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

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What's new this month?

- **All patients currently prescribed domperidone should have their treatment reviewed at their next routine appointment. Prescribers should ensure that treatment for the relief of nausea and vomiting is within recommended dosage and prescribed at the lowest effective dose for the shortest possible time (not usually more than one week). Within this context, domperidone continues to be designated GREEN (see page 4).**
- **Domperidone is now contra-indicated in people: (1) with conditions where cardiac conduction is, or could be, impaired; (2) with underlying cardiac diseases such as congestive heart failure; (3) receiving other medicines known to prolong QT interval or potent CYP3A4 inhibitors (e.g. ketoconazole, erythromycin); and (4) severe hepatic impairment. Where domperidone is now contra-indicated on medical grounds, the patients will need to be switched to an alternative treatment. Patients that are currently prescribed interacting medicines known to prolong the QT interval or inhibit CYP3A4 will need to have their medicines reviewed to either remove the interacting medicine or reconsider the choice of domperidone (see page 4).**
- **PACEF recognize that there are difficulties in identifying an effective alternative to long-term metoclopramide or long-term domperidone, particularly in the treatment of gastroparesis insufficiently responsive to other therapies. The MHRA acknowledge that there may be a clinical need to continue long-term domperidone off-license in some patients. Where this is under consideration, the overall safety profile of domperidone, particularly its cardiac risk and potential interactions with other medicines, must be considered. If continued off-license use is intended, the patient must be informed that the treatment is off-license and given information on the associated risks. This consultation must be recorded in the patient's medical record. New patients should only be initiated on domperidone or metoclopramide longer-term on the advice of a gastroenterologist: designation AMBER without shared care (see page 4).**
- **Sildenafil chewable tablets (*Nipatra*) for the treatment of erectile dysfunction have been designated RED-RED and are not approved for inclusion on the *Lincolnshire Joint Formulary* (see page 6).**
- **Avanafil 50mg, 100mg and 200mg tablets (*Spedra*) for the treatment of erectile dysfunction have been designated RED-RED and are not approved for inclusion in the *Lincolnshire Joint Formulary*. Generic sildenafil tablets (25mg, 50mg and 100mg) remain the first line PDE5 inhibitor of choice (see page 7).**
- **PACEF are convinced that *Resource ThickenUp Clear* offers a genuine alternative to conventional maize starch based thickeners in patients with dysphagia; it may be considered more palatable by some patients and may help to ensure better hydration and nutrition. Subject to recommendation by a Speech and Language Therapist (SALT), *Resource ThickenUp Clear* is approved for use; designation AMBER and approved for inclusion on the *Lincolnshire Joint Formulary.* Food/drink thickeners should never be prescribed in response to an unsupported request from a care home. Wherever possible, bulk packs shared between residents should be prescribed (see page 7).**
- **Following enhancements to the memory size and removal of the deletable memory function, *Omnitest 3* has been approved as one of the preferred lower cost blood glucose testing meters and strips; it is designated GREEN and approved for inclusion**

in the *Lincolnshire Joint Formulary.* The online version of the *PACE Bulletin* evaluating lower cost BGTS (Vol 8 No 2 (February 2014)) provides detailed information on the context within which a lower cost product might be preferred or a switch from a higher cost product advocated (see page 10).

- **The expiry dates of different brands of lower cost blood glucose testing strips are also reviewed (see page 11).**

