FRAMEWORK FOR NEW DRUGS ASSESSMENT IN SCOTLAND

PostScRxipt
from the
GGNHSB Area Drug & Therapeutics Committee
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Website
http://www.show.scot.nhs.uk/ggnhsb/adtc

At present a number of bodies are producing advice, guidance or recommendations on the prescribing of new drugs. Prescribers are at best, confused; at worst, weighed down by bureaucracy. The table clarifies the methods, timescales and status of advice from the Scottish Medicines Consortium (SMC), National Institute for Clinical Excellence (NICE) and the Scottish Intercollegiate Guidelines Network (SIGN).

Some further issues merit clarification:

'Unique' drugs
Since November 2003, the SMC has included the category of approved and 'unique' in its advice categories. 'Unique' has no precise definition, but is likely to apply only to drugs for conditions currently with no effective treatment. So far, the only drug accorded 'unique' status is etanercept for psoriatic arthritis.

NICE advice supersedes SMC advice
SMC aims to provide advice as close to product launch as possible. It is accepted that detailed NICE advice, based on longer utilisation experience, is more robust and, where accepted by NHS Quality Improvement Scotland (QIS), will ***supersede*** SMC advice. Of note, for the first 12 products reviewed by both SMC and NICE, advice was the same (with the exception of detail in the pimecrolimus advice) and SMC advice preceded NICE by 10 months on average.

Harmonisation of SMC and SIGN guidance
The SMC and SIGN both operate under the QIS umbrella, and have established close links. These will ensure that SIGN guideline development groups are aware of recent SMC decisions and work plans, thus minimising the chance of discordant guidance.

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Role of the NHS Glasgow ADTC and Prescribing Management Group (PMG)
The ADTC routinely assesses all SMC recommendations. The main focus for local decision-making is drugs accepted for use but not unique. *Formulary* inclusion may be granted based on perceived advantage over existing products, local specialist input and cost implications. Drugs likely to have major impact on local prescribing practice are referred to the PMG before final *Formulary* decisions are reached. The ADTC and PMG have recently agreed a policy whereby all non-*Formulary* drugs, including those not recommended by the SMC, should only be used exceptionally. Such use must be justified and will be monitored. More detail will be provided in a future *PostScript*.

	SMC	NICE	SIGN
Method	Critique of company information on clinical and cost effectiveness of ***all*** new drugs and major new formulations and indications.	Commissioned review of clinical and cost effectiveness of selected new drugs.	Guidelines on selected clinical topics produced by iterative evidence-based review.
Timing with respect to licensing and launch of new drugs	Quick, minimum 3 months. Depends on company submitting information	Slow, up to 2 years	Variable
Economic evaluation	Included	Included	Not included (at present)
Status of advice	• Unique drugs accepted for use – compulsory • Non-unique drugs accepted for use – local formulary decision • Drugs not recommended – should not be added to local formularies	Drugs reviewed as part of a health technology assessment are reviewed by QIS. If accepted for NHS Scotland, any local variance from NICE guidance must be justified.	Implementation expected as part of clinical governance agenda

Incremental alphabetical list of published SMC advice on which Glasgow decisions have recently been taken.
For further information and a full list of SMC advice, visit **www.scottishmedicines.org**

