



Tayside ADTC Supplement No 159 – February 2017

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

Special Points of Interest for Primary Care

SMC Advice

Published December:

- Cabazitaxel (Jevtana®)
- Cefuroxime (Aprokam®)
- Fentanyl (Ionsys®)
- Ferric maltol (Feraccru®)
- Hydrocortisone (Plenadren®)
- Idelalisib (Zydelig®)
- Ivacaftor (Kalydeco®)
- Pembrolizumab (Keytruda®)
- Pertuzumab (Perjeta®)

Published January:

- Buprenorphine (Butec®)
- Carfilzomib (Kyprolis®)
- Dalbavancin (Xydalba®)
- Daratumumab (Darzalex®)
- Deferasirox (Exjade®)
- Elbasvir/grazoprevir (Zepatier®)
- Eltrombopag (Revolade®)
- Oestrogens, conjugated, bazedoxifene acetate (Duavive®)
- Pembrolizumab (Keytruda®)



Drug Safety Updates

Please follow link - Drug Safety Updates 2017: [January](#) | [February](#)



Prescribing Changes

Oral Thrush - Updated Guidance

NHS Tayside Antimicrobial Management Group have updated the [guidance on treatment of oral thrush in adults](#).

The update was undertaken because the BNF recommended dose of nystatin changed from 1ml four times a day to 4-6mls four times a day. Some manufacturers have already updated the SPC for their product and we expect others to do so in time. Unfortunately there are no plans to increase the pack size which is only 30ml.

The decision was made to change the first line treatment to oral fluconazole or miconazole oral gel with nystatin indicated if there are potential interactions with the first line choices.

The recommended dose for ALL adult patients is now nystatin 5mls four times a day, with the dose split evenly between each side of the mouth.

Please refer to guidance at the link above for full details.

There is likely to be a period of time where patients may receive nystatin at the increased dose but the patient information leaflet states the 1ml dose. Please counsel the patient accordingly and provide a larger syringe or spoon if required.

Discontinuation of Retigabine Tablets (Trobalt®)

[Important communication](#) was sent to relevant healthcare professionals to inform them of the withdrawal of retigabine (Trobalt®) from the market in June 2017. This product is being discontinued because of limited and declining use. The [letter](#) outlines advice for healthcare providers to begin seeking alternative treatment for affected patients, and to withdraw treatment with a gradual dose reduction over at least 3 weeks. No new patients should start retigabine treatment.

There is very low use of retigabine in Tayside and Neurology are reviewing any patient who is on retigabine. Retigabine will be removed from the Tayside Area Formulary and Epilepsy Specialist List.

Creon® 40,000 Unit Capsules back in Stock

The long-term manufacturing problem of Creon® 40,000 unit gastro-resistant capsules (pancreatic enzymes) has now been resolved. During the supply problem patients were advised to take 2 x 25,000 unit capsules instead of 1 x 40,000 unit capsule and 3 x 25,000 unit capsules if on 2 x 40,000 units. To reduce capsule burden patients may now be converted back to the 40,000 unit strength if clinically appropriate.

The recommended starting dose of Creon® 40,000 is 2 capsules with meals and 1 capsule with snacks. However, the dose depends on the fat content of the food consumed each time. Thus, patients should follow the [information leaflet](#) that they are given to guide them with this. Creon® should be taken with all meals and snacks containing fat/protein, including milky drinks.

Betahistine

There is limited evidence for the effectiveness of betahistine on the incidence of vertigo attacks in patients with Meniere's disease. Betahistine is only indicated for the prevention of episodes of Meniere's disease and is not considered of any benefit in patients in the midst of an episode of vertigo of any cause, in which case vestibular sedatives such as prochlorperazine, cinnarizine or cyclizine are indicated.

It has been agreed that prescribing of betahistine should be under the direction of ENT specialists as it is only indicated for the prevention of episodes of Meniere's disease. The place in therapy of betahistine will be reviewed as further evidence on its effectiveness becomes available.

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Formulary Review Recommendations

Treatments for Neuropathic Pain

NHS Tayside [Guidance for the management of neuropathic pain](#) and [post herpetic neuralgia](#) have been updated to include capsaicin cream (0.025% / 0.075%) and menthol 1% in aqueous cream as 1st line topical agents. Capsaicin or menthol cream should be considered 1st line for the treatment of localised neuropathic pain or post-herpetic neuralgia in patients where systemic treatment with amitriptyline or gabapentin is contra-indicated (e.g. frail elderly patients) or in patients who have failed systemic treatment. Effectiveness of treatment should be assessed at 2 weeks for menthol cream & lidocaine plasters and 6 to 8 weeks for capsaicin cream. Treatment effectiveness should be reviewed every 6 months.