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SUMMARY OF PACEF DECISIONS: *MAY/JUNE 2014 UPDATE*

Drug	Indication(s)	Traffic Light and Joint Formulary Status
Aflibercept solution for injection (*Eylea*)	For the treatment of macular oedema secondary to central retinal vein occlusion	RED Approved for inclusion in the *Lincolnshire Joint Formulary* for this indication.
Aflibercept intravenous infusion (*Zaltrap*)	For use in combination with irinotecan/5-fluorouracil/folinic acid (FOLFIRI) chemotherapy for adults with metastatic colorectal cancer (MCRC) that is resistant to or has progressed after an oxaliplatin-containing regimen.	RED-RED Not approved for inclusion in the *Lincolnshire Joint Formulary*
Avanafil 50mg, 100mg and 200mg tablets (*Spedra*)	For the treatment of erectile dysfunction	RED-RED Not approved for inclusion in the *Lincolnshire Joint Formulary*
Domperidone 10mg tablets (generic/*Motilium*) Domperidone 5mg/5ml oral suspension	Relief of symptoms of nausea and vomiting.	GREEN Prescribers should ensure that treatment for the relief of nausea and vomiting is within recommended dosage and prescribed at the lowest effective dose for the shortest possible time (not usually more than one week). Included in the *Lincolnshire Joint Formulary* for this indication.
Domperidone 10mg tablets (generic/*Motilium*) Domperidone 5mg/5ml oral	For the treatment of chronic conditions such as gastroparesis, dyspepsia, and gastro-oesophageal reflux disease.	AMBER without shared care. New patients should only be initiated on the advice of a gastroenterologist. Existing patients should be reviewed at the next routine appointment with

		a view to stopping therapy wherever possible. Where the decision is taken to continue long-term domperidone, the patient should be aware of the unlicensed status of the drug, the maximum recommended dose and the risks of long-term use. Included in the *Lincolnshire Joint Formulary.*
Metoclopramide tablets 10mg (generic/Maxolon) Metoclopramide oral solution 5mg in 5ml	For the symptomatic treatment of nausea and vomiting, including that associated with acute migraine.	GREEN Included in the *Lincolnshire Joint Formulary.* Should only be used short-term (up to 5 days); dose should not exceed the maximum recommended dose (see text).
Metoclopramide tablets 10mg (generic/Maxolon) Metoclopramide oral solution 5mg in 5ml	For the treatment of chronic conditions such as gastroparesis, dyspepsia, and gastro-oesophageal reflux disease.	AMBER without shared care. New patients should only be initiated on the advice of a gastroenterologist. Existing patients should be reviewed at the next routine appointment with a view to stopping therapy wherever possible. Where the decision is taken to continue long-term metoclopramide, the patient should be aware of the unlicensed status of the drug, the maximum recommended dose and the risks of long-term use. Included in the *Lincolnshire Joint Formulary.*
Omnitest 3 meter and blood glucose testing strips	Detection of blood glucose in the range 0.6-33.3mmol/l.	GREEN Included in the Lincolnshire Joint Formulary
Pixantrone infusion (*Pixuvri)*	For the treatment of multiply relapsed or refractory aggressive non-Hodgkin's B-cell lymphoma	RED Approved for inclusion in the *Lincolnshire Joint Formulary* for this indication.
Resource ThickenUp Clear	A xanthan gum based food and drink thickener designed to aid swallowing in patients suffering from oropharyngeal dysphagia.	AMBER Should only be prescribed following an assessment of the patient by a Speech and Language Therapist. Approved for inclusion in the *Lincolnshire Joint Formulary* as an alternative to *Thick and Easy*.
Sildenafil chewable tablets 25mg, 50mg and 100mg (*Nipatra*)	For the treatment of erectile dysfunction	RED-RED Not approved for inclusion 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 NHS in Lincolnshire website (www.lincolnshire.nhs.uk); follow the commissioning link to PACEF. Electronic copies of both the *PACE Bulletin* and our sister publication *PACE Shorts* (a short summary 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 NHS in Lincolnshire 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

DRUG SAFETY ADVICE: DOMPERIDONE - RISK OF CARDIAC SIDE EFFECTS

All patients on domperidone must be reviewed at their next routine appointment following MHRA guidance on cardiac risk and potential interactions.

Following on from recommendations made by the European Medicines Agency in April, the Medicines and Healthcare products Regulatory Agency (MHRA) have now issued their own advice to healthcare professionals on the future role of domperidone (*Motilium*).

