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Lincolnshire Clinical Commissioning Groups, Lincolnshire Community Health Services,
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Lincolnshire Prescribing and Clinical Effectiveness Bulletin

Volume 11 Number 8 **April 2017**

What's new this month?

- ***Alzain*** **capsules (pregabalin) are already approved for use through the *Lincolnshire Joint Formulary* within licensed indications; designation GREEN. Recent changes to the marketing authorisation now mean that *Alzain* is licensed for the treatment of peripheral and central neuropathic pain in adults, excluding the treatment of trigeminal neuralgia pain, acute herpetic pain, post-herpetic pain and causalgia pain. PACEF are now in support of product switching from generic pregabalin or higher cost brands to *Alzain* within licensed indications.**
- ***Axalid*** **capsules(pregabalin) are a newly launched product which are currently the cheapest available pregabalin product. It is however currently only licensed as adjunctive therapy in adults with partial seizures with or without secondary generalisation and for Generalised Anxiety Disorder (GAD) in adults. Axalid have been approved for inclusion on the Lincolnshire Joint Formulary as a treatment option when pregabalin is required for the management of epilepsy or GAD within licensed indications.**
- **Wherever possible and within licensed indications, all new initiations of pregabalin should be prescribed as one of the lower cost brands. (see page 3).**
- **The escalating cost of nabilone 250 microgram and 1mg capsules for neuropathic pain means that the treatment is becoming prohibitively expensive. Nabilone 250 microgram and 1mg capsules continue to be designated AMBER with shared care, but prescribers are urged to review existing patients and seek advice from local pain specialists on possible alternatives (see page 6).**
- ***AirFluSal Forspiro*** **(salmeterol 50 microgram/fluticasone 500 microgram) breath actuated dry powder inhaler is a lower cost alternative to *Seretide Accuhaler 500 (*salmeterol 50 microgram/fluticasone 500 microgram*).* It has already been approved for use through the *Lincolnshire Joint Formulary* designation GREEN as a preferred lower cost alternative to *Seretide Accuhaler 500* for the symptomatic treatment of COPD. It is now licensed for the regular treatment of severe asthma and is also approved by PACEF for this indication. PACEF are not supportive of product switching in patients with asthma as the product is only available as a single strength and step-down will necessitate review and switch to an alternative device (see page 7).**
- **Both dipyridamole/aspirin 200mg/25mg modified release capsules (*Molita*) and dpyridamole 200mg modified release capsules (*Attia*) are designated GREEN and approved for use through the *Lincolnshire Joint Form*ulary as lower cost**

alternatives to originator brands (*Asasantin Retard* and *Persantin Retard*) for licensed indications (see page 8).

- **Reformulation of Lucozade Energy Original. The makers of Lucozade Energy (Lucozade Ribena Suntory) announced in November 2016 that it would be lowering the sugar content in its drinks by more than 50 per cent. The change which affects all flavours, comes into effect from April 2017. People who are advised to take lucozade energy original when their blood sugar is low need to be aware that the amount of drink required will change (see page 10)**

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SUMMARY OF PACEF DECISIONS: *MARCH 2017 UPDATE*

Device, Dressing or Drug	**Indication(s)**	**Traffic Light and *Joint Formulary* Status**
AirFluSal Forspiro (salmeterol 50 microgram / fluticasone propionate 500 microgram) breath actuated dry powder inhaler (Sandoz)	Regular treatment of severe asthma in adults where long-acting beta2 agonist and inhaled corticosteroid is appropriate. Symptomatic treatment of COPD in patients with a pre-bronchodilator FEV1 <60% predicted and a history of exacerbations and with significant symptoms despite regular bronchodilator therapy.	GREEN Included in the *Lincolnshire Joint Formulary* for both indications. *AirFluSal Forspiro* is lower cost than equivalent strength *Seretide Accuhaler* but is only available as a single strength.
Apremilast 10mg, 20mg and 30mg tablets (*Otezla*) (Celgene)	For active psoriatic arthritis (in combination with disease-modifying anti-rheumatic drugs or alone) in patients who have had an inadequate response or who have been intolerant to a prior disease-modifying anti-rheumatic drug therapy	RED. Included in the *Lincolnshire Joint Formulary* for this indication.
Dipyridamole 200mg modified release capsules (*Attia*) (Dr Reddy's)	Secondary prevention of ischaemic stroke and transient ischaemic attacks either alone or in conjunction with aspirin. As an adjunct to oral anti-coagulants in the prophylaxis of thrombosis of prosthetic heart valves.	GREEN Included in the *Lincolnshire Joint Formulary* within licensed indications. Lower cost than *Persantin Retard*.
Dipyridamole/aspirin 200mg/25mg modified release capsules (*Molita*) (Dr Reddy's)	Secondary prevention of ischaemic stroke and transient ischaemic attacks.	GREEN Included in the *Lincolnshire Joint Formulary* within licensed indications. Lower cost than *Asasantin Retard*.
Everolimus 2.5mg, 5mg and 10mg tablets (*Afinitor*) (Novartis Pharmaceuticals UK Ltd)	For the treatment of patients with advanced renal cell carcinoma whose disease has progressed during or after treatment with vascular endothelial growth factor (VEGF) targeted therapy.	RED Included in the *Lincolnshire Joint Formulary* within licensed indications.

