PostScriptOncology

NHS Greater Glasgow and Clyde

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In this issue:

1. Guideline / Policy news

NICE multi-technology appraisals

TA265 Denosumab for the prevention of skeletal-related events in adults with bone metastases from solid tumours

This guidance states that denosumab is recommended as an option for preventing skeletal-related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with bone metastases from breast cancer and from solid tumours other than prostate if bisphosphonates would otherwise be prescribed, and the manufacturer provides denosumab with the discount agreed in the patient access scheme.

Health improvement Scotland has advised that this advice is applicable in NHS Scotland. Therefore, this NICE MTA guidance supersedes the previous SMC advice (752/11). A patient access scheme has been approved for NHSScotland.

This guidance has been reviewed by the Regional Prescribing Advisory Subgroup and local breast cancer team and will now be considered for the GGC Adult Formulary by the New Drugs Sub-committee of ADTC. Until then denosumab remains non-formulary within NHSGGC.

West of Scotland Cancer Network (WOSCAN) – Regional Developments

Recently approved protocols for 'Off-label' Regimens

The WOSCAN Regional Prescribing Advisory Subgroup has recently endorsed a number of protocols which include the use of specific medicines 'off-label'.

These have subsequently been approved by the Cancer Therapeutics Group for use within NHSGGC. They include:

- Dose-dense temozolomide as second line therapy for recurrent glioma (BRWOS-OO2/01)
- Mitomycin / 5FU concomitant with radiotherapy for muscle invasive bladder cancer (URWOS010/01)
- Cisplatin / capecitabine chemoradiation in non-resectable oespophageal cancer (UGWOS-006/01)
- Capecitabine / mitomycin anal cancer chemoradiation (GIWOS011/01)
- Temozolomide for malignant melanoma with brain metastasis (SKWOS-001/01)
- FOLFIRINOX for metastatic / locally advanced pancreatic cancer (HPBWOS-003/01)

As per other WOSCAN protocols these are available at www.intranet.woscan.scot.nhs.uk or by clicking on 'Information sources' within the Chemocare® menu.

Cisplatin - new hydration schedule

A protocol with an accelerated hydration schedule for cisplatin-containing regimens (doses ≤ 80 mg/m^2) was endorsed by the Regional Prescribing Advisory Subgroup and is currently being rolled out to new patients prescribed cisplatin within NHSGGC. Chemocare® regimens for lung cancer, upper GI and urology have been updated to reflect this new hydration schedule.

Germ cell and head and neck cancer regimens, where the dose of cisplatin exceeds 80 mg/m^2, will not be included in the initial roll-out. Patients receiving these regimens will continue to receive the conventional hydration schedule.

Oxaliplatin-related neurotoxicity – prevention and minimisation

Protocols for chemotherapy regimens containing oxaliplatin have been updated to include calcium and magnesium infusions to minimise the risk of oxaliplatin induced neurotoxicity. There are also significant changes to the protocols with regards to assessment and management of neurotoxicity. The updated protocols will be on the WOSCAN intranet site soon. Ready made bags containing calcium and bags containing magnesium are now available through pharmacy.

Guidelines for managing chemotherapy induced nausea and vomiting (CINV) in adults
These guidelines have been updated to include aprepitant (or fosaprepitant) as a first line anti-emetic for all cisplatin based chemotherapy regimens. The use of aprepitant / fosaprepitant for nausea and vomiting associated with highly emetogenic cisplatin based chemotherapy is approved by the Scottish Medicines Consortium.

These updated guidelines will be issued to West of Scotland NHS Boards for consideration. Within NHSGGC, use of aprepitant in this setting no longer requires non-formulary approval. Cisplatin based regimens on Chemocare® will be amended in the near future to reflect this updated guidance.

It should be noted that use of aprepitant / fosaprepitant with moderately emetogenic chemotherapy is not recommended by SMC and therefore remains non-formulary.

2. Medicines Safety

The following issues have been highlighted in recent editions of 'Drug Safety Update' published by the MHRA:

Lenalidomide (Revlimid®): Risk of serious hepatic adverse drug reactions – routine monitoring of liver function now recommended
Routine monitoring of liver function is now recommended for all patients receiving lenalidomide for multiple myeloma. This advice follows a number of reports of serious hepatic reactions.

