PostScriptOncology

NHS Greater Glasgow and Clyde

Issue 17, March 2012 ◆ Produced by A Branch and J Laskey, Cancer Care Pharmacists Clinical Effectiveness

In this issue:

1. Guideline news – local and national

New SIGN guidelines on colorectal cancer
The Scottish Intercollegiate Guidelines Network (SIGN) have recently published guidelines on diagnosis and management of colorectal cancer. This guidance covers primary care and referral, surgery, pathology, treatment with chemotherapy and radiotherapy, and follow up. The guideline can be accessed at www.sign.ac.uk

New NICE multi-technology appraisals:
Health improvement Scotland has advised that the following advice is applicable in NHS Scotland.

TA241 Dasatinib, high-dose imatinib and nilotinib for the treatment of imatinib-resistant chronic myeloid leukaemia (CML)
The Scottish Medicines Consortium (SMC) has previously issued guidance to NHSScotland on the use of dasatinib and nilotinib in this indication (370/07, 440/08). There is a material difference between the NICE and SMC advice. High-dose imatinib has not been assessed by SMC for use in chronic myeloid leukaemia. The NICE MTA guidance supersedes the SMC advice.

The Regional Prescribing Advisory Subgroup have considered this advice and will be issuing a revised Clinical Management Guideline for CML to local boards in the near future.

TA242 Colorectal cancer (metastatic) 2nd line – cetuximab, bevacizumab and panitumomab.
The Scottish Medicines Consortium (SMC) has previously issued guidance to NHSScotland on the use of cetuximab, bevacizumab and panitumumab in this indication (155/05, 469/08, 486/08). This NICE MTA guidance supersedes the SMC advice. There is no material difference between the recommendations of NICE and SMC. Therefore there are no implications for local practice.

TA243 Rituximab for 1st line treatment of stage III-IV follicular lymphoma.
The recommendations replace the recommendations in TA110 relating to the use of rituximabin for this indication. The Scottish Medicines Consortium (SMC) has previously issued guidance to NHSScotland on the use of rituximab in this indication (493/08). The recommendations of NICE and SMC are consistent. Therefore there are no implications for local practice.

West of Scotland Guidelines on the use of bisphosphonates in cancer patients.
The recent WoSCAN guidelines have now been accepted by NHSGGC. The full guidelines and patient information leaflet can be accessed on the WoSCAN intranet site www.intranet.woscan.scot.nhs.uk.

The main changes from the previous version of the guideline are:

- Zoledronic acid recommended as first line in multiple myeloma (was previously recommended as 2nd line)
- More detailed information on dose / administration modifications in patients with renal impairment
- More information on bisphosphonate related osteonecrosis of the jaw (BONJ).
- Calcium supplementation advice
- A statement relating to the most recent advice from MHRA regarding atypical femoral fractures
- A patient information leaflet has been developed for cancer patients receiving bisphosphonates

2. Drug Safety Update

Domperidone safety communication
In December 2011 a safety communication was issued by manufacturers of domperidone (in collaboration with MHRA) highlighting new information regarding cardiac risks associated with domperidone. Some epidemiological studies have shown that domperidone may be associated with an increased risk of serious ventricular arrhythmias including sudden cardiac death. The risks may be higher in patients over 60 years and in those receiving daily doses above 30mg. Domperidone should be avoided in patients taking concomitant medication known to prolong QT.

- The West of Scotland Cancer Network are revising their guidelines for managing chemotherapy induced nausea and vomiting

and will no longer recommend the use of domperidone.
- The updated anti-emetic guidelines will be issued in the near future. In the meantime prescribers are asked to take notice of this safety advice and consider alternative anti-emetics.

It is recognised that a variety of drugs are known to prolong the QT interval. The risk of QT prolongation is determined by underlying patient risk factors, the risk category of the drug involved and the concomitant use of drugs which either carry an additional risk of QT prolongation or increase plasma levels of drugs known to prolong QT (e.g. CYP3A4 inhibitors). Further practical advice for dealing with this prescribing issue is being developed within NHSGGC.

SmPC Changes

(full details at http://www.medicines.org.uk/emc/)

Imatinib (Glivec®)
The summary of product characteristics has recently been updated to include new advice for use of imatinib in patients with renal dysfunction or on dialysis, and also new advice on drug interactions. Caution is advised when co-administering drugs that are CYP3A4 inhibitors (eg ketoconazole), which may increase imatinib plasma concentrations, and result in toxicity. In addition, caution is advised when co-administering CYP3A4 inducers (eg. dexamethasone, phenytoin) which have the potential to decrease exposure to imatinib and increase risk of therapeutic failure.