Nabilone 250 micrograms and 1mg capsules	For the treatment of neuropathic pain in adults (unlicensed)	AMBER with shared care. Included in the *Lincolnshire Joint Formulary* for neuropathic pain (unlicensed)
Pregabalin capsules 25mg, 50mg, 75mg, 100mg, 150mg, 200mg, 225mg, 300mg (*Alzain*) (Dr Reddy's Laboratories UK Ltd)	For the treatment of peripheral and central neuropathic pain in adults, excluding the treatment of trigeminal neuralgia pain, acute herpetic pain, post-herpetic pain, or causalgia pain. For use as adjunctive therapy in adults with partial seizures with or without secondary generalisation and for the treatment of Generalised Anxiety Disorder (GAD) in adults.	GREEN Included in the *Lincolnshire Joint Formulary* within licensed indications only.
Ticagrelor tablets 60mg (*Brilique*) (AstraZeneca)	Co-administered with aspirin for the prevention of atherothrombotic events in adult patients with a history of MI of at least 1 year and a high risk of developing an athero-thrombotic event.	GREEN Included in the *Lincolnshire Joint Formulary* within licensed indications. 60mg twice daily is the recommended dose for extended treatment. Treatment should be stopped when clinically indicated or at a maximum of 3 years.

This *Bulletin* has been created specifically to convey details of decisions taken at the Prescribing and Clinical Effectiveness Forum (PACEF) to all stakeholders across the Lincolnshire Healthcare Community in both primary and secondary care. Back issues of the *PACE Bulletin* and other PACEF publications are available through the PACEF website (http://lincolnshire-pacef.nhs.uk). Electronic copies of the *PACE Bulletin* are circulated to a wide readership via email. If you are not currently on our distribution list and wish to receive regular copies of PACEF publications please contact Cathy Johnson on cathy.johnson@nhs.net or catherine.johnson@optum.com

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The *Lincolnshire Joint Formulary* is available on line and is fully searchable; it can be accessed at www.lincolnshirejointformulary.nhs.uk

RED-RED: This signifies that a product is **not recommended** for prescribing in **either** primary or secondary care. All new products are classified as RED-RED pending assessment by PACEF.
RED: This signifies that a product has been approved for use within secondary care, tertiary care or a primary care hosted specialist service only and **should not be routinely prescribed in primary care**. RED drugs may be used within ULHT or LPFT subject to approval for use within each Trust. ULHT and LPFT reserve the right to determine whether or not RED drugs will be used within their Trusts. RED classification does not automatically signify that a drug will be available within secondary/tertiary care.
AMBER: This signifies that a drug has been approved for use in primary care **subject to specialist initiation; a shared care guideline (SCG) may also be required**. The main purpose of the SCG will be to clearly define both specialist and GP responsibilities. Not all AMBER drugs that require SCGs are currently covered by formal documents; PACEF are working to rectify this.
GREEN: This signifies a product that is **approved for initiation in either primary or secondary care.**

REVIEW: *NEW LICENSED INDICATIONS FOR ALZAIN FORMULATION OF PREGABALIN*

This is an updated version of pregabalin guidance that originally appeared in *PACE Bulletin* Vol 10 No 10 (July 2016).

***Alzain* capsules (pregabalin) are a lower cost branded pregabalin preparation and are already approved for use through the *Lincolnshire Joint Formulary* within licensed indications; designation GREEN. Recent changes to the marketing authorisation now mean that *Alzain* is licensed for the treatment of peripheral and central neuropathic pain in adults, excluding the treatment of trigeminal neuralgia pain, acute herpetic pain, post-herpetic pain and causalgia pain. PACEF are now in support of product switching from generic pregabalin or higher cost brands to *Alzain* within licensed**

indications. Wherever possible and within licensed indications, all new initiations of pregabalin should be branded as *Alzain.*

Since the last PACEF review of pregabalin capsules (*Alzain*), the product has gained a marketing authorisation for the treatment of peripheral and central neuropathic pain in adults, excluding the *Lyrica* patent protected indications: trigeminal neuralgia pain, acute herpetic pain, post-herpetic pain and causalgia pain. *Alzain* is also licensed as adjunctive therapy in adults with partial seizures with or without secondary generalisation and also for the treatment of Generalised Anxiety Disorder (GAD).

The table below compares the marketing authorisations for the new branded formulations of pregabalin with the originator brand, *Lyrica*. Current guidance from NHS England advocates prescribing *Lyrica* by brand for neuropathic pain and only prescribing the newer preparations within license; *Alzain* now has a license for neuropathic pain.

