Arden and Greater East Midlands Commissioning Support Unit

Arden and Greater East Midlands Commissioning Support Unit in association with Lincolnshire Clinical Commissioning Groups, Lincolnshire Community Health Services, United Lincolnshire Hospitals Trust and Lincolnshire Partnership Foundation Trust

Lincolnshire Prescribing and Clinical Effectiveness Bulletin

Volume 10; Number 5 **March 2016**

What's new this month?

- **Following review, avanafil tablets (*Spedra*) have been approved for use as the second line PDE5 inhibitor of choice after generic sildenafil for the treatment of erectile dysfunction. A complete review of PDE5 inhibitors for ED has resulted in tadalafil, both on-demand and once daily, being removed from the *Formulary*; designation RED-RED No new patients should be initiated and existing patients reviewed (see page 4).**
- **The *Flutter* oscillating positive expiratory pressure (PEP) device was approved for use by PACEF in February 2013 for patients with mucus producing conditions that are insufficiently responsive to active cycle of breathing techniques (ACBT). It should only be prescribed following patient assessment and recommendation of a PEP device by a specialist respiratory physiotherapist. Designation: AMBER (see page 6).**
- **Two additional devices, *Acapella vibratory PEP therapy system* and *Lung Flute secretion mobilization device* have also been evaluated by PACEF and designated AMBER subject to the same restrictions. (i.e. they should only be prescribed in those insufficiently responsive to ACBT following patient assessment and recommendation of a PEP device by a specialist respiratory physiotherapist) (see page 6).**
- **Specialist physiotherapists have produced a treatment algorithm to clearly identify when prescriptions for these products are likely to be requested from GPs (see page 15).**
- ***CliniFast Elasticated Tubular Bandages* are now the preferred elasticated bandage on the *Wound Management Formulary*; *Tubifast 2-way stretch* bandages are prohibitively expensive and should not be prescribed (see page 7).**
- **Emollients with high paraffin content can constitute a fire risk, particularly in patients who are smokers or who are receiving home oxygen therapy. No or low paraffin content products are preferable in these high risk groups (see page 8).**
- **Levonorgestrel 52mg T-shaped intrauterine system (*Mirena*) is the first line levonorgestrel containing IUS of choice on the grounds of effectiveness, safety, cost-effectiveness and range of authorised indications. It is designated GREEN and available through the *Lincolnshire Joint Formulary*. It should always be prescribed by brand name (see page 12).**
- **Levonorgestrel 13.5mg T-shaped intrauterine system (*Jaydess*) is recommended as a second line option for women requiring a shorter duration of contraception and/or a smaller device or lower dose; designation GREEN. It should also be prescribed by brand name (see page 12).**
- **Desmopressin is a life sustaining medicine in the treatment of cranial diabetes insipidus; there is a risk of severe harm or even death if doses are omitted or delayed (see page 13).**
- **Following an incident in which a patient experienced hearing loss following azithromycin overdose, prescribers are urged to query regular daily doses in excess of 500mg. The only exceptions are: (1) uncomplicated *Chlamydia trachomatis* urethritis**

and cervicitis where 1g or 2g as a single oral dose is indicated and (2) gonorrhoea where a single 1g or 2g dose is sometimes used in combination with ceftriaxone (see page 13).

- **Shire Pharmaceuticals have written out to all healthcare professionals to highlight the risk of serious skin reactions with galantamine hydrobromide (*Reminyl*). To date five cases have been identified worldwide including Stevens-Johnson syndrome (SJS), acute generalised exanthematous pustulosis (AGEP) and erythema multiforme (EM). Patients and carers are advised to watch out for warning signs (see page 14).**

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SUMMARY OF PACEF DECISIONS: *FEBRUARY 2016 UPDATE*

Device, Dressing or Drug	Indication(s)	Traffic Light and *Joint Formulary* Status
Acapella Vibratory PEP Therapy System (Smiths Medical)	Oscillating positive expiratory pressure device for use in patients with lung diseases with secretory problems such as COPD, asthma, bronchiectasis and cystic fibrosis.	AMBER Should only be prescribed following assessment and recommendation by a specialist respiratory physiotherapist.
Avanafil 50mg, 100mg and 200mg tablets *(Spectra)* (Menarini)	On-demand treatment for erectile dysfunction	GREEN Approved for inclusion in the *Lincolnshire Joint Formulary*. Second line for on-demand treatment of ED after sildenafil. Subject to restriction under Part XVIIIB of the *Drug Tariff.*
CliniFast Elasticated Tubular Bandage	Elasticated viscose stockinette bandage.	GREEN
Comfifast Elasticated Tubular Bandage	Elasticated viscose stockinette bandage.	GREEN
Eumocream (glycerol 25%) (GlaxoSmith Kline)	For dry or flaky skin conditions including eczema and dermatitis	GREEN Approved for inclusion on the *Lincolnshire Joint Formulary*. Should be reserved for when a paraffin free product is required.
Flutter oscillating positive expiratory pressure device (Evergreen Nebulisers Ltd)	Oscillating positive expiratory pressure device for patients with COPD, asthma, bronchiectasis and cystic fibrosis..	AMBER Should only be prescribed following assessment and recommendation by a specialist respiratory physiotherapist.
Lung Flute Secretion Mobilization Device for PEP/ bronchial hygiene therapy (Medical Acoustics)	Oscillating positive expiratory pressure device for patients with chronic mucus congestion caused by COPD, asthma, emphysema, bronchitis, pneumonia and other respiratory ailments.	AMBER Should only be prescribed following assessment and recommendation by a specialist respiratory physiotherapist.
Levonorgestrel 13.5mg T-shaped	Contraception	GREEN.