Medicine	Reason for consideration	Indication	SMC decision	Glasgow decision
Aprepitant (Emend®)	New medicine	Prevention of acute and delayed nausea and vomiting associated with highly emetogenic cisplatin-based chemotherapy.	Accepted for restricted use within NHS Scotland. Restricted to initiation only by appropriate hospital based specialists	**Non-*Formulary*** on advice of New Drugs in Oncology Group. Place in therapy will be considered in review of anti-emetic treatment policy.
Atomoxetine (Strattera®)	New medicine	Treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children ≥ 6 years and in adolescents.	Not recommended for use within NHS Scotland.	**Non-*Formulary.***
Bivalirudin (Angiox®)	New medicine	Anticoagulant in patients undergoing percutaneous coronary intervention.	Accepted for restricted use within NHS Scotland. Restricted to patients who would have been considered for unfractionated heparin plus a glycoprotein IIb/IIIa antagonist.	**Non-*Formulary.*** Decision deferred to allow consultation with cardiologists
Bortezomib (Velcade®)	New medicine	Treatment of patients with multiple myeloma who have received at least two prior therapies and have demonstrated disease progression on the last therapy and are unresponsive to alternative licensed treatments for this stage of disease.	Accepted for use within NHS Scotland.	***Formulary.*** Restricted to use according to Haematology protocol.
Caspofungin (Cancidas®)	New indication	Empirical therapy for presumed fungal infections (such as candida or aspergillus) in febrile, neutropenic adult patients.	Accepted for restricted use within NHS Scotland.	***Formulary.*** Acknowledge new indication. Restricted to use on the advice of microbiologists or specialists in infectious diseases.
Cetuximab (Erbitux®)	New medicine	In combination with irinotecan for the treatment of patients with epidermal growth factor receptor expressing metastatic colorectal cancer after failure of irinotecan-including cytotoxic therapy.	Not recommended for use within NHS Scotland.	**Non-*Formulary.***
Conjugated Oestrogen, Medroxyprogesterone (Premique® Low Dose)	New formulation	Hormone replacement therapy in postmenopausal women with an intact uterus.	Accepted for use within NHS Scotland.	***Formulary.***
Creon Micro®	New formulation	Treatment of pancreatic exocrine insufficiency.	Accepted for restricted use within NHS Scotland. Suitable for use in infants and young cystic fibrosis sufferers who are unable to swallow capsules.	***Formulary.*** SMC restrictions apply.
Efalizumab (Raptiva®)	New medicine	Treatment of adult patients with moderate to severe chronic plaque psoriasis who have failed to respond to, or have a contra-indication to, or are intolerant to other therapies, including ciclosporin, methotrexate and PUVA.	Not recommended for use within NHS Scotland.	**Non-*Formulary.***
Eplerenone (Inspra®)	New medicine	In addition to standard therapy including beta-blockers, to reduce the risk of cardiovascular disease after recent MI in stable patients with left ventricular dysfunction and clinical evidence of heart failure.	Accepted for restricted use within NHS Scotland. Restricted to patients who cannot tolerate spironolactone due to non-specific hormonal adverse effects.	**Non-*Formulary.*** Awaiting outcome of licence holder's appeal to SMC regarding the restriction.
Ertapenem (Invanz®)	New medicine	Treatment of abdominal infections in adults caused by bacteria known or likely to be susceptible to ertapenem and when parenteral therapy is required.	Accepted for restricted use in NHS Scotland. Restricted to second or third line treatment of community acquired abdominal infections resistant to conventional treatments and under the advice of local microbiologists or specialists in infectious diseases.	***Formulary.*** SMC restrictions apply.
Etomidate (Lipuro®)	New formulation	Induction of general anaesthesia in patients ≥ 6 months where appropriate.	Accepted for use within NHS Scotland.	***Formulary.***
Gemcitabine (Gemzar®)	New indication	In combination with paclitaxel, for the treatment of patients with metastatic breast cancer who have relapsed following adjuvant/neo-adjuvant chemotherapy. Prior chemotherapy should have included an anthracycline unless clinically contraindicated.	Not recommended for use within NHS Scotland.	**Non-*Formulary.***
Laronidase (Aldurazyme®)	New medicine Resubmission	For long-term enzyme replacement therapy in patients with a confirmed diagnosis of Mucopolysaccharidosis I.	Not recommended for use within NHS Scotland.	**Non-*Formulary.***
Letrozole (Femara®)	New indication	Treatment of invasive early breast cancer in postmenopausal women who have received prior standard adjuvant tamoxifen therapy.	Accepted for use within NHS Scotland.	***Formulary.*** Acknowledge new indication.
Levetiracetam (Keppra®) 750 mg film-coated tablets 100mg/ml oral solution	New formulation	Adjunctive therapy in the treatment of partial onset seizures.	Accepted for restricted use within NHS Scotland. Restricted as an additional dosage form for adjunctive therapy in the treatment of partial seizures with or without secondary generalisation in appropriate patients. Its use should be initiated by physicians who have appropriate experience in the treatment of epilepsy.	***Formulary.*** Acknowledge new formulation. SMC restrictions apply.
Metformin prolonged release tablets (Glucophage SR®)	New formulation	Treatment of Type 2 diabetes mellitus in adults, particularly in overweight patients, when dietary management and exercise alone do not result in adequate glycaemic control.	Not recommended for use within NHS Scotland.	**Non-*Formulary.***
Miglustat (Zavesca®)	New medicine	Treatment of mild to moderate Type 1 Gaucher's disease in adult patients for whom enzyme replacement therapy is unsuitable.	Accepted for use within NHS Scotland. Restricted to initiation by physicians experienced in the management of Gaucher's disease.	**Non-*Formulary.*** To be added to a list of orphan drugs which may be used occasionally.
Mycophenolate sodium (Myfortic®)	New medicine	In combination with ciclosporin and corticosteroids for the prophylaxis of acute transplant rejection in adult patients receiving renal transplants.	Accepted for restricted use within NHS Scotland. Restricted to use by transplant specialists.	***Formulary.*** SMC restrictions apply. Switching between mycophenolate sodium and mycophenolate mofetil is not recommended.
Nicotinic Acid Modified Release Tablets (Niaspan®)	New medicine Resubmission	Adjunct therapy to exercise and dietary measures for the treatment of hyperlipidaemia and mixed dyslipidaemia.	Not recommended for use within NHS Scotland.	**Non-*Formulary.***
Paracetamol Infusion (Perfalgan®)	New formulation	Short-term treatment of moderate pain following surgery and fever, when administration by intravenous route is clinically justified.	Accepted for use within NHS Scotland.	***Formulary.***
Pregabalin (Lyrica®)	New medicine	Adjunctive therapy in adults with partial seizures with or without secondary generalisation.	Accepted for restricted use within NHS Scotland. Restricted to initiation by physicians who have appropriate experience in the treatment of epilepsy and principally in patients who have not benefited from treatment with an older anti-convulsant drug such as carbamazepine or sodium valproate, or for whom these drugs are unsuitable.	***Formulary.*** SMC restrictions apply.
Pregabalin (Lyrica®)	New medicine	Treatment of peripheral neuropathic pain in adults.	Not recommended for use within NHS Scotland.	**Non-*Formulary.***
Rituximab (MabThera®)	New indication	Treatment of previously untreated patients with stage III-IV follicular lymphoma in combination with CVP chemotherapy.	Accepted for restricted use in NHS Scotland. Restricted to use only by oncologists or haematologists who have expertise in treating lymphoma. It should be administered in a hospital environment where full resuscitation facilities are available.	**Non-*Formulary.*** Decision deferred; awaiting endorsement from CMT
Rosiglitazone Maleate / Metformin Hydrochloride (Avandamet®)	Product update	Treatment of Type 2 diabetes mellitus in patients for whom a combination of rosiglitazone and metformin is appropriate.	Accepted for use within NHS Scotland in formulations containing rosiglitazone (2mg or 4mg) plus metformin (1000mg).	***Formulary.***