Authorised indications

	Licensed indications
Pregabalin capsules 25mg, 50mg, 75mg, 100mg, 150mg, 200mg, 225mg, 300mg (*Alzain*, Dr Reddy's Laboratories UK Ltd),	*Neuropathic pain* For the treatment of peripheral and central neuropathic pain in adults, excluding the treatment of trigeminal neuralgia pain, acute herpetic pain, post-herpetic pain, or causalgia pain. *Epilepsy* As adjunctive therapy in adults with partial seizures with or without secondary generalisation. *Generalised Anxiety Disorder* For the treatment of Generalised Anxiety Disorder (GAD) in adults.
Pregabalin capsules 25mg, 50mg, 75mg, 100mg, 150mg, 200mg, 225mg, 300mg (*Axalid,* Kent Pharmaceuticals Ltd.	*Epilepsy* Axalid is indicated as adjunctive therapy in adults with partial seizures with or without secondary generalisation. *Generalised Anxiety Disorder* Axalid is indicated for the treatment of Generalised Anxiety Disorder (GAD) in adults.
Pregabalin capsules 25mg, 50mg, 75mg, 100mg, 150mg, 200mg, 225mg, 300mg (*Lecaent* , Actavis UK Ltd)	*Epilepsy* As adjunctive therapy in adults with partial seizures with or without secondary generalisation. *Generalised Anxiety Disorder* For the treatment of Generalised Anxiety Disorder (GAD) in adults.
Pregabalin capsules 25mg, 50mg, 75mg, 100mg, 150mg, 200mg, 225mg, 300mg (*Lyrica*, Pfizer)	*Neuropathic pain* For the treatment of peripheral and central neuropathic pain in adults, including the treatment of trigeminal neuralgia pain, acute herpetic pain, post-herpetic pain, or causalgia pain. *Epilepsy* *A*s adjunctive therapy in adults with partial seizures with or without secondary generalisation. *Generalised Anxiety Disorder* For the treatment of Generalised Anxiety Disorder (GAD) in adults.
Pregabalin capsules 25mg, 50mg, 75mg, 100mg, 150mg, 200mg, 225mg, 300mg (*Pregabalin Zentiva*, Zentiva)	*Epilepsy* As adjunctive therapy in adults with partial seizures with or without secondary generalisation. *Generalised Anxiety Disorder* For the treatment of Generalised Anxiety Disorder (GAD) in adults.
Pregabalin capsules 25mg, 50mg, 75mg, 100mg, 150mg, 200mg, 225mg, 300mg (Rewisca, Consilient	*Epilepsy* As adjunctive therapy in adults with partial seizures

Health Ltd)	with or without secondary generalisation. *Generalised Anxiety Disorder* For the treatment of Generalised Anxiety Disorder (GAD) in adults.

Approximately, 70% of all pregabalin prescribing is for neuropathic pain. Despite NHSE guidance, the majority of pregabalin prescribing is still generic. This means that virtually all of the pregabalin prescribing in Lincolnshire at present is still being reimbursed at *Lyrica* prices despite the availability of lower cost brands.

Cost Comparison (lowest cost products highlighted in **bold**)

	Dose	**Cost (28 Days)**
Pregabalin 75mg capsules (*Alzain*) (Dr Reddy's Laboratories)	**75mg twice daily**	**£24.95***
Pregabalin 75mg capsules (Axalid) (Kent Pharmaceuticals ltd)	**75mg twice daily**	**£19.95**
Pregabalin 75mg capsules (*Lecaent*) , (Actavis UK Ltd)	75mg twice daily	£64.39
Pregabalin 75mg capsules (*Lyrica*) (Pfizer)	75mg twice daily	£64.40
Pregabalin 75mg capsules (*Pregabalin Zentiva*) (Zentiva)	75mg twice daily	£64.40
Pregabalin 75mg capsules (*Rewisca*) (Consilient Health Ltd)	**75mg twice daily**	**£48.30**
Gabapentin 300mg capsules	300mg three times daily	£2.37
Pregabalin 50mg capsules (*Alzain*)	**50mg three times daily**	**£44.95***
Pregabalin 50mg capsules (*Axalid)*)	**50mg three times daily**	**£29.93**
Pregabalin 50mg capsules (*Lecaent*)	50mg three times daily	£96.59
Pregabalin 50mg capsules (*Lyrica*)	50mg three times daily	£96.60
Pregabalin 50mg capsules (*Pregabaliin Zentiva)*)	50mg three times daily	£96.60
Pregabalin 50mg capsules (*Rewisca*)	**50mg three times daily**	**£72.45**
Gabapentin 300mg capsules	300mg three times daily	£2.37
Pregabalin 100mg capsules (*Alzain*)	**100mg three times daily**	**£44.95***
Pregabalin 100mg capsules (*Axalid*)	**100mg three times daily**	**£29.93**
Pregabalin 100mg capsules (*Lecaent*)	100mg three times daily	£96.59
Pregabalin 100mg capsules (*Lyrica*)	100mg three times daily	£96.60
Pregabalin 100mg capsules (*Pregabalin Zentiva*)	100mg three times daily	£96.60
Pregabalin 100mg capsules (*Rewisca*)	**100mg three times daily**	**£72.45**
Gabapentin 600mg tablets	600mg three times daily	£7.33
Pregabalin 150mg capsules (*Alzain*)	**150mg twice daily**	**£24.95***
Pregabalin 150mg capsules *(Axalid)*	**150mg twice daily**	**£19.95**
Pregabalin 150mg capsules (*Lecaent*)	150mg twice daily	£64.39
Pregabalin 150mg capsules (*Lyrica*)	150mg twice daily	£64.40
Pregabalin 150mg capsules (*Pregabalin Zentiva*)	150mg twice daily	£64.40
Pregabalin 150mg capsules (*Rewisca*)	**150mg twice daily**	**£48.30**
Gabapentin 600mg tablets	600mg three times daily	£7.33
Pregabalin 200mg capsules (*Alzain*)	**200mg three times daily**	**£44.95***
Pregabalin 200mg capsules (*Axalid)*	**200mg three times daily**	**£29.93**
Pregabalin 200mg capsules (*Lecaent*)	200mg three times daily	£96.59
Pregabalin 200mg capsules (*Lyrica*)	200mg three times daily	£96.60
Pregabalin 200mg capsules (*Pregabalin Zentiva*)	200mg three times daily	£96.60
Pregabalin 200mg capsules (*Rewisca*)	**200mg three times daily**	**£72.45**
Gabapentin 300mg capsules	THREE 300mg (900mg) capsules three times daily	£7.11