intrauterine system (*Jaydess*) (Bayer)		Second line for women requiring a shorter duration of contraception and/or a smaller device. *Always prescribe by brand name.*
Levonorgestrel 52mg T-shaped intrauterine system (Levosert) (Actavis)	Contraception Idiopathic menorrhagia.	RED-RED Not approved for inclusion in the *Lincolnshire Joint Formulary.* *If prescribing is unavoidable, prescribe by brand name.*
Levonorgestrel 52mg T-shaped intrauterine system (*Mirena*) (Bayer)	Contraception. Idiopathic menorrhagia. Protection from endometrial hyperplasia during oestrogen replacement therapy.	GREEN – first line Available through the *Lincolnshire Joint Formulary.* *Always prescribe by brand name.*
Sildenafil 25mg, 50mg and 100mg tablets (generic)	On-demand treatment for erectile dysfunction	GREEN Included in *the Lincolnshire Joint Formulary*. First line for on-demand treatment of ED; no longer subject to restriction under Part XVIIIB of the *Drug Tariff.*
Tadalafil 10mg and 20mg tablets *(Cialis) (Lilly)*	On-demand treatment for erectile dysfunction	RED-RED No new patients should be initiated and existing patients reviewed. No longer approved for use through the *Lincolnshire Joint Formulary*.
Tadalafil 2.5mg tablets (*Cialis*) (Lilly)	Once daily treatment for erectile dysfunction	RED-RED No new patients should be initiated and existing patients reviewed. No longer approved for use through the *Lincolnshire Joint Formulary*.
Tadalafil 5mg tablets (*Cialis*) (Lilly)	Once daily treatment for erectile dysfunction Benign Prostatic Hypertrophy.	RED-RED No new patients should be initiated and existing patients reviewed. No longer approved for use through the *Lincolnshire Joint Formulary*.
Tubifast 2-way stretch Elasticated Tubular Bandage (Molnlyke Health Care)	Elasticated viscose stockinette bandage.	RED-RED Lower cost equivalents *CliniFast* and *Comfifast* are preferred.
Vardenafil 5mg,10mg and 20mg tablets (*Levitra*) (Bayer)	Erectile dysfunction	RED-RED Not included in the *Lincolnshire Joint Formulary*.
Vardenafil 10mg orodispersible tablets (*Levitra Orodispersible*) (Bayer)	Erectile dysfunction	RED-RED Not included in the *Lincolnshire Joint Formulary*.

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 Sandra France on sandra.france@gemcsu.nhs.uk.

Google searching can be a quick and effective way of finding back numbers of the *PACE Bulletin* relevant to a specific topic of interest. Searchers are advised to use the official version of the *Bulletin* available from the PACEF website rather than depend on a potentially unreliable draft or variant found through Google or an alternative search engine.
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: *AVANAFIL 5OMG, 100MG AND 200MG (SPEDRA)*

Following review, avanafil tablets (*Spedra*) have been approved for use as the second line PDE5 inhibitor of choice after generic sildenafil for the treatment of erectile dysfunction (ED). A complete review of PDE5 inhibitors for ED has resulted in tadalafil, both on-demand and once daily, being removed from the *Formulary*; designation RED-RED No new patients should be initiated and existing patients reviewed.

This is an updated version of a New Drug Assessment that originally appeared in *PACE Bulletin* Volume 8 No 12 (June 2014)

Avanafil (*Spedra*) is a phosphodiesterase type-5 inhibitor licensed for the treatment of erectile dysfunction. Supporting evidence comes from three placebo controlled trials, two of which were performed in diabetics and post prostatectomy patients, specific populations that correlate with priority groups on the current NHS Selected List. Results from the trials demonstrate the clinical efficacy of avanafil over placebo in the treatment of erectile dysfunction and confirm the licensed recommended initial dose of 100mg increased to 200mg or decreased to 50mg based on individual efficacy and tolerability.

There are no comparative trials between avanafil and any other PDE5 inhibitors, making it difficult to judge whether the product has any advantages over currently available therapies. In terms of timing of administration, both avanafil and tadalafil are faster acting and can be given 30 minutes prior to sexual activity, while the timing of sildenafil is 60 minutes before and vardenafil between 25 and 60 minutes before (see table).

The overall safety of avanafil appears to be similar to that of other PDE5 inhibitors with common adverse events including headache, flushing, nasal and sinus congestion and back pain.