Dasatinib (Sprycel®)
The summary of product characteristics for dasatinib has recently been updated. Under "important adverse reactions" there is new advice on management of myelosuppression, which occurs more frequently with advanced phase CML or Ph+ ALL than in chronic phase CML. Advice is given on frequency of blood count monitoring for imatinib resistant or intolerant patients and in patients with newly diagnosed chronic phase CML. Guidance is given regarding management of myelosuppression by temporary interruption of therapy or dose reduction.

3. MHRA Yellow card reporting scheme

Prescribers are reminded of the importance of reporting adverse drug reactions to the MHRA via the yellow card reporting scheme. This can be done at http://yellowcard.mhra.gov.uk/ The Yellow Card Scheme is vital in helping the MHRA monitor the safety of the medicines and vaccines that are on the market. Even if it is only a suspicion that a medicine or combination of medicines has caused a side effect, this should be reported.

Established therapy
Regardless of how long a drug has been on the market, **any** serious adverse event thought to be associated with a medicine or vaccine should be reported. Serious reactions are those that are fatal, life-threatening, incapacitating or those that require hospitalisation (or prolong stay in hospitalised patients); such reactions range from anaphylaxis to an effect on fertility.

For established drugs (those without black-triangle status), there is no need to report well-known non-serious adverse effects (eg low-grade fever with vaccines or constipation with opioid analgesics).

New therapies
The MHRA's surveillance of adverse effects of new medicines is more intensive; for such medicines, an inverted black triangle (▼) is shown against the name of the medicine in the Summary of Product Characteristics (SmPC) and in compendia such as the British National Formulary (BNF) and MIMS. **Any** adverse effect suspected to be associated with black-triangle medicines should be reported on a Yellow Card. Medicines are under intensive surveillance typically for a couple of years, after which the black-triangle denotation is removed. However, if there is doubt about the risk profile of a medicine then the black triangle is retained longer (or sometimes reinstated).
All suspected adverse reactions in children should be reported, whether from established medicines or newly launched ones, whether from off-label use or from licensed use.

A learning package on pharmacovigilance for clinical practitioners is available.

4. Recent Clinical Audit Highlights

A medicines use evaluation of sunitinib for renal cell carcinoma in the West of Scotland
A medicines use evaluation was recently carried out to determine treatment response, tolerability and compliance with the West of Scotland protocol. The results have now been analysed and provide useful information on:

- duration of therapy
- frequency of monitoring for adverse effects
- incidence of toxicities
- dose adjustments/omissions
- response to treatment
- reasons for stopping

A key finding was the importance of monitoring for toxicities at every cycle and ensuring adverse effects are managed promptly in order to minimise reductions in dose intensity. A further finding was the inconsistent documentation of toxicities. The results have also been compared with the pivotal trial for sunitinib in terms of duration of therapy and tolerability.
For more details please contact Dr Nicholas MacLeod (nicholas.macleod@ggc.scot.nhs.uk) or Jennifer Laskey (jennifer.laskey@ggc.scot.nhs.uk).

5. Recent National Guidance and GGC formulary decisions

Table 1 provides an overview of GGC formulary decisions, from January to February 2012, relating to SMC advice / relevant NICE advice

Drug	Indication	SMC / NICE advice	GGC formulary status
azacitidine (Vidaza®)	Treatment of adult patients not eligible for haematopoietic stem cell transplant (SCT) with intermediate-2 and high risk myelodysplastic syndrome (MDS), chronic myelomoncytic leukaemia (CMML) or acute myeloid leukaemia (AML)	SMC No. 589/09 Sep 2011 (resubmission) Accepted for use	WoSCAN protocol has been developed and is being sent to NHSGGC ADTC for consideration.
erlotinib (Tarceva®)	1st line treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating EGFR	SMC No 749/11 Jan 2012 Accepted for use	WoSCAN protocol has been developed and is being sent to NHSGGC ADTC for consideration.
nilotinib (Tasigna®)	Treatment of adult patients with newly diagnosed Philadelphia chromosome positive chronic myelogenous leukaemia (CML) in the chronic phase.	SMC No. 709/11 Aug 2011 Accepted for use	WoSCAN protocol has been developed and is being sent to NHSGGC ADTC for consideration
fentanyl single dose nasal spray (Instanyl®)	Management of breakthrough pain in adults already receiving maintenance opioid therapy for chronic cancer pain	SMC No 750/11 Jan 2012 Accepted for restricted use* *restricted to patients who are unsuitable for other short-acting oral opioids (e.g. oral morphine) as an alternative to other buccal and sublingual fentanyl preparations.	Non-formulary the medicine does not represent sufficient added benefit to other comparator medicines already available in the Formulary.

All WoSCAN protocols available at www.intranet.woscan.scot.nhs.uk

If there is anything you would like to see included in future issues of this bulletin please let us know. Please direct any feedback to aly.branch@ggc.scot.nhs.uk or jennifer.laskey@ggc.scot.nhs.uk