TAYSIDE PRESCRIBER

NHS Tayside

Tayside DTC Supplement No 124 – February 2013

Produced by NHS Tayside Drug and Therapeutics Committee Medicines Advisory Group (MAG)

Special points of interest for Primary Care

SMC advice:

- Brentuximab vedotin (Adcetris®)
- Budesonide capsule (Budenofalk®)
- Budesonide granules(Budenofalk®)
- Ceftaroline fosamil (Zinforo®)
- Clostridium botulinum type A (Dysport®)
- Dapagliflozin (Forxiga®)
- Decitabine (Dacogen®)
- Etoricoxib (Arcoxia®)
- Glycopyrronium (Seebri Breezhaler®)
- Hydrocortisone (Plenadren®)
- Ivacaftor (Kalydeco®)
- Tadalafil (Cialis®)
- Vildagliptin (Galvus®)

Inside this issue :

Prescribing Changes

Dapagliflozin

Dapagliflozin (Forxiga®) is the first in class SGLT2 inhibitor and has been approved for use in Scotland where Sulphonylureas are inappropriate as add on to metformin monotherapy, SGLT2 (sodium glucose transporter 2) is expressed in the renal tubule and acts to reabsorb glucose from the tubular fluid. Therefore SGLT2 inhibitors lower the renal threshold for glucose and induce glycosuria. This has a number of beneficial effects including 1) lowering of the blood glucose concentrations and 2) excretion of calories in the form of glucose resulting in net weight loss. As expected, the clinical trials show an increase in urinary tract infections and genital infections such as candidiasis; these respond to the usual treatment.

Dapagliflozin has reduced efficacy as eGFR falls and should not be used in those with eGFR<60ml/min. The SPC also states that dapagliflozin is not recommended for use in patients receiving loop diuretics or who are volume depleted, e.g. due to acute illness (such as gastrointestinal illness). Caution should be exercised in patients for whom a dapagliflozin-induced drop in blood pressure could pose a risk, such as patients with known cardiovascular disease, patients on anti-hypertensive therapy with a history of hypotension or elderly patients. For patients receiving dapagliflozin, in case of intercurrent conditions that may lead to volume depletion, careful monitoring of volume status (e.g. physical examination, blood pressure measurements, laboratory tests including haematocrit) and electrolytes is recommended. Temporary interruption of treatment with dapagliflozin is recommended for patients who develop volume depletion until the depletion is corrected.

Denosumab

NICE issued a Multiple Technology Appraisal (MTA) on the use of denosumab (Xgeva®) for the prevention of skeletal-related events in adults with bone metastases from solid tumours in October 2012

Whilst the MTA recommends denosumab as an alternative option to a bisphosphonate, it is categorised as Non-formulary for this indication within NHS Tayside. Bisphosphonates remain the local choice for prevention of skeletal-related events in cancer patients with established metastatic bone disease.

Inhalers

Flutiform® (fluticasone propionate and formoterol fumarate 50microgram/5microgram, 125 microgram/5microgram and 250microgram/10microgram per actuation inhalation suspensions) A combination inhaled corticosteroid and long acting beta agonist (LABA), indicated in the regular treatment of asthma at BTS step 3, in patients over 12 years. Flutiform® is cost-equivalent to Fostair®, but less expensive than Seretide® and Symbicort®. In Tayside, it has been added to the formulary as an alternative to these other agents. Flutiform® is available in a pressurised meter dose inhaler, which should be used with the Aerochamber Plus® device.

Glycopyrronium (44 micrograms inhalation powder – Seebri Breezhaler®) is an antimuscarinic bronchodilator indicated for the maintenance treatment of adults with chronic obstructive pulmonary disease (COPD) at a dose of 44 micrograms per day. This agent is second line. The first line formulary choice is tiotropium.

Inhalers continued

Aclidinium (322 micrograms inhalation powder - Eklira Genuair®) is an antimuscarinic bronchodilator indicated for the maintenance treatment of adults with COPD at a dose of 322micrograms aclidinium twice daily. This agent is third-line.

Indacaterol (Onbrez Breezhaler® 150 microgram inhalation powder, hard capsules and Onbrez Breezhaler® 300 microgram inhalation powder, hard capsules) is a LABA bronchodilator indicated for the maintenance treatment of COPD. It is administered once daily. Capsules must always be stored in the blister to protect from moisture and only removed immediately before use. This agent is the first line formulary choice.