A cost comparison reveals the following:

PDE5 inhibitor	Dose (before sexual activity)	Indications	Cost (£) 28 days	Cost per dose
Avanafil 100mg tablets (*Spedra*) (Menarini)	**100mg approximately 30 minutes before sexual activity (usual starting dose)**	**Erectile dysfunction**	**£10.94 (4)**	**£2.74**
Avanafil 50mg tablets (*Spedra*) (Menarini)	**50mg approximately 30 minutes before sexual activity (preferred dose for patients on alpha blocker therapy)**	**Erectile dysfunction**	**£14.08 (4)**	**£3.52**
Avanafil 200mg tablets (*Spedra*) (Menarini)	**200mg approximately 30 minutes before sexual activity (maximum single dose in 24 hours)**	**Erectile dysfunction**	**£21.90 (4)**	**£5.48**
Sildenafil 50mg tablets (generic)	**50mg approximately one hour before sexual activity (usual starting dose)**	**Erectile dysfunction**	**£1.03 (4)**	**26p**
Sildenafil 25mg tablets (generic)	**25mg approximately one hour before sexual activity**	**Erectile dysfunction**	**£0.97 (4)**	**24p**
Sildenafil 100mg tablets (generic)	**100mg approximately one hour before sexual**	**Erectile dysfunction**	**£1.13 (4)**	**28p**

	activity (maximum single dose in 24 hours)			
Tadalafil 10mg tablets (*Cialis*) (Lilly)	10mg at least 30 minutes before sexual activity (usual starting dose)	Erectile dysfunction	£26.99 (4)	£6.74
Tadalafil 20mg tablets (*Cialis*) (Lilly)	20mg at least 30 minutes before sexual activity (maximum single dose in 24 hours)	Erectile dysfunction (20mg *Adcirca* is also licensed for Pulmonary Arterial Hypertension)	£26.99 (4)	£6.74
Tadalafil 2.5mg tablets (*Cialis*) (Lilly)	2.5mg once daily (in patients who anticipate at least twice weekly sexual activity)	Erectile dysfunction	£54.99 (28)	£1.97 a day
Tadalafil 5mg tablets (*Cialis*) (Lilly)	5mg once daily (in patients who anticipate at least twice weekly sexual activity)	Erectile dysfunction Benign Prostatic Hypertrophy (BPH)	£54.99 (28)	£1.97 a day
Vardenafil 10mg tablets (*Levitra*) (Bayer)	10mg taken 25 to 60 minutes prior to sexual activity (usual starting dose)	Erectile dysfunction	£14.08 (4)	£3.52
Vardenafil 5mg tablets (*Levitra*) (Bayer)	5mg taken 25 to 60 minutes prior to sexual activity	Erectile dysfunction	£7.56 (4)	£1.89
Vardenafil 20mg tablets (*Levitra*) (Bayer)	20mg taken 25 to 60 minutes prior to sexual activity (maximum single dose in 24 hours)	Erectile dysfunction	£23.48 (4)	£5.87
Vardenafil 10mg orodispersible tablets (*Levitra Orodispersible*) (Bayer)	10mg taken 25 to 60 minutes prior to sexual activity (usual starting dose)	Erectile dysfunction	£17.88 (4)	£4.47

Formulary approved products are highlighted in **bold.**

PACEF Recommendation:

Generic sildenafil tablets (25mg, 50mg and 100mg) remain the first line PDE5 inhibitor of choice in the treatment of erectile dysfunction. Generic sildenafil is no longer subject to Part XVIIIB of the *Drug Tariff* and can be prescribed for ED outside of the constraints of the selected list of approved conditions and patient groups. After a full review of the evidence, PACEF acknowledge that avanafil is the lowest cost agent after sildenafil with similar efficacy and tolerability to alternative PDE5 inhibitors. As a result of this avanafil 50mg, 100mg and 200mg tablets (*Spedra*) are approved for inclusion in the *Lincolnshire Joint Formulary*; designation GREEN for second line use after generic sildenafil. On demand tadalafil 10mg and 20mg tablets (*Cialis*) are no longer approved for use and are designated RED-RED; no new patients should be initiated on treatment and existing patients should be reviewed. Once daily formulations of tadalafil 2.5mg and 5mg tablets are also no longer approved for patients with erectile dysfunction even in those with benign prostatic hypertrophy and should not be initiated in new patients; it is acknowledged that some patients with benign prostatic hypertrophy will already be receiving prescriptions for the 5mg strength and this should remain unchallenged until the patient or clinician considers it appropriate to stop. As a result of this, tadalafil 2.5mg and 5mg tablets (*Cialis Once a Day*) are designated RED-RED and should not be initiated in new patients. Once daily tadalafil is no longer cost-effective even for those who anticipate at least twice weekly sexual activity as the cost per dose of sildenafil has fallen to less than 30p and lower cost on-demand alternatives such as avanafil are now available. Vardenafil 5mg, 10mg and 20mg tablets (*Levitra*) have been re-classified from GREEN to RED-RED; no new patients should be initiated on treatment and existing patients should be reviewed. Vardenafil 10mg orodispersible tablets (*Levitra Orodispersible*) remain RED-RED.