[Click Here](#) for Tayside neuropathic pain algorithm.

Key Messages

- Amitriptyline or gabapentin are 1st line oral agents
- Half of patients will not respond to first line systemic treatment
- Menthol or capsaicin cream are 1st line topical agents
- Lidocaine plasters are restricted to use in patients where 1st line agents, including topical menthol or capsaicin have been tried and found to be ineffective.
- It is essential to review effectiveness of treatment regularly
- The drug/topical agent should be stopped if not effective

Mental Health Formulary Review

The Mental Health Specialist list and corresponding sections of the formulary, namely antipsychotic and antidepressant medication (see pages 5 & 6 of TAF updates for details), have been reviewed and rationalised on the basis of cost effectiveness and current usage.

Key Messages

- All preparations (with the exception of lithium & clozapine) should be prescribed generically
 - Use immediate release preparations first line as modified release preparations are more expensive. See [Tayside Prescriber 145](#) for guidance on quetiapine
 - Use tablets/capsules first line and only use orodispersible/liquids where clinically indicated due to high cost. Examples include amisulpiride, risperidone and aripiprazole
 - Consider using a typical depot preparation 1st line. Atypical depots are more expensive.
- Examples of monthly/4 weekly costs of atypical Vs typical:*
- | |
|---|
| Paliperidone palmitate: 50 to 150mg monthly (~£180 to £400) |
| Vs |
| Haloperidol decanoate: 50 to 300mg 4 weekly (~£4 to £15) |
| or |
| Zuclopenthixol decanoate: 100 to 600mg weekly (~£21 to £28) |

Medicine	Condition Being Treated	NHS Board Decision	Comments and Useful Links
<p>Cabazitaxel 60mg concentrate and solvent for solution for infusion (Jevtana®) SMC No. 735/11 Second resubmission under end of life process Accepted restricted</p>	<p>In combination with prednisone or prednisolone is indicated for the treatment of adult patients with hormone refractory metastatic prostate cancer previously treated with a docetaxel-containing regimen.</p> <p>SMC Restriction: for use in patients who have received at least 225mg/m² (three cycles) of docetaxel and have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.</p>	<p>Not routinely available as local implementation plans are being developed or the ADTC is waiting for further advice from local clinical experts – decision expected by April 2017</p>	<p>SMC Link SPC Link</p>
<p>Cefuroxime 50mg powder for solution for injection (Aprokam®) SMC No. 932/13 Abbreviated submission Accepted</p>	<p>Antibiotic prophylaxis of postoperative endophthalmitis after cataract surgery.</p>	<p>Not routinely available as local implementation plans are being developed or the ADTC is waiting for further advice from local clinical experts – decision expected by April 2017</p>	<p>SMC Link SPC Link</p>
<p>Fentanyl 40 micrograms per dose transdermal system (Ionsys®) SMC No. 1207/16 Absence of a submission from the holder of the marketing authorisation Not recommended</p>	<p>Management of acute moderate to severe post-operative pain in adult patients</p>	<p>Not available as not recommended for use in NHS Scotland</p>	<p>SMC Link</p>
<p>Ferric maltol 30mg hard capsules (Feracru®) SMC No. (1202/16) Full submission Not recommended</p>	<p>In adults for the treatment of iron deficiency anaemia (IDA) in patients with inflammatory bowel disease (IBD).</p>	<p>Not available as not recommended for use in NHS Scotland</p>	<p>SMC Link</p>
<p>Hydrocortisone 5mg and 20mg modified-release tablets (Plenadren®) SMC No. 848/12 Full submission under orphan process Not recommended</p>	<p>Treatment of adrenal insufficiency in adults</p>	<p>Not available as not recommended for use in NHS Scotland</p>	<p>SMC Link</p>
<p>Idelalisib 100-mg, 150-mg film-coated tablets (Zydelig®) SMC No: 1212/16 Absence of a submission from the holder of the marketing authorisation Not recommended</p>	<p>In combination with ofatumumab for the treatment of adult patients with chronic lymphocytic leukaemia who have received at least one prior therapy, or first line treatment in the presence of 17p deletion or TP53 mutation in patients who are not eligible for any other therapies.</p>	<p>Not available as not recommended for use in NHS Scotland</p>	<p>SMC Link</p>
<p>Ivacaftor 150mg film coated tablets (Kalydeco®) SMC No. 1193/16 Submission considered under ultra-orphan process Not recommended</p>	<p>For the treatment of patients with cystic fibrosis (CF) aged 18 years and older who have an R117H mutation in the CF transmembrane conductance regulator (CFTR) gene</p>	<p>Not available as not recommended for use in NHS Scotland</p>	<p>SMC Link</p>
<p>Pembrolizumab 50mg powder for concentrate for solution for infusion (Keytruda®) SMC No. 1087/15 Resubmission assessed under the end of life orphan process Not recommended</p>	<p>As monotherapy for the treatment of advanced (unresectable or metastatic) melanoma in adults. This submission relates to use in adults previously treated with ipilimumab.</p>	<p>Not available as not recommended for use in NHS Scotland</p>	<p>SMC Link</p>