The European review confirmed a small increased risk of serious cardiac side effects associated with domperidone. A higher risk was observed particularly in:

- people older than 60 years.
- people taking daily oral domperidone in doses of more than 30mg.
- people taking QT prolonging medicines or CYP3A4 inhibitors at the same time as domperidone.

For indications other than the relief of nausea and vomiting, the cardiac risks were considered to outweigh the benefits.

Crucially, the MHRA acknowledge that there may be a clinical need to use it at doses or durations greater than those authorized. However, they stress that, where this is under consideration, the clinician must consider the overall safety profile of domperidone, particularly its cardiac risk and potential interactions with other medicines.

Domperidone: Revised Indications

The table below illustrates the changes to authorized indications that are likely to be made in response to this review:

Approved Indications	**Indications No Longer Approved**
Children: Relief of symptoms of nausea and vomiting. [MHRA report that use of domperidone in children is under further investigation. Domperidone license-holders are required to conduct studies to provide further data to support domperidone efficacy in children]. In children under 12 and weighing less than 35kg, the recommended maximum dose in 24 hours is 0.75mg/kg body weight (dose interval:0.25mg/kg body weight up to three times a day)	
Adults: Relief of symptoms of nausea and vomiting. For adults and adolescents over 12 years of age and weighing 35kg or more, the recommended maximum dose in 24 hours is 30mg (dose interval: 10mg up to three times a day).	Adults: Relief of epigastric sense of fullness, upper abdomen discomfort and regurgitation of gastric contents. Domperidone should no longer be used for the treatment of bloating and heartburn. (e.g. For the treatment of chronic conditions such as gastroparesis, dyspepsia, and gastro-oesophageal reflux disease).

Advice to healthcare professionals is as follows:

- Domperidone is restricted to use in the relief of nausea and vomiting. All other indications should be considered as off-license.

- When prescribed, domperidone should be used at the lowest effective dose for the shortest possible time. This means that long-term use for chronic conditions is now problematic,
- Domperidone is now contra-indicated in people: (1) with conditions where cardiac conduction is, or could be, impaired; (2) with underlying cardiac diseases such as congestive heart failure; (3) receiving other medicines known to prolong QT interval or potent CYP3A4 inhibitors (e.g. ketoconazole, erythromycin); and (4) severe hepatic impairment. All of these contra-indications, except for severe hepatic impairment, were previously cautions rather than conta-indications.
- Prescribers should ensure that treatment for the relief of nausea and vomiting is within recommended dosage and prescribed at the lowest effective dose for the shortest possible time (not usually more than one week).
- Patients currently receiving long-term treatment with domperidone should be reassessed at a routine appointment to advise on treatment continuation, dose change or cessation.

Treatment of gastroparesis

In gastroparesis, unresponsive to removal of any iatrogenic causes, prokinetic agents, such as metoclopramide and domperidone are still considered the mainstays of therapy. Both drugs are of equivalent efficacy in reducing symptoms and both are now restricted in terms of authorised indications, contra-indications and safety concerns. Domperidone does not cross the blood brain barrier and has not been associated with dystonic reactions or tardive dyskinesia; it has been shown to be as effective as metoclopramide in terms of gastric emptying. However, as detailed above, domperidone has been associated with arrhythmias due to prolongation of the QT interval and potentially hazardous drug interactions.

In patients for whom domperidone or metoclopramide are not appropriate, alternative options are very limited. For example, low dose erythromycin (250 to 500mg three times daily for up to four weeks) is of some benefit, but it is unlicensed for this indication and long-term efficacy is limited by tachyphylaxis.