NEW DEVICE ASSESSMENTS: *ACAPELLA VIBRATORY POSITIVE EXPIRATORY PRESSURE THERAPY SYSTEM* AND *LUNG FLUTE SECRETION MOBILIZATION DEVICE*

There is limited evidence to suggest that oscillating PEP devices like *Acapella*, *Flutter* and *Lung Flute* are helpful in enabling patients with mucus producing chest conditions to clear secretions. All three devices are designated AMBER and can be prescribed on the recommendation of a specialist respiratory physiotherapist.

Acapella Vibratory PEP Therapy System

Acapella is a vibratory PEP therapy system which may be of use in patients with lung diseases with secretory problems such as COPD, asthma and cystic fibrosis. The *Acapella* generates vibration in the chest wall on expiration through the device due to vibration of a counterweighted plug and magnet. Following use of the device further huffing and coughing can help to clear any sputum. The usual treatment cycle takes 10 to 20 minutes or until all sputum has been cleared.

Flutter oscillating PEP device

Flutter is an oscillating positive expiratory pressure (PEP) device which may be of use in the alleviation of mucus producing conditions such as atelectasis, bronchitis, bronchiectasis, cystic fibrosis (CF), chronic obstructive pulmonary disease (COPD) and asthma. It is a pipe shaped device with a mouthpiece at one end and a perforated plastic cover at the other; inside is a high density steel ball which rests within a plastic circular cone. Before exhalations the steel ball blocks the conical canal of the device. The ball is moved by a combination of the pressure of exhaled air, the force of gravity on the ball and the angle of the cone. During exhalation the steel ball rolls and bounces up and down, creating an opening and closing cycle within the valve like device which repeats many times during each exhalation. The oscillations in expiratory pressure and airflow that are created by the device result in vibrations occurring within the airways. This can be felt as a fluttering sensation, hence the name given to the device. The result of the vibrations is to loosen mucus from the airway walls. *Flutter* therapy is complete when no further mucus can be expectorated. Frequency of use and duration of each session varies with each patient, but usually the whole process takes between 5 to 15 minutes and is repeated twice daily, once in the morning and once in the late afternoon or evening.

Lung Flute Secretion Mobilization Device for PEP/ bronchial hygiene therapy

The *Lung Flute* creates vibrations to loosen the mucus when the patient blows gently into the flute over a reed. Reed oscillation, tube design and the lung cavity itself act in parallel to produce a sound frequency between 16-25Hz. This artificially vibrates the airways and cilia with the result that it makes secretions thinner and more easily expelled by coughing. Generally, morning and late afternoon/evening sessions are recommended, each lasting 5 to 10 minutes

There is little published evidence to support the use of these devices. A Cochrane review published in 2009 concluded that there was no clear evidence that oscillation was more or less effective overall than other forms of physiotherapy. The authors recommended that more long term randomised controlled trials were needed.

The Cystic Fibrosis Trust recommend that oscillatory devices should be considered as an option for airway clearing in patients with CF. The British Thoracic Society (BTS) have stated

that PEP and oscillating PEP devices have been shown to be equally effective as traditional chest physiotherapy in sputum clearance; they are also recognised as useful techniques in the NICE guidelines on COPD. Patient preference should be taken into consideration when selecting which airway clearance techniques or devices would be most appropriate for individual patients. There is a published trial conducted in a very small number of COPD patients which demonstrates the effectiveness of *Lung Flute* in improving symptoms associated with COPD.

A cost comparison reveals that the three devices are broadly comparably priced:

Device	***Drug Tariff* price (March 2016)**
Acapella Vibratory PEP Therapy System (Smiths Medical)	£40.50
Flutter oscillating positive expiratory pressure device (Evergreen Nebulisers Ltd)	£40.50
Lung Flute Secretion Mobilization Device for PEP/ bronchial hygiene therapy (Medical Acoustics)	*£37.50*

PACEF Recommendation

There is evidence to suggest that oscillating PEP devices like *Acapella*, *Flutter* and *Lung Flute* are helpful in enabling patients with mucus producing chest conditions to clear secretions, increase expectorated sputum volume and improve respiratory function. This may, in turn, reduce the risk of respiratory infection and improve the patient's general health and wellbeing. However, oscillating PEP devices are not easy to use effectively and patients must be trained in their use by specialist physiotherapy services. The patient must also have tried and gained insufficient benefit from alternative techniques such as the active cycle of breathing technique (ACBT). As a result of this, the *Acapella Vibratory PEP Therapy System ,* the *Flutter* PEP device and the *Lung Flute* Secretion Mobilization Device are all designated AMBER. They should only be prescribed following patient assessment and recommendation of a PEP device by specialist respiratory physiotherapist. They should not be prescribed in response to a direct patient request to a GP as physiotherapist assessment and training is crucial to ensure selection of appropriate patients and maximum benefit from the device. The treatment algorithm provided at the end of this *Bulletin* details the place in therapy of these three devices as defined by the specialist physiotherapists who will in certain circumstances request that one of these devices should be prescribed by the patient's GP.