Medicine	Condition Being Treated	NHS Board Decision	Comments and Useful Links
Pertuzumab 420mg concentrate for solution for infusion (Perjeta®) SMC No. 1121/16 Resubmission assessed under the orphan process Not recommended	For use in combination with trastuzumab and chemotherapy for the neoadjuvant treatment of adult patients with human epidermal growth factor receptor 2 (HER2)-positive, locally advanced, inflammatory, or early stage breast cancer at high risk of recurrence.	Not available as not recommended for use in NHS Scotland	SMC Link

Local processes exist to allow prescribing of non-SMC approved medicines for individual patients and are available in the [NHS Tayside Policy on the Prescribing of Medicines that are Non-formulary \(including Individual Patient Treatment Requests\)](#).

Medicine	Condition Being Treated	NHS Board Decision	Comments and Useful Links
Buprenorphine 5, 10, 15 and 20 microgram/hour transdermal patch (Butec®) SMC No. 1213/17 Following a full submission Accepted restricted	In adults, for the treatment of chronic non-malignant pain of moderate intensity when an opioid is necessary for obtaining adequate analgesia. <u>SMC Restriction:</u> for use in patients over 65 years	Not routinely available as local implementation plans are being developed or the ADTC is waiting for further advice from local clinical experts – decision expected by April 2017	SMC Link SPC Link
Carfilzomib 60mg powder for solution for infusion (Kyprolis®) SMC No. 1171/16 Resubmission assessed under the orphan medicine process Not recommended	In combination with lenalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy	Not available as not recommended for use in NHS Scotland	SMC Link
Dalbavancin 500mg powder for concentrate for solution for infusion (Xydalba®) SMC No. 1105/15 Following a full submission Accepted restricted	Treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults. <u>SMC Restriction:</u> for second-line use or when methicillin-resistant Staphylococcus aureus (MRSA) infection is suspected, or on the advice of local microbiologists or specialists in infectious disease, and the patient is initially hospitalised due to ABSSSI, requires intravenous antibiotics, but is eligible for early discharge as soon as their medical condition does not require further inpatient treatment	Not routinely available as local implementation plans are being developed or the ADTC is waiting for further advice from local clinical experts – decision expected by April 2017	SMC Link SPC Link
Daratumumab 20mg/mL concentrate for solution for infusion (Darzalex®) SMC No. 1205/17 End of life and orphan process Not recommended	As monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor and an immunomodulatory agent and who have demonstrated disease progression on the last therapy.	Not available as not recommended for use in NHS Scotland	SMC Link
Deferasirox 125mg, 250mg, 500mg dispersible tablets (Exjade®) SMC No. (347/07) Resubmission under ultra-orphan process Accepted restricted	Treatment of chronic iron overload due to blood transfusions when deferoxamine therapy is contraindicated or inadequate, in adult and paediatric patients aged 2 years and older with rare acquired or inherited anaemias. The current advice relates only to use in the myelodysplastic syndrome (MDS) population. <u>SMC Restriction:</u> use in patients with MDS with an International Prognostic Scoring System (IPSS) score of low or intermediate -I risk.	Not routinely available as local implementation plans are being developed or the ADTC is waiting for further advice from local clinical experts – decision expected by April 2017	SMC Link SPC Link
Elbasvir 50 mg, grazoprevir 100mg film-coated tablet (Zepatier®) SMC No. 1203/17 Following a full submission Accepted	Treatment of chronic hepatitis C (CHC) in adults. (The efficacy of elbasvir-grazoprevir has not been demonstrated in genotypes 2, 3, 5 and 6. Elbasvir-grazoprevir is not recommended in patients infected with these genotypes).	Not routinely available as local implementation plans are being developed or the ADTC is waiting for further advice from local clinical experts – decision expected by April 2017	SMC Link SPC Link