Further information on all these inhalers, including instructions on how to use the devices, can be found on the Electronic Medicines Compendium.

Isosorbide Mononitrate - supply problems

Due to problems with the availability of raw materials, there is currently a shortage of standard release isosorbide mononitrate preparations:

- Isosorbide mononitrate 10mg, 20mg and 40mg

The availability of modified release formulations appears to be unaffected by this shortage.

The shortage may last until the end of April 2013. As with other medicine supply problems the situation may change at short notice.

It is recommended that patients should be switched to the nearest practical total daily dose of the least expensive once daily modified release preparation.

Information on the dose equivalence of these products is uncertain and patients should be monitored closely for effectiveness and tolerability. If any clinician has concern about prescribing for a particular patient, advice from a consultant cardiologist should be sought.

Community pharmacists who are unable to obtain stock of the standard release preparation should refer patients back to their prescriber so that an alternative can be prescribed.

The following modified release isosorbide mononitrate preparations should be prescribed generically:

- Isosorbide mononitrate m/r capsules 25mg, 50mg
- Isosorbide mononitrate m/r tablets 60mg

Patients should be switched back to a standard release formulation when the shortage has been resolved.

Click here for further information.

Guidelines and Protocols

Local treatment protocol for octreotide and lanreotide

The local treatment protocol for lanreotide (Somatuline® LAR, Somatuline Autogel®) and the depot preparation of octreotide (Sandostatin Lar®) is now available from the endocrinology specialist list.

GPs may prescribe under the direction of hospital endocrinologists, oncologists or surgeons for the treatment of neuroendocrine and pituitary tumours deemed to require somatostatin analogue treatment by the hospital team.

Drug Safety Updates

Please follow link - Volume 6, Issue 7, February 2013

Medicine	Indication	Local recommendation category	Comments and useful links
Brentuximab vedotin (Adcetris®) 50 mg powder for concentrate for solution for infusion (845/12) *- Non-submission*	Treatment of adult patients with relapsed or refractory CD30+ Hodgkin lymphoma (HL): 1. following autologous stem cell transplant (ASCT); or 2. following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option; and treatment of adult patients with relapsed or refractory systemic anaplastic large cell lymphoma (sALCL).	**Not recommended**	***SMC advice***
Budesonide 3mg gastro-resistant capsule (Budenofalk®) (828/12) *- Full submission*	Symptomatic relief of chronic diarrhoea due to collagenous colitis.	GPs may prescribe under the direction of the GI Clinic **GI specialist list**	***SMC advice*** ***SPC link***
Budesonide 9mg gastro-resistant granules (Budenofalk®) (831/12) *- Abbreviated submission*	Induction of remission in patients with active collagenous colitis.	GPs may prescribe under the direction of the GI Clinic **GI specialist list**	***SMC advice*** ***SPC link***
Ceftaroline fosamil, 600mg, powder for concentrate for solution for infusion (Zinforo®) (830/12) *- Full submission*	Treatment of complicated skin and soft tissue infections in adults.	Non-formulary - alternatives preferred SMC restriction: use in patients with known or suspected MRSA infections – for Gram+ve only infection where vancomycin iv is inappropriate and daptomycin iv or linezolid iv is normally used. – for polymicrobial Gram+ve and common Gram-ve pathogens, where vancomycin iv with gentamicin iv is inappropriate and daptomycin iv with gentamicin iv, or tigecycline iv is normally used.	***SMC advice*** ***SPC link*** Daptomycin iv or linezolid iv are used locally for gram +ve infections. Daptomycin iv with gentamicin iv is used locally if mixed growth. In both cases treatment is under the direction of ID/ Micro. ***MRSA treatment protocol***
Clostridium botulinum type A toxin-haemagglutinin complex 300 units and 500 units (Dysport®) (353/07) *- Resubmission*	For focal spasticity, including the treatment of arm symptoms associated with focal spasticity in conjunction with physiotherapy.	Non-formulary—alternatives preferred SMC restriction: for focal spasticity of the upper limbs associated with stroke	***SMC advice*** ***SPC link*** Botox® is the botulinum toxin type A preparation on the Stroke and MFE specialist lists
Dapagliflozin 5mg and 10mg film-coated tablets (Forxiga®) (799/12) *- Full submission*	For use in adults aged 18 years and older with type 2 diabetes mellitus to improve glycaemic control in combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control. Dapigliflozin is also indicated for use as monotherapy when diet and exercise do not provide adequate glycaemic control in patients for whom use of metformin is considered inappropriate due to intolerance	<u>Combination therapy</u> **Formulary** Restricted to dual therapy in combination with metformin when a sulphonylurea inappropriate <u>Monotherapy</u> Not recommended	***SMC advice*** ***SPC link***
Decitabine (Dacogen®) 50 mg powder for concentrate for solution for infusion (846/12) *- Non-submission*	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.	**Not recommended**	***SMC advice***
Etoricoxib (Arcoxia®) 30mg, 60 mg, 90 mg & 120 mg film-coated Tablets 30mg, 60 mg, 90 mg & 120 mg Film-coated Tablets(847/12) *- Non-submission*	Short-term treatment of moderate pain associated with dental surgery.	**Not recommended**	***SMC advice***