PACEF Recommendations:
All patients currently prescribed domperidone should have their treatment reviewed at their next routine appointment. Prescribers should ensure that treatment for the relief of nausea and vomiting is within recommended dosage and prescribed at the lowest effective dose for the shortest possible time (not usually more than one week). Within this context, domperidone continues to be designated GREEN. Patients for whom domperidone is now contra-indicated will need to switch to an alternative treatment. Patients that are currently prescribed interacting medicines known to prolong the QT interval or inhibit CYP3A4 will need to have their medicines reviewed to either remove the interacting medicine or reconsider the choice of domperidone. As with our recent guidance on long-term use of metoclopramide, PACEF recognize that there are difficulties in identifying an effective alternative to long-term metoclopramide or long-term domperidone, particularly in the treatment of gastroparesis insufficiently responsive to other therapies. The MHRA acknowledge that there may be a clinical need to continue long-term domperidone off-license in some patients. Where this is under consideration, the overall safety profile of domperidone, particularly its cardiac risk and potential interactions with other medicines, must be considered. If continued off-license use is intended, the patient must be informed that the treatment is off-license and given information on the associated risks. This consultation must be recorded in the patient's medical record. New patients should only be initiated on domperidone or metoclopramide longer-term on the advice of a gastroenterologist: designation AMBER without shared care.

References:
Drug Safety Update, Vol 7 No 10, May 2014, Domperidone – risks of cardiac side effects.
PACE Bulletin, Vol 7 No 21, December 2013, Metoclopramide – risk of neurological effects

RAPID DRUG RE-ASSESSMENT: *SILDENAFIL CHEWABLE TABLETS 25MG, 50MG AND 100MG (NIPATRA)*

Following a significant price reduction, sildenafil chewable tablets (*Nipatra*) are still not approved for use.

Sildenafil chewable tablets 25mg, 50mg and 100mg (*Nipatra*) hold a marketing authorisation for the treatment of erectile dysfunction. A cost comparison with other formulations of sildenafil and alternative PDE5 inhibitors reveals that *Nipatra* is comparably priced to low cost generic sildenafil and much lower cost than alternatives. Prescribing data for Lincolnshire reveals that there is virtually no market in Lincolnshire at present for the alternative orodispersible formulation of a PDE5 inhibitor, vardenafil 10mg orodispersible tablet (*Levitra Orodispersible*)

Product	**Pack size**	**Cost (£)**
Sildenafil chewable tablets 25mg (*Nipatra*)	**4 tabs**	**£1.05**
	8 tabs	**£2.10**
Sildenafil chewable tablets 50mg (*Nipatra*)	**4 tabs**	**£1.03**
	8 tabs	**£2.06**
Sildenafil chewable tablets 100mg (*Nipatra*)	**4 tabs**	**£1.11**
	8 tabs	**£2.22**
Sildenafil tablets 25mg (generic)	4 tabs	£1.08
Sildenafil tablets 50mg (generic)	4 tabs	£1.15
Sildenafil tablets100mg (generic)	4 tabs	£1.23
Sildenafil 25mg tablets (*Viagra*)	4 tabs	£16.59
	8 tabs	£33.19
Sildenafil 50mg tablets (*Viagra*)	4 tabs	£21.27
	8 tabs	£42.54
Sildenafil 100mg tablets (*Viagra*)	4 tabs	£23.50
	8 tabs	£46.99
Avanafil 50mg tablets (*Spedra*)	4 tabs	£10.94
	8 tabs	£19.70
Avanafil 100mg tablets (*Spedra*)	4 tabs	£14.08
	8 tabs	£26.26
Avanafil 200mg tablets (*Spedra*)	4 tabs	£21.90
	8 tabs	£39.40
Tadalafil 10mg tablets (*Cialis*)	4 tabs	£26.99
Tadalafil 20mg tablets (*Cialis*)	4 tabs	£26.99
	8 tabs	£53.98
Vardenafil 5mg tablets (*Levitra*)	4 tabs	£7.56
	8 tabs	£15.12
Vardenafil 10mg tablets (*Levitra*)	4 tabs	£14.08
	8 tabs	£28.16
Vardenafil 20mg tablets (*Levitra*)	4 tabs	£23.48
	8 tabs	£46.96
Vardenafil 10mg orodispersible tablets (*Levitra Orodispersible*)	4 tabs	£17.88