Pregabalin 300mg capsules (*Alzain)*	**300mg twice daily**	**£24.95***
Pregabalin 300mg capsules (*Axalid*)	**300mg twice daily**	**£19.95**
Pregabalin 300mg capsules (*Lecaent)*	300mg twice daily	£64.39
Pregabalin 300mg capsules (*Lyrica*)	300mg twice daily	£64.40
Pregabalin 300mg capsules (*Pregabalin Zentiva*)	300mg twice daily	£64.40
Pregabalin 300mg capsules (*Rewisca*)	**300mg twice daily**	**£48.30**
Gabapentin 300mg capsules	THREE 300mg (900mg) capsules three times daily	£7.11

*Prices for Alzain in effect from 1st May 2017.

The potential saving for each of the Lincolnshire CCGs if 80% of generic pregabalin or *Lyrica* is switched to *Alzain* prescribed by brand:

	Potential saving pa
Lincolnshire East CCG	£805,267
Lincolnshire West CCG	£734,044
South Lincolnshire CCG	£389,665
South West Lincolnshire CCG	£391,544

Dr Reddy's, the manufacturer of *Alzain*, have circulated a letter to all CCG Heads of Medicines Optimisation to guarantee that *Alzain* will remain at least 40% below Category C price and at least 5% below Category M price for at least the next 2 years. The *Lyrica* patent is due to expire in July 2017 with low cost generic products likely to become available soon afterwards. Some 'skinny labelled' generics are already available, but lack the range of licensed indications of *Lyrica* and *Alzain.*

PACEF Recommendations:

(1)When prescribing pregabalin for the treatment of anything other than trigeminal neuralgia pain, acute herpetic pain, post-herpetic pain, or causalgia pain, pregabalin should be prescribed as *Alzain*, the lowest cost brand. Open generic scripts for pregabalin are still reimbursed at the higher *Lyrica* price; only branded prescribing of preferred lower cost products will reduce prescribing costs.

(2)Prescribers should ensure that, as far as reasonably possible, branded *Lyrica* continues to be prescribed by name for all patients requiring pregabalin for the patent protected indications of trigeminal neuralgia pain, acute herpetic pain, post-herpetic pain, or causalgia pain. The *Lyrica* patent is still in contention in the High Court and this guidance is subject to change pending the outcome of this case.

(3)Community pharmacies and dispensing practices should ensure that, as far as reasonably possible, branded *Lyrica* is dispensed against all prescriptions for pregabalin for patients suffering from the patent protected indications of trigeminal neuralgia pain, acute herpetic pain, post-herpetic pain, or causalgia pain. Prescribers are asked to be supportive of community pharmacy requests to change generic prescriptions to branded *Lyrica* for a patent protected indication.

(4)Practices should review all patients currently prescribed pregabalin for neuropathic pain (excepting trigeminal neuralgia pain, acute herpetic pain, post-herpetic pain, or causalgia pain), generalized anxiety disorder or epilepsy to ensure that *Alzain* is prescribed by brand wherever possible.

(6) Following review *Alzain, Axalid* and *Rewisca* are the three lower cost brands approved for use through the *Lincolnshire Joint Formulary*; designation GREEN. In order to achieve the cost saving these products must be prescribed by brand. They should only be prescribed for non-patent protected indications (see table of authorised indications above). *Axalid* is significantly lower cost than *Rewisca* and should be considered when pregabalin is required to treat epilepsy or generalized anxiety disorder.