WOUND MANAGEMENT COST COMPARISON: *CLINIFAST ELASTICATED TUBULAR BANDAGE VS COMFIFAST VS TUBIFAST*

***CliniFast Elasticated Tubular Bandages* are now the preferred elasticated bandage on the *Wound Management Formulary*; *Tubifast 2-way stretch* bandages are prohibitively expensive and should not be prescribed.**

CliniFast elasticated tubular bandages are equivalent in price to the current preferred tubular bandage on the *Wound Management Formulary* (WMF), *Comfifast.*

FP10 prices

Product	***Comfifast* bandages**	***CliniFast* bandages**	***Tubifast 2-way stretch* bandages**
Size	**Cost**	**Cost**	**Cost**
7.5cm x 1m	£0.77	£0.77	£1.32
7.5cm x 3m	£2.13	£2.13	£3.72
7.5cm x 5m	£3.74	£3.74	£6.48
10.75 cm x 1m	£1.20	£1.20	£2.11
10.75 cm x 3m	£3.49	£3.49	£6.05
10.55 cm x 5m	£6.04	£6.04	£10.39
17.5 cm x 1m	£1.83	£1.83	-

However, as *CliniFast* elasticated tubular bandages are significantly lower in cost than *Comfifast* when ordered through NHS Supply Chain (NHSSC) (see below), it makes sense that they should be preferred through the *WMF*, particularly where NHSSC are the supplier (e.g. as part of the Non-Prescription Supply of Wound Management Products Service).

NHS Supply Chain Prices

Product	***Comfifast* bandages**	***CliniFast* bandages**	**Saving per bandage**
Size	**Cost**	**Cost**	
7.5cm x 1m	**£0.73**	£0.87	+14p
7.5cm x 3m	**£2.01**	£1.85	16p
7.5cm x 5m	**£3.53**	£3.41	12p
10.75 cm x 1m	**£1.13**		
10.75 cm x 3m	**£3.28**	£2.68	60p
10.75 cm x 5m	**£5.43**	£5.19	24p
17.5 cm x 1m	**£1.83**	£1.73	10p

Additional savings can be made across the healthcare community by changing from *Tubifast, 2-way stretch*, a non-formulary product, to either *Comfifast* or *CliniFast*.

PACEF Recommendation:
Where an elasticated tubular bandage is indicated, *CliniFast* are preferred; designation GREEN. *Tubifast 2-way* stretch elasticated bandages are prohibitively expensive in comparison to alternatives and are designated RED-RED (i.e. they should not be prescribed).

COST EFFECTIVE EMOLLIENTS WITH NO OR LOW PARAFFIN CONTENT

Emollients with high paraffin content can constitute a fire risk, particularly in patients who are smokers or who are receiving home oxygen therapy. No or low paraffin content products are preferable in these high risk groups.

In November 2007, the National Patient Safety Agency (NPSA) issued an alert to all healthcare staff involved in the prescribing, dispensing or administration of paraffin based skin products. The NPSA highlighted that the topical administration of paraffin based skin-products carries a potential fire risk as dressings and clothing coated with paraffin can become highly flammable and easily ignited with a naked flame or cigarette. The risk is greatest when these preparations are applied to large areas of the body with dressings and clothing becoming soaked or coated with the ointment. Products with a particularly high paraffin content, such as emulsifying ointment or 50% liquid paraffin/ 50% white soft paraffin

(WSP) ointment are particularly high risk. Patients should be told to keep away from fire or flames, and not to smoke when using these preparations.

In May 2013, PrescQIPP published a bulletin entitled '*Cost effective emollients with no or low paraffin content*' in which they advised NHS organisations to ensure that at least one product should be included in local formulary guidance which: (1) takes into account the warnings in the NPSA alert and (2) is suitable for patients using home oxygen therapy. Wherever possible, low paraffin content cream preparations should be used in these patients rather than paraffin-containing ointments.

PrescQIPP define low paraffin content as 30% w/w or less. The Emollients section of the Lincolnshire Joint Formulary has been revised in order to include low paraffin options at every stage:

Preferred products for first line use in those with mild dry skin

Drug	Paraffin content	Indication(s)	Traffic Light and Joint Formulary Status
Aveeno Cream (1% colloidal oatmeal) £3.97 100g £6.80 300ml pump £7.19 500ml pump	Paraffins listed in ingredients No information supplied from manufacturer.	For endogenous and exogenous eczema, xeroderma, ichthyosis and senile pruritus (pruritus of the elderly) associated with dry skin	GREEN Possible first line choice for mild dryness. Included in the *Lincolnshire Joint Formulary.*
Aveeno Lotion (1% colloidal oatmeal) £6.66 500ml	Paraffins listed in ingredients No information supplied from manufacturer.	For endogenous and exogenous eczema, xeroderma, ichthyosis and senile pruritus (pruritus of the elderly) associated with dry skin	GREEN Possible first line choice for mild dryness Included in the *Lincolnshire Joint Formulary.*
Diprobase **cream** £1.28 50g £6.32 500g pump	liquid paraffin 6%, white soft paraffin (WSP) 15% Low paraffin content	For dry skin conditions	GREEN Possible first line choice for mild skin conditions. .Included in the *Lincolnshire Joint Formulary.*
E45 **cream** £1.61 50g £2.91 125g £5.62 500g pump	liquid paraffin 12.6% WSP14.5% Low paraffin content	Ichthyosis, traumatic dermatitis, dry stages of eczema, dry psoriasis, dry skin conditions	GREEN Possible first line choice for mild skin conditions. .Included in the Lincolnshire Joint Formulary.
Hydromol Cream (sodium pyrrolidone carboxylate 2.5%) £2.04 50g £4.09 100g £11.92 500g pump	Liquid paraffin 13.8%w/w Low paraffin content	For dry skin conditions	GREEN Possible first line choice for mild skin conditions Included in the Lincolnshire Joint Formulary
Eumocream 30g £2.28 100g £3.70	Contains glycerol 25% Paraffin free	Dry or flaky skin conditions including eczema and dermatitis	GREEN Should be reserved for when a paraffin free product is required.