PACEF Recommendation:
Generic sildenafil tablets (25mg, 50mg and 100mg) remain the first line PDE5 inhibitor of choice in the treatment of erectile dysfunction. Forthcoming guidance from the Department of Health is likely to lift current restrictions on prescribing of PDE5 inhibitors in primary care, but only for generic sildenafil tablets. Prescribers are urged to review all patients currently receiving alternative higher cost branded PDE5

inhibitors to ensure that as many patients as possible are prescribed generic sildenafil. Prescribing patterns across the county reveal that there is virtually no demand for an orodispersible or chewable formulation of a PDE5 inhibitor. Despite their low cost, PACEF felt that there was no role for sildenafil chewable tablets (*Nipatra*) and they were designated RED-RED and not approved for inclusion on the *Lincolnshire Joint Formulary.*

RAPID DRUG ASSESSMENT: *AVANAFIL 50MG, 100MG AND 200MG TABLETS (SPEDRA)*

Avanafil tablets (*Spedra*) have not been approved for use for the treatment of erectile dysfunction.

Avanafil (*Spedra*) is a newly launched PDE5 inhibitor authorised 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. Certain patient groups included in SLS criteria were excluded from these trials, including patients with erectile dysfunction related to spinal cord injury, other neurological disorders and severe renal impairment. As a result of this, there is a lack of data in some of the NHS approved patient groups.

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 can h 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.

The cost comparison above confirms that avanafil (*Spedra*) is a higher cost branded PDE5 inhibitor compared to the preferred low cost first line option: generic sildenafil tablets

PACEF Recommendation:
Having assessed the evidence, PACEF can see no reason to approve avanafil 50mg, 100mg and 200mg tablets (Spedra) for inclusion in the *Lincolnshire Joint Formulary*; designation RED-RED. Generic sildenafil tablets (25mg, 50mg and 100mg) remain the first line PDE5 inhibitor of choice.

RAPID REVIEW: *RESOURCE THICKENUP CLEAR*

***Resource ThickenUp Clear* is approved for use as a xanthan gum based food and drink thickener for patients with dysphagia.**

Resource ThickenUp Clear (*RTUC*) is a xanthan gum based food and drink thickener designed to aid swallowing in patients suffering from oropharyngeal dysphagia.
While there are many other thickening products available on the market, the majority of the alternatives are maize starch based (e.g. *Multi-Thick, Nutilis, Resource ThickenUp, Thick and Easy, Thicken Aid, Thixo-D* and *Vitaquick*). In Lincolnshire the Fresenius Kabi product, *Thick and Easy*, is most widely used both within United Lincolnshire Hospitals Trust and in primary care, particularly in care homes.

Although maize starch based products are widely used, they are not without their problems. For example:

(1) they alter the odour and taste of liquid or food and can render food or drink unappetising. Clear drinks, like water, are rendered opaque and this can deter the patient from drinking or finishing a drink once started. Patients can become dehydrated if they are not able to consume sufficient fluids and unappetising drinks can act as a barrier to this.
(2) starch based thickeners continue to thicken over time rendering a drink progressively thicker as time goes on. This can result in patients starting a drink, but never finishing one.
(3) people with dysphagia can have a tendency to hold food or drink in their mouth longer than non-dysphagic patients. Amylase enzymes in saliva can begin to break down maize starch in the mouth before it can be swallowed. As a result of this, a thickened drink can become thinner in the mouth, re-creating swallowing difficulties.

Resource ThickenUp Clear is one of only two xanthan gum based products currently available on the UK market; the other product is *Nutilis Clear*. RTUC is visually clear and flavourless and when added to food or drink does not change the odour or taste; it also leaves the food or drink looking visually more appealing and appetising. Clear drinks thickened with *RTUC* remain fully transparent (i.e. water continues to look like water) and do not continue to thicken over time as maize starch containing products do. *RTUC* is also amylase resistant and is not broken down by saliva.