Advice for healthcare professionals:
- Routine monitoring of liver function with the same frequency as haematological monitoring is recommended for patients receiving lenalidomide i.e. weekly for the first 8 weeks and monthly thereafter. This is particularly important in patients with a history of, or concurrent, viral liver infection, or when lenalidomide is given at the same time as other medications known to be associated with liver injury.
- Prescribers should consider the possibility of lenalidomide-induced liver injury in patients presenting with otherwise unexplained deterioration of liver function.
- Impairment of liver function generally resolves when lenalidomide treatment is stopped. Once abnormal liver function parameters return to baseline, reintroduction of lenalidomide at a lower dose may be considered.
- Reminder advice: lenalidomide is excreted predominantly by the kidney. It is important to adjust the dose of lenalidomide in patients with renal impairment to avoid high plasma levels which may increase the risk of severe hepatotoxicity, as well as haematological side effects.

The WOSCAN protocol for lenalidomide is being revised to incorporate these recommendations and highlight the risk of hepatotoxicity.

Denosumab (Xgeva®): fatal cases of severe symptomatic hypocalcaemia and risk of hypocalcaemia at any time during treatment – monitoring recommended
Cases of severe symptomatic hypocalcaemia have been reported in patients receiving denosumab 120 mg or 60 mg. Denosumab 120 mg (Xgeva®) is licensed for prevention of skeletal related events in adults with bone metastases from solid tumours. Denosumab 60 mg (Prolia®) is licensed for the treatment of osteoporosis. Some of these cases were fatal in patients receiving the 120 mg dose. Although hypocalcaemia most commonly occurs within the first 6 months of treatment, it may occur at any time during treatment.

Advice for healthcare professionals:
The following precautions should be followed to minimise the risk of hypocalcaemia with denosumab:
Contra-indications:
- Denosumab 120 mg (Xgeva®) should not be used in patients with severe, untreated hypocalcaemia. (Denosumab 60 mg (Prolia®) should not be used in patients with hypocalcaemia, regardless of severity.)

Warnings and recommendations:
- Pre-existing hypocalcaemia must be corrected prior to initiating denosumab, and supplementation of calcium and vitamin D is required in all patients receiving 120 mg denosumab unless hypercalcaemia is present.
- Adequate intake of calcium and vitamin D is important in all patients receiving 60 mg denosumab
- Patients with severe renal impairment (creatinine clearance <30 mL/min; eGFR 15 – 29 mL/min/1.73m^2) or receiving dialysis are at greater risk of developing hypocalcaemia, and monitoring of calcium levels in these patients is recommended.

Denosumab is currently non-formulary within NHSGGC, however this is being reviewed. Any approved protocols will reflect this latest advice and include information regarding supplemental calcium and vitamin D and the need to correct hypocalcaemia prior to initiation.

MHRA Safety Letters to Healthcare professionals

Letters have been sent to healthcare professionals in relation to the following:

Pegylated liposomal doxorubicin (Caelyx®) – Information about reintroduction onto market following production problems.

Lapatinib (Tyverb®) – Information from recent trials demonstrating that lapatinib in combination with capecitabine has poorer efficacy, in terms of progression-free and overall survival, compared to trastuzumab and capecitabine. The effect was particularly pronounced in patients who had no prior exposure to trastuzumab. Prescribers are reminded that lapatinib is not licensed in combination with capecitabine unless the patient has progressed on trastuzumab. **It should be noted that lapatinib is non-formulary within NHSGGC.**

Denosumab (Xgeva®) – Information about risk of atypical femoral fractures associated with use of denosumab. The risk relates to both Prolia® (for osteoporosis) and Xgeva® (for prevention of skeletal related events in adults with bone metastases from solid tumours).

Further information on the MHRA (Medicines & Healthcare Regulatory Agency) advice and safety letters can be found at www.mhra.gov.uk . The MHRA also has a new Twitter channel **@MHRAmedicines.**

In addition, **Drug Safety Update** is an extremely useful monthly publication from the MHRA.

Local Safety Issues Highlighted

Use of LHRH analogues in prostate cancer
An article in PostScript (March 2013) highlighted a couple of cases where patients received their LHRH analogue at the wrong interval. It reminds prescribers / pharmacists to check frequency of administration coincides with strength of LHRH analogue prescribed. The full article can be viewed here.

Oral anti-cancer medicines in acutely unwell patients
An article in PostScript Acute (April 2013) highlights the potential implications of continuing oral anti-cancer medicines in acutely unwell patients admitted to hospital. The full article can be viewed here.