Preferred products containing an antimicrobial

Drug	Paraffin content	Indication(s)	Traffic Light and Joint Formulary Status
Dermol Cream £2.86 100g £6.63 500g	liquid paraffin 10% Low paraffin content	For dry and pruritic skin conditions including eczema and dermatitis, Can be used as a soap substitute	GREEN First choice when a product for mild dryness is indicated where there is evidence of a high bacterial load. Recommended for short-term use only. Included in the *Lincolnshire Joint Formulary*
Dermol Lotion £6.04 500ml pump	liquid paraffin 2.5% Low paraffin content	For dry and pruritic skin conditions including eczema and dermatitis,	GREEN First choice when a product for mild dryness is indicated

		Can be used as a soap substitute	where there is evidence of a high bacterial load. Recommended for short-term use only. Included in the *Lincolnshire Joint Formulary*

Preferred products for moderate dryness

Drug	Paraffin content	Indication(s)	Traffic Light and Joint Formulary Status
Aquamax Cream £1.89 100g £3.99 500g	WSP 20%, liquid paraffin 8% Low paraffin content	Eczema, psoriasis and other dry skin conditions	GREEN Possible first line choice for moderate dryness. Included in the *Lincolnshire Joint Formulary.*
***Cetraben* cream** £3.98 150g £5.99 500g £11.62 1050g	WSP13.2%, light liquid paraffin 10.5% Low paraffin content	Dry skin conditions,eczema.	GREEN Possible first line choice for moderate dryness. Included in the *Lincolnshire Joint Formulary.*
Doublebase gel £2.65 100g £5.83 500g pump	liquid paraffin 15% Low paraffin content	Dry skin conditions	GREEN Possible first line choice for moderate dryness. Included in the *Lincolnshire Joint Formulary.*
Epaderm Cream £1.70 50g £6.95 500g	(yellow soft paraffin , liquid paraffin, emulsifying wax) No information supplied from manufacturer.	Dry skin conditions	GREEN Possible first line choice for moderate dryness. Included in the Lincolnshire Joint Formulary.

Preferred products containing urea

Drug	Paraffin content	Indication(s)	Traffic Light and Joint Formulary Status
Balneum Cream (5% urea) £2.85 50g £9.97 500g	Liquid paraffin 5.35% (information supplied by manufactuerer) Low paraffin content	Dry skin conditions	GREEN For short term use only for dry thickened skin in conjunction with another emollient. Included in the *Lincolnshire Joint Formulary.*
Balneum Plus Cream (5% urea) £3.29 500g pump	Liquid paraffin 1.0% (information supplied by manufacturer) Low paraffin content	Pruritis, eczema, dermatitis and scaling skin conditions.	GREEN For short term use only for dry thickened skin in conjunction with another emollient. Included in the *Lincolnshire Joint Formulary.*
***Hydromol Intensive* cream** (10% urea) £1.64 30g £4.37 100g	White soft paraffin 28.15% w/w Low paraffin content	Dry skin and hyperkeratosis	GREEN For short term use only for dry thickened skin in conjunction with another emollient when higher strength urea product is indicated. Included in the *Lincolnshire Joint Formulary.*
Calmurid cream (10% urea) £9.97 100g £35.70 500g pump	Galderma UK Ltd confirmed product is paraffin free.	Dry skin and hyperkeratosis	GREEN – second line Should be reserved for very hyperkeratotic lesions and for those intolerant to treatment with *Hydromol Intensive* crem. Included in the *Lincolnshire Joint Formulary.*

Preferred products for severe dry skin

Drug	Paraffin content	Indication(s)	Traffic Light and Joint Formulary Status
Emulsifying ointment	50% WSP	Dry skin	GREEN