* 'pending' means that no local recommendation to support use is in place at the current time

Medicine	Indication	Local recommendation category	Comments and useful links
Glycopyrronium 44 micrograms hard capsules of inhalation powder (Seebri Breezhaler®) (829/12) *- Full submission*	As a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD).	**Formulary** Restricted to use as second-choice long-acting muscarinic antagonist (LAMA)	***SMC advice*** ***SPC link*** Tiotropium Handihaler® is the first-choice LAMA in the formulary
Hydrocortisone (Plenadren®) 5mg and 20mg tablets (848/12) *- Non-submission*	Treatment of adrenal insufficiency in adults.	**Not recommended**	***SMC advice***
Ivacaftor 150mg film-coated tablets (Kalydeco®) (827/12) *- Full submission*	Treatment of cystic fibrosis (CF) in patients age 6 years and older who have a *G551D* mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.	**Not recommended**	***SMC advice*** Special arrangements are in place to facilitate patient access via the Rare Conditions Medicines Fund
Tadalafil (Cialis®) 5mg film coated tablets (849/12) *- Non-submission*	Treatment of the signs and symptoms of benign prostatic hyperplasia in adult males.	**Not recommended**	***SMC advice***
Vildagliptin 50mg tablets (Galvus®) (826/12) *- Full submission*	Treatment of type 2 diabetes mellitus in adults as monotherapy in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance.	Non-formulary - alternatives preferred	***SMC advice*** ***SPC link*** Sitagliptin is the first-choice DPP-4 inhibitor in the formulary

* 'pending' means that no local recommendation to support use is in place at the current time

SMC Advice issued in February 2013 **SMC website: www.scottishmedicines.org.uk**

Medicine	Indication	Local recommendation category	Comments and useful links
Colecalciferol 800 international units (equivalent to 20 micrograms vitamin D_3) tablets (Desunin 800 IU®) (840/13) *- Abbreviated submission*	Prevention and treatment of vitamin D deficiency in adults and adolescents. In addition to specific osteoporosis treatment of patients who are at risk of vitamin D deficiency, supplemental calcium should be considered.	*Vitamin D deficiency* Formulary - restricted to treatment of vitamin D deficiency *Osteoporosis* Formulary - restricted to patients in whom a combined vitamin D and calcium supplement is unsuitable	***SMC advice*** ***SPC link*** ***NHS Tayside Guidelines for Investigation and Treatment of Vitamin D Deficiency*** *is under development* Vitamin D for maintenance therapy should normally be purchased OTC. Combined vitamin D and calcium supplementation is recommended first-line as an adjunct to osteoporosis therapy. TAF first-choice is Calceos®. Desunin® has replaced Fultium D_3® on the formulary.