3. Recent Clinical Audit Highlights

A medicines use evaluation (MUE) of 2nd line treatments for non-small cell lung cancer (NSCLC) in the West of Scotland

A medicines use evaluation of 2nd line treatments for NSCLC (erlotinib, pemetrexed or docetaxel) was carried out between January 2011 and January 2012. The aims of this MUE were to quantify uptake of off-trial second-line NSCLC treatment in WoS and determine compliance with the corresponding WoS protocol, to compare response and toxicities of treatments and compare to pivotal trials. The results have now been analysed and provide useful information on:

- patient demographics
- choice of therapy
- duration of therapy
- incidence of toxicities
- dose adjustments/omissions
- response to treatment
- reasons for stopping

The results were compared to the pivotal trials in terms of duration of therapy, toxicity and overall survival. Performance status was found to correlate with overall survival. The results have been shared with the WOSCAN Lung Cancer Managed Clinical Network.
For more details please contact jennifer.laskey@ggc.scot.nhs.uk

4. Cancer Information available online

StaffNet

Background information on some common tumour types (which was previously within the GGC Cancer Care Clinical handbook) is now available on StaffNet. In addition, the procedure for semen storage in male cancer patients is also available. The information can be found by using the search function in StaffNet or by clicking here

WOSCAN intranet site

The West of Scotland Cancer Network intranet site (www.intranet.woscan.scot.nhs.uk) is available to all NHS Scotland staff. A database has been added to the site that contains the local formulary status of systemic anticancer medicines reviewed by SMC or HIS/NICE MTA processes within the last 2 years or on the SMC timetable for review. The database can be found within the Prescribing Advisory Subgroup menu or by clicking here.

5. GGC Adult Formulary decisions

Table 1 provides an overview of GGC Formulary decisions, from Sep 2012 until March 2013, relating to SMC advice / relevant NICE advice

Drug	Indication	SMC / NICE HIS advice	GGC Formulary status
abiraterone acetate (Zytiga®)	Use with prednisone or prednisolone for the treatment of metastatic castration-resistant prostate cancer (mCRPC) in adult men whose disease has progressed on or after a docetaxel-based chemotherapy regimen	SMC No. 764/12 Aug 2012 (resubmission) Accepted for restricted use	**Added to Formulary** Restricted to use according to WOSCAN protocol URWOS-011/1
bortezomib Subcutaneous (Velcade®)	In combination with melphalan and prednisolone for treatment of patients with previously untreated mutiple myeloma who are not eligible for high dose chemotherapy with bone marrow transplant	SMC No 822/12 November 2012 Accepted for use	**Added to Formulary** Restricted to use according to WOSCAN protocol MMWOS-004/02
everolimus (Afinitor®)	Treatment of unresectable or metastatic, well- or moderately-differentiated neuroendocrine tumours of pancreatic origin (pNET) in adults with progressive disease.	SMC No771/12 May 2012 Accepted for use	**Added to Formulary** Restricted to use according to WOSCAN protocol RCWOS002/1
tegafur/ gimerecil/ oteracil (Teysuno®)	Advanced gastric cancer in adults when given in combination with cisplatin	SMC No 802/12 August 2012 Accepted for restricted use	**Added to Formulary** Restricted to use according to WOSCAN protocol UGWOS-007/01 (available on WOSCAN site soon)
palonosetron capsules (Aloxi®)	Prevention of nauea and vomiting associated with moderately emetogenic chemotherapy	SMC No 838/13 January 2013 Accepted for use	**Non-Formulary (no added benefit to other comparator medicines)**
bevacizumab (Avastin®) with carboplatin and paclitaxel	Front-line treatment of advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer	SMC No 806/12 September 2012 Not recommended	**Non-Formulary**
bevacizumab (Avastin®) with carboplatin and gemcitabine	Adult patients with first recurrence of platinum-sensitive epithelian ovarian, fallopian tube or primary peritoneal cancer who have not received prior therapy with bevacizumab or other VEGF inhibitors or VEGF receptor–targeted agents.	SMC No 853/13 March 2013 Not recommended	**Non-Formulary**
brentuximab (Adcetris®)	Treatment of adult patients with relapsed or refractory CD30+ Hodgkin lymphoma	SMC No 845/12 December 2012 Not recommended (non-submission)	**Non-Formulary**
decitabine (Dacogen®)	Treatment of adult patients aged 65 years and above with newly diagnosed de novo or secondary acute myeloid leukaemia (AML), according to the World Health Organisation (WHO) classification, who are not candidates for standard induction chemotherapy	SMC No 846/12 December 2012 Not recommended (non-submission)	**Non-Formulary**
pazopanib (Votrient®)	Adult patients with selective subtypes of advanced soft tissue sarcoma (STS) who have received prior chemotherapy for metastatic disease or who have progressed within 12 months after (neo) adjuvant therapy.	SMC No 820/12 November 2012 Not recommended	**Non-Formulary**
vemurafenib (Zelboraf®)	Monotherapy for the treatment of adults patients with BRAF V600 mutation-positive unresectable or metastatic melanoma	SMC No 792/12 August 2012 Not recommended	**Non-Formulary**

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

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