£2.48 500g			Possible first line choice for severe dryness. Included in the *Lincolnshire Joint Formulary.*
Hydromol Ointment £2.88 125g £4.89 500g £9.09 1kg	Yellow soft paraffin 30% Emulsifying wax 30%, Liquid paraffin 40%)	Dry skin including eczema and as a soap substitute.	GREEN Possible first line choice for severe dryness. Included in the *Lincolnshire Joint Formulary.*
Diprobase Ointment £1.28 50g £5.99 500g	Liquid paraffin 5%, WSP 95%	Dry skin conditions	GREEN Possible first line choice for severe dryness. Included in the *Lincolnshire Joint Formulary.*
White soft paraffin/liquid paraffin 50:50 £1.83 250g £3.66 500g	Liquid paraffin 50%, WSP 50%	Dry skin conditions	GREEN Possible first line choice for severe dryness. Included in the *Lincolnshire Joint Formulary.*
Emollin spray (liquid paraffin 50%, WSP 50%)	Liquid paraffin 50%, WSP 50%	Dry, scaly, sensitive or sore skin.	GREEN To be used for bullous skin conditions. Included in the *Lincolnshire Joint Formulary.*

Reference: *PrescQIPP Bulletin* 49 'Cost effective emollients with no or low paraffin content''(May 2013)

SHARED CARE GUIDELINES

PACEF have reviewed, updated and approved the following shared care guidelines:

- *Nabilone unlicensed use in the management of chronic neuropathic pain that has failed to respond to other first and second line treatments.*
- *Ketamine for use in palliative care for the management of pain unresponsive to standard therapies and as a third/fourth-line choice for the management of chronic neuropathic pain that has failed to respond to alternative treatments.*
- *Mercaptopurine: unlicensed use of mercaptopurine for the treatment of inflammatory bowel disease.*
- *Azathioprine in dermatology and gastroenterology.*
- *Methotrexate in dermatology.*
- *Ciclosporin in dermatology.*
- *Dronedarone for the treatment of patients with non-permanent atrial fibrillation.*
- *Erythropoiesis Stimulating Agents (ESA's) in the treatment of anaemia of chronic kidney disease (CKD) stages 4 & 5.*
- *Sirolimus for maintenance of immunosuppression after kidney transplantation in adults.*
- *Tacrolimus (Adoport and Prograf) for maintenance of immunosuppression after kidney transplantation in adults.*
- *Tacrolimus (Advagraf) for maintenance of immunosuppression after kidney transplantation in adults.*
- *Mycophenolate mofetil for maintenance of immunosuppression after kidney transplantation in adults.*
- *Mycophenolic acid for maintenance of immunosuppression after kidney transplantation in adults.*

These SCGs are now available through the PACEF website or by contacting Cathy Johnson on cathy.johnson@ardengemcsu.nhs.uk

MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY: *DRUG SAFETY UPDATE* (JANUARY 2016)

Levonorgestrel-releasing intrauterine systems: prescribe by brand name

Levonorgestrel-releasing intrauterine systems should always be prescribed by brand name because products have different indications, durations of use, and introducers.

A summary table comparing the three available products was published in *PACE Bulletin* Volume 10 No 2 (January 2016):

Product	Releasing	Indications	Replace after	Cost per pack	Cost per year
Levonorgestrel 52mg T-shaped intrauterine system (*Levosert*) (Actavis)	20 microgram in 24 hours	Contraception. Idiopathic menorrhagia.	3 years	£66.00	£22.00 per year
Levonorgestrel 52mg T-shaped intrauterine system (*Mirena*) (Bayer)	20 microgram in 24 hours	Contraception. Idiopathic menorrhagia. Protection from endometrial hyperplasia during oestrogen replacement therapy.	5 years	£88.00	£17.60 per year
Levonorgestrel 13.5mg T-shaped intrauterine system (*Jaydess*) (Bayer)	6 microgram in 24 hours	Contraception	3 years	£69.22	£23.07 per year.

Products containing 52 mg levonorgestrel (*Levosert* and *Mirena*)

A levonorgestrel-releasing intrauterine system (IUS) has been available as the brand *Mirena* for a number of years. Recently, a second product called *Levosert* was licensed for use in the UK. As *Mirena* has a wider range of licensed indications, can be used over a longer time period and is lower cost (in terms of cost per year), it is approved for use through the *Lincolnshire Joint Formulary*; designation GREEN.

Although *Mirena* and *Levosert* both contain 52 mg levonorgestrel, they differ in two important ways:

(1) Indications for use

Mirena is licensed for 5 years' use and *Levosert* is licensed for 3 years' use for contraception or heavy menstrual bleeding. Clinical data for long-term efficacy and safety of *Mirena* for these indications are available for 5 years of use, whereas only 3 years of data are currently available for *Levosert*. This is the primary reason why *Mirena* is available through the *Lincolnshire Joint Formulary* and *Levosert* is not; designation RED-RED.

Mirena is also licensed for 4 years' use for endometrial protection as part of a hormone replacement therapy regimen; *Levosert* is not licensed for this indication.

(2) Introducer or insertion device

Mirena and *Levosert* have different introducers, requiring different insertion techniques. Insertion (and removal) of any intra-uterine device (IUD) may be associated with pain,

bleeding, and (in some cases) perforation of the uterus. Therefore, IUDs should only be inserted by healthcare professionals who are experienced in insertion or who have had training in the relevant insertion techniques.