'Local processes exist to allow consideration of prescribing outwith SMC advice or outwith NHS Tayside formulary. Details are available in the NHS Tayside Policy on the Prescribing of Medicines that are Non-formulary (including Individual Patient Treatment Requests)'

Updates from previous SMC Advice

Medicine	Indication	Local recommendation category	Comments and useful links
Colecalciferol 800 international units (equivalent to 20 micrograms vitamin D_3) capsules (Fultium-D_3®) (801/12) *- Full submission*	In adults, the elderly and adolescents for the prevention and treatment of vitamin D deficiency and as an adjunct to specific therapy for osteoporosis in patients with vitamin D deficiency or at risk of vitamin D insufficiency.	Non-formulary—alternatives preferred	***SMC advice*** ***SPC*** Desunin® has replaced Fultium D_3® on the formulary
Fingolimod (as hydrochloride), 0.5mg hard capsules (Gilenya®) (763/12) *- Re-submission*	As single disease modifying therapy in highly active relapsing remitting multiple sclerosis (RRMS) for the following adult patient groups: - Patients with high disease activity despite treatment with a beta-interferon; OR - Patients with rapidly evolving severe RRMS.	**HOSPITAL ONLY** (MS Clinic) Second-line disease modifying therapy. Restricted to patients with high disease activity despite treatment with beta-interferon. Supplied via a Patient Access Scheme (PAS).	***SMC advice*** ***SPC link*** ***Fingolimod Protocol***
Ranibizumab, 10mg/mL solution for injection (Lucentis®) (711/11) *- Resubmission*	Treatment of visual impairment due to diabetic macular oedema (DMO) in adults.	**HOSPITAL ONLY** (Ophthalmology Clinic) Restricted to patients with best corrected visual acuity 75 ETDRS letters or less at baseline. Supplied via a Patient Access Scheme (PAS).	***SMC advice*** ***SPC link***
Ticagrelor 90mg film-coated tablets (Brilique®) (699/11) *- Full submission*	Co-administered with aspirin, for the prevention of atherothrombotic events in adult patients with acute coronary syndromes; including patients managed medically, and those who are managed with percutaneous coronary intervention (PCI) or coronary artery by-pass grafting (CABG).	GPs may prescribe under the direction of the Cardiology Clinic Restricted to use in high risk PCI in patients >75yrs, <60kg or with history of previous TIA/stoke **Cardiology specialist list**	***SMC advice*** ***SPC link*** ***Angioplasty Algorithm*** *under review* Clopidogrel in combination with aspirin is the first-choice antiplatelet for ACS in the formulary

Tayside Area Formulary (TAF) Updates - Feb 2013

TAF Section	Drug(s)/topic	Changes
1.5	Treatment of inflammatory bowel disease	Budesonide 3mg gastro-resistant modified release capsules (Entocort®) replaced by budesonide 3mg gastro-resistant capsules (Budenofalk®) for the treatment of mild to moderate crohn's disease.
1.5 GI Specialist List	Treatment of inflammatory bowel disease	Budesonide 3mg gastro-resistant capsules and 9mg gastro-resistant granules (Budenofalk®) added to the formulary and gastrointestinal specialist list.
2.9 Cardiology Specialist List	Antiplatelet drugs	Ticagrelor▼* added to formulary and cardiology specialist list.
6.1	Drugs used in diabetes	Dapagliflozin▼* 5mg and 10mg tablets added to the formulary.

Tayside Area Formulary (TAF) Updates - continued...

TAF Section	Drug(s)/topic	Changes
9.5 Renal Specialist List	Minerals	Lanthanum carbonate 750mg and 1000mg oral powder added to the formulary and renal specialist list. GPs may prescribe under the direction of the renal clinic or dialysis unit.
9.6	Vitamins	Colecalciferol (Desunin®) 800international units (20micrograms) added to the formulary
13.5.2	Psoriasis	Alphosyl HC® cream (coal tar 5% / hydrocortisone 0.5%) has been discontinued. If a topical steroid is required to be used in conjunction with the coal tar preparations, they should be used in an alternating regime.
13.6	Preparations for Acne and Rosacea	All strengths of Panoxyl Aquagel® (benzoyl peroxide) have been discontinued. Alternative preparations are available in the formulary (4%, 5% and 10%). Oxy On The Spot® (2.5%) is available to buy over the counter.

SMC Briefing Note:
Click here for January Briefing Note

Forthcoming SMC Advice

This bulletin is produced by the Medicines Advisory Group (MAG), which is a sub-group of the NHS Tayside Drug and Therapeutics Committee.

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