Medicine	Condition Being Treated	NHS Board Decision	Comments and Useful Links
Eltrombopag film-coated tablets 25mg and 50mg (Revolade®) SMC No. (1206/17) Abbreviated submission Accepted restricted	Chronic immune (idiopathic) thrombocytopenic purpura (ITP) patients aged 1 year to 17 years who are refractory to other treatments (e.g. corticosteroids, immunoglobulins). <u>SMC Restriction:</u> use in patients with severe symptomatic ITP or a high risk of bleeding.	Not routinely available as local implementation plans are being developed or the ADTC is waiting for further advice from local clinical experts – decision expected by April 2017	SMC Link SPC Link
Oestrogens, conjugated, bazedoxifene acetate (Duavive®) 0.45mg / 20mg modified-release tablets SMC No: 1220/17 Absence of a submission from the company Not recommended	Treatment of oestrogen deficiency symptoms in postmenopausal women with a uterus (with at least 12 months since the last menses) for whom treatment with progestin-containing therapy is not appropriate	Not available as not recommended for use in NHS Scotland	SMC Link
Pembrolizumab 50mg powder for concentrate for solution for infusion (Keytruda®) SMC No. 1204/17 Under the end of life and orphan medicine process Accepted restricted	The treatment of locally advanced or metastatic non-small cell lung carcinoma (NSCLC) in adults whose tumours express programmed death ligand 1 (PD-L1) and who have received at least one prior chemotherapy regimen. <u>SMC Restriction:</u> treatment with pembrolizumab is subject to a two-year clinical stopping rule.	Not routinely available as local implementation plans are being developed or the ADTC is waiting for further advice from local clinical experts – decision expected by April 2017	SMC Link SPC Link

Local processes exist to allow prescribing of non-SMC approved medicines for individual patients and 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 - No updates this month



Tayside Area Formulary (TAF) Updates - Jan/Feb 2017

Medicines within the Tayside Area Formulary are intended to guide choice on a rational selection of medicines for **adults** which have been included on the basis of clinical efficacy, safety, patient acceptability and cost-effectiveness.

TAF Section	Drug(s)/Topic	Changes
01.05.03	Drugs affecting the immune response	Methotrexate subcutaneous injection – now Amber traffic light in formulary and Gastroenterology specialist formulary list as per updated Shared Care Agreement . For further information see Tayside ADTC Supplement No 158 - December 2016 .
Chapter 2	Cardiovascular system	Links to SIGN 148 Acute coronary syndrome, April 2016 updated throughout Chapter 2.
02.09	Antiplatelet drugs	Ticagrelor now listed as a second choice antiplatelet in formulary and Cardiology specialist formulary list (Amber traffic light – GPs may prescribe under direction of Cardiology). Ticagrelor is indicated in combination with aspirin only on the recommendation of Cardiology for confirmed acute coronary syndrome in accordance with SIGN 148 Acute coronary syndrome, April 2016 . Clopidogrel is first choice in combination with aspirin for acute coronary syndrome now clarified as first choice for suspected acute coronary syndrome in combination with aspirin. Prasugrel is now non-formulary. Angioplasty antiplatelet algorithm removed from formulary as superseded by SIGN 148.
02.12	Other lipid modifying agents	Alirocumab subcutaneous injection - link added to Alirocumab (PCSK9) - Consultant Only (CV risk clinic) Prescribing flow chart .
Chapter 3	Respiratory System	Links throughout chapter to BTS/SIGN guideline on the management of asthma updated to latest version (September 2016).
04.02	Drugs used in psychoses and related disorders	Formulary and Mental Health specialist formulary list antipsychotics reviewed and rationalised. Levomepromazine (for use in schizophrenia), sulpiride and lurasidone now non-formulary. Antipsychotics used only by specialist Mental Health services removed from main formulary and listed only on Mental Health specialist formulary list : zuclopenthixol acetate injection (Clopixol Acuphase®), and aripiprazole injection (Abilify®). Olanzapine and quetiapine now listed as first choice atypical (second-generation) antipsychotics in addition to risperidone. Fluphenazine decanoate depot injection now non-formulary. Several oral solution/liquid or oro-dispersible tablet formulations removed from formulary due to cost and notes added to highlight these.