A cost comparison of all of the available food and drink thickening products reveals the following:

	Unit size and cost	**No of doses per tin**	**Cost per dose**
Multi-thick (maize starch)	250g -£4.83	62.5	£0.08
Nutilis Powder (maize starch)	300g - £4.92 20 x 12g sachets - £6.40	50-75 20 (sachets)	£0.07 - £0.10 £0.32 (per sachet)
Nutilis Clear (xanthan gum)	175g - £8.46	87.5	£0.09
Resource ThickenUp (maize starch)	227g - £4.55 75 X 4.5g sachets - £17.28	50.44 75 (sachets)	£0.09 £0.23 (per sachet)
***Resource ThickenUp Clear* (xanthan gum)**	**125g - £8.46** **24 x 1.2g sachets - £5.28**	**104** **24 (sachets)**	**£0.08** **£0.22 (per sachet)**
Thick and Easy (maize starch)	225g - £4.93 4.5kg - £82.56 100 x 9g sachet - £30.00	50 1000 100 (sachets)	£0.10 £0.08 £0.30 (per sachet)
Thicken Aid (maize starch)	225g -£3.71 100 x 9g sachet - £22.40	50 100 (sachets)	£0.07 £0.22 (per sachet)
Thixo-D Original (maize starch)	375g - £5.79	75	£0.08
Vitaquick (maize starch)	300g - £6.87 2kg -£37.93	100 667	£0.07 £0.06

From this it can be concluded that:

(1) *RTUC* is no more expensive than maize starch based alternatives, particularly at syrup consistency.
(2) It is much more expensive to prescribe these products as individual sachets rather than bulk packs. Prescribers should ensure that bulk packs are prescribed wherever possible.
(3) The number of scoops of each product required to thicken food or drink for each stage of dysphagia influences the overall cost of the product. Because *Resource ThickenUp Clear* dosage increases by one scoop for each stage of dysphagia while other products increase by smaller increments, *RTUC* can be more expensive than competitors at the custard and pudding consistencies (see below).

	Stage 1 dysphagia (syrup)	**Stage 2 dysphagia (custard)**	**Stage 3 dysphagia (pudding)**
Multi-thick (maize starch)	1.5 scoops (4g) in 100ml	2 - 2.5 scoops (5.4-6.75g)	2.5 – 3.5 scoops (6.75 – 9.45g) in 100ml
Nutilis Powder (maize starch)	1 – 1.5 scoops (4-6g)in 100ml	1.5 – 2 scoops (6-8g) in 100ml	2-3 scoops (8-10g) in 100ml
Nutilis Clear (maize starch)	0.5 scoops (2g) in 100ml	1.5 scoops (6g) in 100ml	3 scoops (12g) in 100ml
Resource Thickenup (maize starch)	1 scoop (4.5g) in 100ml	1.5 scoops (6.75g) in 100ml	2 scoops (9g) in 100ml
***Resource ThickenUp Clear* (xanthan gum)**	**1 scoop (1.2g) in 100ml**	**2 scoops (2.4g) in 100ml**	**3 scoops (3.6g) in 100ml**
Thick and Easy (maize starch)	1 scoop (4.5g) in 100ml	1.5 scoops (6.8g) in 100ml	2 scoops (9g) in 100ml
Thicken Aid (maize starch)	1 scoop (4.5g) in 100ml	1.5 scoops (6.75g) in 100ml	2 scoops (9g) in 100ml
Thixo-D Original (maize starch)	1 scoop (5g) in 100ml	1.25 scoops (6.25g) in 100ml	1.5 scoops (7.5g) in 100ml
Vitaquick (starch powder)	1 scoop (5g) in 150ml	2 – 2.5 scoops (10g – 12.5g) in 150ml	4 scoops (20g) in 150ml

The presence of a deteriorating condition can result in the long-term use of a thickener. Conversely, following a stroke or head injury, thickeners may only be required short-term. Anything that improves the patient's ability to drink is likely to improve hydration and quality of life. The length of time that thickened fluids are required varies from a few days to several months to the end of life in some cases.