(7) There is considerable activity in the pregabalin market at present with the potential for more products to gain additional licenses, and the emergence of lower

cost brands or price reductions for existing brands. PACEF will continue to review these products and update guidance as soon as practical in response to these changes.
(8) *Lecaent* and *Pregabalin Zentiva* are new higher cost branded formulations of pregabalin priced very similarly to the originator brand *Lyrica*. As a result, both products are not approved for use through the *Lincolnshire Joint Formulary* and are designated RED-RED.
(9) Significant reductions in pregabalin prescribing costs can also be achieved through strength and dose optimisation. For example 150mg twice daily is significantly lower cost than 100mg three times daily.
(10) Generic gabapentin provides an even lower cost alternative. Gabapentin is approved for use on the *Lincolnshire Joint Formulary* (designation: GREEN) and is licensed for peripheral neuropathic pain. While upward dose titration is more complex and dosage potentially more frequent, prescribers should consider gabapentin preferentially in new patients requiring treatment with a GABA analogue for neuropathic pain.
(9) PACEF have approved switching from higher cost generic and branded pregabalin to *Alzain* as part of the Prescribing QIPP Programme 2017/18. Practices are encouraged to support this switch. Potential savings by CCG are tabulated above.

REVIEW: *INCREASING COST OF NABILONE 250 MICROGRAM AND 1MG CAPSULES*

The escalating cost of nabilone 250 microgram and 1mg capsules for neuropathic pain means that the treatment is becoming prohibitively expensive. Nabilone continues to be designated AMBER with shared care, but prescribers are urged to review existing patients and seek advice from local pain specialists on possible alternatives.

Nabilone 250 micrograms and 1mg capsules are designated AMBER with shared care and approved for use through the *Lincolnshire Joint Formulary* for the management of chronic neuropathic pain unresponsive to first and second line treatments (unlicensed). A shared care protocol has been developed and was last reviewed and updated in February 2016.

PACEF are aware that the cost of nabilone therapy has increased significantly over the past 12 months with use across Lincolnshire primary care declining. To illustrate the scale of the increase: the 28 day cost of 1mg twice daily has more than doubled in the last 12 months and from some suppliers has more than quadrupled. Nabilone was already an expensive therapy 12 months ago with 1mg twice daily costing £352.35 for 28 days' supply.

PACEF Recommendation:
Nabilone 250 micrograms and 1mg capsules continue to be designated AMBER with shared care in accordance with local shared care guidelines. Practices currently prescribing nabilone should seek advice from the chronic pain service on possible alternatives. PACEF have contacted local pain specialists for advice on the role of nabilone in the management of neuropathic pain and will publish further guidance on this later in the year.

NEW INDICATION ASSESSMENT: *AIRFLUSAL FORSPIRO 50/500 FOR ASTHMA*

***AirFluSal Forspiro* (salmeterol 50 microgram/fluticasone 500 microgram) breath actuated dry powder inhaler is now licensed for the regular treatment of adults with severe asthma.**

AirFluSal Forspiro (salmeterol 50 microgram/fluticasone 500 microgram) breath actuated dry powder inhaler is a lower cost alternative to *Seretide Accuhaler 500 (*salmeterol 50 microgram/fluticasone 500 microgram). It has already been approved for use through the *Lincolnshire Joint Formulary* designation GREEN as a preferred lower cost alternative to *Seretide Accuhaler 500* for the symptomatic treatment of COPD within licensed indications. *AirFluSal Forspiro* 50/500 now has a license extension to cover its use in the regular treatment of adults with severe asthma. PACEF reviewed bioequivalence data against the alternative dry powder inhaled formulation *Seretide Accuhaler 500*, and accepted the products as equivalent.

A cost comparison reveals that *AirFluSal Forspiro* is significantly lower in cost than all equivalent formulations:

Drug	**Marketing Authorisation**	**Daily dose**	**Cost (£) (doses)**
AirFluSal Forspiro (salmeterol 50 microgram / fluticasone propionate 500 microgram) breath actuated dry powder inhaler (Sandoz)	Regular treatment of severe asthma in adults where long-acting beta2 agonist and inhaled corticosteroid is appropriate. Symptomatic treatment of COPD in patients with a pre-bronchodilator FEV1 <60% predicted and a history of exacerbations and with significant symptoms despite regular bronchodilator therapy.	One inhalation twice daily	£32.74 (60)
Seretide Accuhaler 500 (salmeterol 50 microgram / fluticasone propionate 500 microgram) breath actuated dry powder inhaler (GlaxoSmithKline)	Regular treatment of asthma in adults where long-acting beta2 agonist and inhaled corticosteroid is appropriate. Symptomatic treatment of COPD in patients with a pre-bronchodilator FEV1 <60% predicted and a history of exacerbations and with significant symptoms despite regular bronchodilator therapy.	One inhalation twice daily	£40.92 (60)
	Meter dose devices (for comparison)		
Seretide 250 Evohaler (salmeterol 25 microgram/ fluticasone propionate 250 microgram per actuation) (GlaxoSmithKline)	Regular treatment of asthma in adults and children over 4 years where long-acting beta2 agonist and inhaled corticosteroid is appropriate.	Two puffs twice daily	£59.48 (120 puffs)
Sirdupla 250 (salmeterol 25 microgram/	Regular treatment of asthma in adults where long-acting	Two puffs twice daily	£44.61 (120 puffs)

fluticasone propionate 250 microgram per actuation) (Mylan)	beta2 agonist and inhaled corticosteroid is appropriate.		

