocs/PDFs/EPAR/Plavix/32895609en.pdf
2. *JAMA.* 2009;301(9):937-944.

Long Acting Reversible Contraceptives

1. Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit. Intra-uterine guidance, 2007.
2. National Institute for Health and Clinical Excellence. Long acting reversible contraception: the effective and appropriate use of long-acting reversible contraception, 2005.
3. Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit Guidance. Progestogen-only implants, 2008.
4. Scottish Intercollegiate Guidelines Network. The Management of Genital Chlamydia Trachomatis Infection, 2009.
5. Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit. UK Medical Eligibility Criteria for Contraceptive Use, 2006. http://www.ffprhc.org.uk/admin/uploads/UKMEC200506.pdf
6. ISD Scotland. Key Clinical Indicators for Sexual Health, 2006-2007.
7. The Scottish Government. Respect and Responsibility, Sexual Health Strategy, 2007.