Medicine	Reason for consideration	Indication	SMC decision	Glasgow decision
Solifenacin (Vesicare®)	New medicine	Treatment of urge incontinence and/or increased urinary frequency and urgency that can occur in overactive bladder syndrome.	Not recommended for use within NHS Scotland.	**Non-*Formulary.***
Testosterone 30mg mucoadhesive buccal tablets (Striant®)	New medicine	Testosterone replacement in primary or secondary hypogonadism.	Accepted for restricted use within NHS Scotland. Restricted to patients who would particularly benefit from this mode of administration where intramuscular treatment is not suitable.	***Formulary.*** SMC restrictions apply.
Voriconazole (VFEND®)	Product update	Treatment of invasive fungal infections.	Accepted for restricted use within NHS Scotland. Restricted to use only in suspected or confirmed cases of invasive aspergillosis; for infections caused by *Fusarium spp* and *Scedosporium spp*; or serious invasive candidiasis unresponsive to fluconazole. It should be administered primarily to immunocompromised patients with progressive, possibly life-threatening, infections.	***Formulary.*** SMC restrictions apply.
Triptorelin acetate 11.25mg (Decapeptyl SR®)	ADTC appeal	Treatment of advanced prostate cancer.	Accepted for restricted use within NHS Scotland. Restricted to patients for whom the use of triptorelin is appropriate and who would benefit from reduced frequency of administration.	***Formulary.*** SMC restrictions apply.

Clopidogrel in acute coronary syndrome and the updated GGNHS antiplatelet guideline

The ADTC has noted SMC advice and extended the *Formulary* indication for clopidogrel to include restricted use in acute coronary syndrome (ACS). Clopidogrel blocks platelet aggregation through an action distinct from that of aspirin. It is licensed for prevention of atherosclerotic events in peripheral arterial disease, myocardial infarction (MI) and ischaemic stroke, and, in combination with low-dose aspirin, for patients suffering non-ST segment elevation ACS.

The SMC accepted clopidogrel for restricted use in ACS. It should be initiated only during an inpatient stay when a diagnosis of ACS is confirmed by ECG changes or raised cardiac enzymes/markers. The maximum benefit appears within 3 months and absolute benefit is greatest in high risk patients. The CURE trial assessed aspirin and clopidogrel in this patient group.[1] For every 100 patients, addition of clopidogrel to aspirin for a mean of 9 months prevented two cardiovascular deaths, non-fatal MIs or strokes, but led to one or two additional major bleeds. Current evidence only supports combination therapy for up to 12 months; most (or all) of the benefit appears within 4 weeks.

Prescribing in Glasgow has been evaluated in a sample of 432 patients from 22 practices. 45 patients (10%) had ACS; the vast majority had treatment initiated in hospital, mainly by a cardiologist. Advice on appropriate duration of therapy was given in 7 cases (16%). Use ranged from 1 - 30 months (median 9 months). Local consensus on clopidogrel use after ACS is now available in new antiplatelet guidelines. The duration of clopidogrel treatment in ACS should range from **4 weeks** in those not undergoing any intervention to **12 weeks** in those having angiography or angioplasty with a bare metal stent to **24 weeks** in those undergoing angioplasty with a drug-eluting stent.

A recent trial looked at aspirin plus clopidogrel compared to clopidogrel alone after recent ischaemic stroke or TIA. There was a non-significant difference in major vascular events, but the risk of life-threatening or major bleeding was increased by the addition of aspirin. It is appropriate to review therapy in patients receiving combination therapy for this indication.[2]

In view of the greater cost of clopidogrel (£35.31 for 28 days) than aspirin dispersible 75mg (37p for 28 days), it is incumbent on primary and secondary care to review use carefully in line with local policy, especially with regard to duration of therapy.

PostScript

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1. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med* 2001;345:494-502
2. Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high risk patients (MATCH): randomised, double-blind, placebo-controlled trial. Lancet 2004;364:331-337