PACEF Recommendation:
***AirFluSal Forspiro 50/500* dry powder inhaler is significantly lower in cost than equivalent dose *Seretide Accuhaler 500*. Both products now hold marketing authorisations for asthma and COPD and both are designated GREEN and approved for inclusion in the *Lincolnshire Joint Formulary* for both indications. PACEF recognise that *AirFluSal Forspiro* is only available in one strength (salmeterol 50 microgram / fluticasone propionate 500 microgram) and consider this to be a disadvantage as *Seretide Accuhaler* is available in three strengths with the potential for the dose to be stepped down where necessary. If the dose of *AirFluSal Forspiro* needs to be stepped down, the patient will need to be transferred to an alternative device such as *Seretide Accuhaler*. Prescribers should also be aware that in line with current PACEF guidance on the treatment of asthma, fluticasone should be considered to be a third line corticosteroid after beclometasone and budesonide. Due to these reservations, PACEF expect *AirFluSal Forspiro* to be a relatively marginal product for the treatment of asthma and are not supportive of product switching from higher cost products to *AirFluSal Forspiro* in asthmatic patients.**

RAPID COST COMPARISON: *DIPYRIDAMOLE 200MG MODIFIED RELEASE CAPSULES (ATTIA) AND DIPYRIDAMOLE/ASPIRIN 200MG/25MG MODIFIED RELEASE CAPSULES (MOLITA)*

New lower cost brands of dipyridamole 200mg modified release capsules (*Attia*) and dipyridamole 200mg/aspirin 25mg modified release (*Molita*) are now available.

Dipyridamole 200mg modified release capsules (*Attia*) are licensed for both the secondary prevention of ischaemic stroke and transient ischaemic attacks either alone or in conjunction with aspirin and as an adjunct to oral anti-coagulation for prophylaxis of thromboembolism associated with prosthetic heart valves. The recommended dose is one capsule twice daily, usually one in the morning and one in the evening preferably with meals. They are less costly than the originator brand dipyridamole 200mg MR capsules (*Persantin Retard*).

Dipyridamole 200mg/aspirin 25mg modified release (*Molita*) is licensed solely for the secondary prevention of ischaemic stroke and transient ischaemic attack. The recommended dose is one capsule twice daily. It is less costly than the originator brand, *Asasantin.*

Product	Marketing Authorisation	Dose	Cost (£) 28 days
Dipyridamole/aspirin 200mg/25mg modified release capsules (*Asasantin Retard*) (Boehringer Ingelheim Ltd)	Secondary prevention of ischaemic stroke and transient ischaemic attacks.	1 twice daily	£9.19
Dipyridamole/aspirin 200mg/25mg modified release capsules (*Molita*) (Dr Reddy's)	Secondary prevention of ischaemic stroke and transient ischaemic attacks.	1 twice daily	£5.24
Dipyridamole 200mg modified release	Secondary prevention of ischaemic stroke and	1 twice daily	£9.39

capsules (*Persantin Retard*) (Consilient Health Ltd, Boehringer Ingelheim Ltd)	transient ischaemic attacks either alone or in conjunction with aspirin. As an adjunct to oral anti-coagulants in the prophylaxis of thrombosis of prosthetic heart valves.		
Dipyridamole 200mg modified release capsules (*Attia*) (Dr Reddy's)	Secondary prevention of ischaemic stroke and transient ischaemic attacks either alone or in conjunction with aspirin. As an adjunct to oral anti-coagulants in the prophylaxis of thrombosis of prosthetic heart valves.	1 twice daily	£8.92

The estimated 100% cost savings if all dipyridamole 200mg modified release products are brand prescribed as *Attia* and all dipyridamole/aspirin combination products brand prescribed as *Molita* are as follows:

Product switch to:	**LECCG**	**LWCCG**	**SLCCG**	**SWLCCG**
Attia	£2,763	£1,942	£1,558	£1,239
Molita	£1,631	£1,406	£1,343	£742

PACEF Recommendation:
Both dipyridamole/aspirin 200mg/25mg modified release capsules (*Molita*) and dpyridamole 200mg modified release capsules (*Attia*) are designated GREEN and approved for use through the *Lincolnshire Joint Form*ulary for licensed indications. Prescribing all dipyridamole/aspirin 200mg/25mg modified release capsules and dpyridamole 200mg modified release capsules as *Molita* and *Attia* respectively would generate annual savings across the county of £12,624.