TAF Section	Drug(s)/Topic	Changes
04.03	Antidepressant drugs	Tayside guidance for using antidepressants in primary care updated. Formulary and Mental Health specialist formulary list antidepressants reviewed and rationalised. Amitriptyline (for use as an antidepressant) and nortriptyline now non-formulary. Isocarboxazid and tranylcypromine now non-formulary. Paroxetine now non-formulary. Sertraline listed as second choice SSRI, fluoxetine remains the first choice SSRI. Tryptophan (unlicensed) now non-formulary. Several oral solution/liquid formulations removed from formulary due to cost and notes added to highlight these.
04.06	Other drugs for Ménière's disease	Green traffic light removed for betahistine (changed to Amber traffic light) - may be prescribed by GPs under specialist direction as it is only indicated for the prevention of episodes of Ménière's disease.
04.07.03	Neuropathic pain	New sub-section added on topical treatments for neuropathic pain. This is following a review of the management of neuropathic pain . Menthol 1% in aqueous cream has been added to the formulary as a first choice option for symptomatic relief of post-herpetic neuralgia or neuropathic pain in patients for whom a topical treatment is preferred (off-label). Capsaicin cream 0.025% and 0.075% has also been listed as a first choice option for the same indication (also off-label). Axsain® 0.075% cream is licensed for post-herpetic neuralgia. Lidocaine 5% medicated plasters are now restricted to use for patients who don't respond to or are intolerant of first and second line systemic therapies or first choice topical treatments (i.e. menthol 1% in aqueous cream or capsaicin cream). It is now recommended that lidocaine plasters are reviewed at 2 weeks after initiation and 6 monthly thereafter.
04.08.01	Retigabine	Changed to non-formulary as manufacturer is discontinuing this.
05.03.03.02	Chronic hepatitis C	Link to National Clinical Guideline on treatment of HCV in adults updated to latest version (January 2017).
06.04.01.02	Progestogens and progesterone receptor modulators	Additional indication added to formulary and Obstetrics & Gynaecology specialist formulary list for ulipristal acetate (Esmya®) – for the intermittent treatment of moderate or severe symptoms of uterine fibroids in adult women of reproductive age.
10.01.03	Drugs affecting the immune response	Methotrexate subcutaneous injection – now Amber traffic light in formulary and Rheumatology specialist formulary list as per updated Shared Care Agreement . For further information see Tayside ADTC Supplement No 158 - December 2016 .
10.02.02	Skeletal muscle relaxants	Baclofen now green traffic light (non-specialist initiation) for relief of spasticity of voluntary muscle associated with neurological damage including stroke. Tizanidine remains as Amber traffic light (GPs can prescribe under specialist direction). Note added to baclofen and tizanidine entries to remind prescribers there are numerous drug interactions possible with baclofen or tizanidine.
12.01	Drugs acting on the ear	Acetic acid 2% (Earcalm®) added to formulary for mild otitis externa as per ENT Infection Management Guidance . Note on when to use ear drops or ear spray added to anti-inflammatory preparations for otitis externa. Ciprofloxacin 0.3% (Ciloxan® ophthalmic solution) off-label use for otitis externa replaced by licensed ciprofloxacin 0.3% / dexamethasone 0.1% ear drops (Cilodex®) (Green traffic light) as per ENT Infection Management Guidance .
12.02	Drugs acting on the nose	Xylometazoline hydrochloride 0.1% nasal spray/drops (Otrivine Adult®) added to formulary as a topical nasal decongestant (maximum duration of treatment 7 days). Chlorhexidine dihydrochloride and neomycin sulfate nasal cream (Naseptin®) note added that this contains arachis oil and is not suitable for those with allergies to peanuts or soya.
12.03	Drugs acting on the oropharynx	Links to NHS Tayside Oral Thrush Guidance updated to new version (December 2016). Fluconazole and miconazole now first choice treatments for oral candidiasis, nystatin oral suspension listed as second choice. Note on updated dose added to Nystatin entry. See page 1 for further information. Tranexamic acid oral solution (unlicensed) for use as mouthwash no longer listed in this section – information moved to section 02.11.
13.02.01	Emollients	Link to cost chart for emollients updated for February 2017.
13.05.03	Systemic treatments	Methotrexate subcutaneous injection – now Amber traffic light in formulary and Dermatology specialist formulary list as per updated Shared Care Agreement . For further information see Tayside ADTC Supplement No 158 - December 2016 .
13.07	Imiquimod	Local protocol for the use of imiquimod 5% cream in actinic keratoses removed as no longer required.

Forthcoming SMC Advice

Local implementation of SMC recommendations is taken forward by the Tayside Prescribing Support Unit (PSU). This bulletin is based on evidence available to Tayside PSU at time of publication and is covered by the Disclaimer and Terms & Conditions of Use.

[CLICK HERE](#) for access to the Medicines Governance section of the Pharmacy Staffnet site.

This bulletin is produced by the Medicines Advisory Group (MAG), which is a sub-group of the NHS Tayside Drug and Therapeutics Committee. Please direct any queries to either:

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