Product containing 13.5 mg levonorgestrel (*Jaydess*)

A smaller IUS that contains 13.5 mg levonorgestrel (called *Jaydess*) has been marketed since 2014 and is licensed for 3 years' use for contraception only. This product has also been approved for use through the *Lincolnshire Joint Formulary*; designation GREEN.

PACEF Recommendations:
Levonorgestrel 52mg T-shaped intrauterine system (*Mirena*) is the first line product of choice on the grounds of effectiveness, safety, cost-effectiveness and range of authorised indications. It is designated GREEN and available through the *Lincolnshire Joint Formulary*. It should always be prescribed by brand name. Levonorgestrel 13.5mg T-shaped intrauterine system (*Jaydess*) is recommended as a second line option for women requiring a shorter duration of contraception and/or a smaller device or lower dose; designation GREEN. It should also be prescribed by brand name. In the absence of data beyond 3 years and with a relatively high cost per year, levonorgestrel 52mg T-shaped intrauterine system (*Levosert*) is designated RED-RED and not approved for inclusion in the *Lincolnshire Joint Formulary* at this stage, pending the publication of further trial data on longer-term use.

PATIENT SAFETY ALERT: *RISK OF SEVERE HARM OR DEATH WHEN DESMOPRESSIN IS OMITTED OR DELAYED IN PATIENTS WITH DIABETES INSIPIDUS* (FEBRUARY 2016)

Desmopressin is a life sustaining medicine in the treatment of cranial diabetes insipidus; there is a risk of severe harm or even death if doses are omitted or delayed.

Desmopressin is a synthetic form of antidiuretuc hormone used to treat cranial diabetes insipidus; in this situation it is considered to be a life sustaining medication. For this indication, it is most commonly prescribed as:

- Desmopressin 100 and 200 microgram tablets (*DDAVP*/*Desmopressin*)
- Desmopressin nasal spray 10 microgram per actuation (*Desmopspray*)
- Desmopressin acetate injection 4 microgram per ml (*DDAVP*)

NHS England are aware on 80 incidents in the past seven years where a dose of desmopressin has been omitted or delayed; in 76 of these cases the error was detected and acted on before the patient became critically ill; in four cases the patients experienced severe dehydration and died.

One of the main themes emerging from the subsequent investigation of these incidents was the lack of awareness among medical, pharmacy and nursing staff of the critical nature of desmopressin therapy in patients with cranial diabetes insipidus

AZITHROMYCIN INCIDENT

Following an incident in which a patient experienced hearing loss following azithromycin overdose, prescribers are urged to query regular daily doses in excess of 500mg.

In a recent incident reported from outside of Lincolnshire, a patient with complex rheumatological disease associated with recurrent respiratory tract infections was prescribed

prophylactic azithromycin therapy. The recommended dose was azithromycin 500mg three times a week taken on Monday Wednesday and Friday. Unfortunately, the dose was transcribed as 500mg x 3 times per day (Monday, Wednesday, Friday) in the clinic letter and the GP went on to prescribe azithromycin 1500mg three times a week as a result. After taking this dose for just over a month the patient became unwell and eventually presented with diarrhoea, shivering episodes, general ill health and increasingly impaired hearing. Hearing loss is a well-documented complication of azithromycin overdose, but is usually reversible within 5 weeks of discontinuation. In this case, the patient has not regained hearing nine months after the error occurred and is likely to continue to be hearing impaired for the remainder of their life.

PACEF Recommendation:
Prescribers are urged to query regular daily doses of azithromycin in excess of 500mg. The only exceptions are: (1) uncomplicated *Chlamydia trachomatis* urethritis and cervicitis where 1g or 2g as a single oral dose is indicated and (2) gonorrhoea where a single 1g or 2g dose is sometimes used in combination with ceftriaxone.

GALANTAMINE (REMINYL) CAN CAUSE SERIOUS SKIN REACTIONS

Shire Pharmaceuticals have written out to all healthcare professionals to highlight the risk of serious skin reactions with galantamine hydrobromide (*Reminyl*). To date five cases have been identified worldwide including Stevens-Johnson syndrome (SJS), acute generalised exanthematous pustulosis (AGEP) and erythema multiforme (EM). Patients and carers are advised to watch out for signs of serious skin reactions including:

- severe rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals (SJS).
- Red rash covered with small pus-filled bumps that can spread over the body, sometimes with a fever (AGEP).
- Rash that may blister, with spots that look like small targets (EM).

Patients should stop galantamine immediately and seek medical help if any of these signs appear.

Acknowledgements

Many thanks to: Cathy Johnson, Interface Lead Pharmacist, Arden GEM Commissioning Support Unit and Lorna Adlington, Medicines Optimisation Lead, Lincolnshire Community Health Services, for their help with the preparation of this *Bulletin.* Also thanks to Sue Smith from NHS Nene CCG and NHS Corby CCG for sharing with us the learning from the azithromycin incident. Many thanks to Kate Parrot, Trust Clinical Specialist Physiotherapist for Cardiovascular and Respiratory at ULH for her contribution to the evaluation of the *Acapella* and *Lung Flute* devices.

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March 2016

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Appendix: *Clinical Pathway for Use of Oscillating Positive Expiratory Pressure Devices*