REFORMULATION of LUCOZADE – REDUCTION IN SUGAR CONTENT

The makers of Lucozade Energy (Lucozade Ribena Suntory) announced in November 2016 that it would be lowering the sugar content in its drinks by more than 50 per cent. This change which affects all flavours comes into effect from April 2017, although there will be a period of time when both old and new formulations will be on sale due to the transition period.
The reformulated product will be completely unsuitable fororal Glucose Tolerance tests (OGTT) and information from Path Links on suitable alternatives has been sent out to all Lincolnshire Medical Practices.
Diabetes UK have issued the following advice.
If diabetics have been advised to drink Lucozade Energy Original when their blood glucose is low the volume of lucozade required needs to change.
For example:

- to obtain 10g of carbohydrate you now need 110mls
- to obtain 15g of carbohydrate you now need 170ml

There is a need to check the label before use, as the amount of drink required to obtain certain levels of carbohydrate will vary between different flavours.

NICE TECHNOLOGY APPRAISAL 420: *TICAGRELOR FOR PREVENTING ATHEROTHROMBOTIC EVENTS AFTER MYOCARDIAL INFARCTION* (DECEMBER 2016)

NICE Recommendation

Ticagrelor in combination with aspirin, is recommended within its marketing authorisation as an option for preventing atherothrombotic events in adults who had a myocardial infarction and who are at high risk of a further event. Treatment should be stopped when clinically indicated or **at a maximum of 3 years.**

Notes

PACEF last reviewed ticagrelor (*Brilique*) as part of the development of the *Guidance on the prescribing of aspirin, clopidogrel, prasugrel and ticagrelor for the prevention of atherothrombotic events in patients with acute coronary syndromes* (*PACE Bulletin* Vol 7 No 9 (June 2013).

Marketing authorisation

Ticagrelor is an oral antagonist of the P2Y12 adenosine diphosphate receptor that inhibits platelet aggregation and thrombus formation in atherosclerotic disease.

Ticagrelor (Brilique) 60mg twice daily co-administered with aspirin has a marketing authorisation for the prevention of atherothrombotic events in adult patients with a history of MI of at least 1 year and a high risk of developing an atherothrombotic event. Treatment may be started without interruption (continuation therapy) after the initial 1 year treatment with ticagrelor 90mg or other adenosine diphosphate (ADP) receptor inhibitor therapy in patients with acute coronary syndrome (ACS) and with a high risk of an atherothrombotioc event. Treatment can also be started up to 2 years from the MI or within 1 year after stopping previous ADP receptor inhibitor treatment.

60mg twice daily is the recommended dose for extended treatment.

Unless contraindicated, ticagrelor should always be given with a daily low maintenance dose of aspirin 75mg to 150mg.

There are limited data on the efficacy and safety of ticagrelor beyond 3 years of extended treatment.

PEGASUS-TIMI 54

The NICE decision to extend the recommended duration of ticagrelor/aspirin therapy to 3 years in adults who had a myocardial infarction and who are at high risk of a further event derives from the PEGASUS-TIMI 54 study summarised below:

- Enrolled patients had a history of MI occurring between 12 and 36 months before entry. Patients also had at least one additional risk factor for subsequent atherothrombotic events (i.e. age 65 or over, diabetes mellitus needing medication, second prior MI, evidence of multivessel coronary artery disease (CAD) or chronic non-end-stage renal dysfunction).

PACEF Comment:
Patients potentially eligible for three years ticagrelor/aspirin therapy should be post MI and have at least one of the following risk factors: (1) 65 or over; (2) DM needing medication; (3) a second prior MI; (4) evidence of multivessel CAD; or (5) chronic non-end-stage renal dysfunction.
ULHT based cardiology department have confirmed that they will be responsible for identifying all patients eligible for three years ticagrelor/aspirin therapy.

- 84% of patients in each treatment arm received clopidogrel plus aspirin as their previous antiplatelet therapy; clopidogrel was switched to ticagrelor in the active comparator group.
- Trial compared ticagrelor (n=7.045) with placebo (n=7,067) concurrently prescribed with aspirin. This means that aspirin alone was compared to ticagrelor/aspirin.
- NICE reviewed the results of a pre-specified sub-group analysis of patients who had had a myocardial infarction1 to 2 years previously (ticagrelor n=4,331; placebo n=4,333). The results of the pre-specified sub-group analysis were more favourable to ticagrelor than the results from the overall trial.
- In the group of patients who had a MI between 1 and 2 years previously, ticagrelor reduced the risk of MI, stroke or death from CV causes by 23% compared to placebo.
- NICE concluded that ticagrelor is clinically effective in people with a history of MI and a high risk of an atherothrombotic event.
- The mean length of treatment in PEGASUS-TIMI 54 was 25.3 months; there are limited data on efficacy and safety beyond 3 years. NICE concluded that they could only approve a maximum duration of treatment of up to 3 years.

PACEF Comment:
Due to limited data on efficacy and safety beyond three years, ticagrelor/aspirin therapy post-MI should not extend beyond 3 years.
ULHT cardiology department will ensure that both the patient and their registered GP practice are aware of the intended dose of ticagrelor and proposed duration of treatment.

- Clopidogrel/aspirin was not used as a comparator because it did not hold a marketing authorisation for use for more than 12 months after MI. While clopidogrel/aspirin is commonly used as initial antiplatelet therapy for up to 12 months after MI, it is not used in clinical practice when continued treatment is needed for patients with a history of MI or at high risk of atherothrombotic event.
- Ticagrelor has potential advantages over clopidogrel in preventing atherthrombotc events after MI because of faster antiplatelet action, although it also has a higher bleeding risk.

PACEF Comment:
ULH Cardiology have informed us that they are likely to initiate ticagrelor/aspirin for 3 years in new patients at high risk of ACS (i.e. due to Left Main Coronary Artery Disease, Ostial Left Anterior Descending Coronary Artery Disease, Complex Multivessel Primary Percutaneous Coronary Intervention (PPCI) or In-Stent Stenosis) where additional bleeding risk is balanced against the risk of further events.
It is expected, based on current data, that patient numbers will be low.

PACEF Recommendation:
Ticagrelor (*Brilique*) in combination with aspirin is recommended as an option for preventing atherothrombotic events in adults who had a myocardial infarction and who are at high risk of a further event. 60mg twice daily is the recommended dose for extended treatment. Unless contraindicated, ticagrelor should always be given with a low maintenance daily dose of aspirin 75mg to 150mg. Treatment should be stopped when clinically indicated or at a maximum of 3 years.
ULHT cardiology department will be responsible for identifying those patients eligible for this treatment as recommended by NICE TA 420.

NICE UPDATE

NICE Technology Appraisal	Guidance	PACEF Recommendation
TA432 *Everolimus for advanced renal cell carcinoma after previous treatment* (February 2017)	Everolimus is recommended within its marketing authorisation as an option for treating advanced renal cell carcinoma that has progressed during or after treatment with vascular endothelial factor targeted therapy.	Everolimus (*Afinitor*) 2.5mg, 5mg and 10mg tablets have a marketing authorisation for the treatment of patients with advanced renal cell carcinoma whose disease has progressed during or after treatment with vascular endothelial growth factor (VEGF) targeted therapy. Designated: RED and approved for use through the *Lincolnshire Joint Formulary* for this indication. Everolimus is already on-Formulary for advanced breast cancer and renal cell carcinoma.
TA433 *Apremilast for treating active psoriatic arthritis* (February 2017)	Apremilast, alone or in combination with disease-modifying antirheumatic drugs (DMARDs), is recommended as an option for treating active psoriatic arthritis in adults only if: they have peripheral arthritis with 3 or more tender joints and 3 or more swollen joints and their disease has not responded to adequate trials of at least 2 standard DMARDs, given either alone or in combination.	Apremilast 10mg, 20mg and 30mg tablets (*Otezla*) are designated RED for this indication and are approved for use through the *Lincolnshire Joint Formulary.*

POLYPHARMACY IN THE FRAIL ELDERLY

Frailty is a distinctive health state related to the ageing process in which multiple body systems gradually lose their in-built reserves. Approximately 10% of people aged over 65 years have frailty, rising to between a quarter and a half of those aged over 85 years. Older people living with frailty are at risk of adverse outcomes such as dramatic change in their physical and mental well-being after an apparently minor event, such as an infection or change in medication, which challenges their health.

Screening tools for frailty are available. In Lincolnshire, the Edmonton Frail Scale is being used by secondary care and community services, but GPs may use shorter tools such as the PRISMA 7 questionnaire.

Polypharmacy in frail older people is common. Since many drugs are associated with adverse outcomes, such as falls, increasing confusion and risk of drug interactions, review of medication is important. A number of validated medication checklists are available, with the STOPP and START guidelines most commonly used in Lincolnshire. Although these guidelines are a welcome aid for older people, including those with frailty, they do not address the issue of people with frailty in the last year of life. Individual goals of treatment for this patient group often focus on comfort and dignity rather than prolongation of life at the expense of side effects or drug interactions.
In patients with frailty who fulfil criteria for being in the last year of their life consider:

- stopping statins and ezetimibe.
- stopping antianginals, particularly nicorandil (associated with a high risk of ulceration).
- stopping calcium channel blockers where there is constipation or ankle oedema.
- reviewing CCBs where there is reflex tachycardia or cardio-depression.
- stopping nifedipine in CHD/CHF.
- reviewing diltiazem and verapamil (should only be used with extreme caution in the frail).
- stopping sulfonylurea in frail elderly patients with an HbA1c level less than 50.
- stopping metformin in the frail elderly where there is CKD with eGFR frequently falling under 35ml/min.
- stopping dementia treatment unless the drug helps with behaviour.
- stopping oxybutynin and other antimuscarinic drugs in the same class; ensure that the patient is adequately padded and toileted.
- stopping calcium and vitamin D supplementation in the frail immobile (i.e.those who are bed-bound or unable to walk.
- stopping bisphosphonates due to risk of ulceration.

This is an abridged version of guidance that original appeared in *Polypharmacy and the Frail Elderly* by Dr Gill Garden (Consultant Older People's Services) and David Ewen (Pharmacist) (September 2016).

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