PACEF Recommendation:

PACEF are convinced that *Resource ThickenUp Clear* offers a genuine alternative to conventional maize starch based thickeners in patients with dysphagia; it may be considered more palatable by some patients and may help to ensure better hydration and nutrition. At syrup consistency, the product is no more expensive than competitors, but may become so at the custard and pudding consistency required for stage 2 and stage 3 dysphagia respectively. It is crucial that patients should only be prescribed a food/drink thickener following assessment by a Speech and Language Therapist. Subject to recommendation by a SALT, *Resource ThickenUp Clear* is approved for use. It is designated AMBER and approved for inclusion on the *Lincolnshire Joint Formulary* as an alternative to the maize starch based product *Thick and Easy.* The table below summarizes the likely quantities per month that might be required per patient dependent upon the consistency required. Food/drink thickeners should never be prescribed in response to an unsupported request from a

care home. Wherever possible, bulk packs should be prescribed to avoid the excessive cost associated with prescribing as individual sachets.

Resource ThickenUp Clear: Likely monthly usage (28 days) and monthly cost

Fluid amount per day	Stage 1 (syrup)	Stage 2 (custard)	Stage 3 (pudding)
200ml	1 tin (£8.46)	2 tins (£16.92)	2 tins (£16.92)
600ml *	**2 tins (£16.92)**	**4 tins (£33.84)**	**5 tins (£42.30)**
1000ml	3 tins (£25.38)	6 tins (£50.76)	9 tins (£76.14)
1500ml	5 tins (£42.30)	9 tins (£76.14)	13 tins (£109.98)
2000ml	6 tins (£50.76)	11 tins (£93.06)	17 tins (£143.82)

*It is reasonable to assume that a person with stage 1 dysphagia requiring syrup consistency fluids will use approximately 2 tins per month at a cost of £16.92.

RAPID RE-ASSESSMENT: *OMNITEST 3 METER AND BLOOD GLUCOSE TESTING STRIPS*

Earlier in the year PACEF evaluated all of the available lower cost blood glucose testing strips and meters against a number of key criteria. As part of that process, most of the products evaluated were approved for use within certain criteria (see *PACE Bulletin*, Volume 8 No 2, *Prescribing Lower Cost Blood Glucose Testing Strips and Meters* (February 2014 and subsequent updates)). One of the products that failed to meet key criteria first time round was the B.Braun product *Omnitest 3*. The two problems identified were that: (1) the design of the meter allowed for test results to be deleted and (2) the memory capacity for test results was felt to be insufficient (i.e. below the threshold of 450 tests).

Since the publication of the *PACE Bulletin*, B.Braun have modified the software of the existing meter to increase memory capacity for test results to 500 tests and to remove the test result delete function. As a result of this, the *Omnitest 3* meter now complies with all of the PACEF essential criteria and is approved for use as one of the preferred lower cost products.

Supplies of the new meter have been available in the UK since April 28th 2014 and priority will be given for supplies in those areas that have included the updated meter on their formulary or approved lists. There are currently no plans to replace the older style *Omnitest 3* meters that have already been distributed to patients. However, for group 2 drivers or those requiring a meter with larger memory capacity, arrangements can be made to replace with the updated version through B.Braun.

The updated evaluation of *Omnitest 3* against key criteria is included in the summary table below:

Blood Glucose Testing Meter and Strip	Compliant with ISO 15197: 2013?	Is the memory capacity more than 450 tests?	Is the memory easily deletable?	Can results be down loaded?	Is calibration required?	Are results displayed in mmol/l?	Does the device turn on automatically?
Accu-Chek Active	Fully compliant	Yes	No	Yes	No	Yes	Yes
Element	Fully compliant	Yes	No	Yes	No	Yes	Yes
GlucoLab	Fully compliant	Yes	No	Yes	No	Yes	Yes
GlucoMen GM	Fully compliant	No	No	Yes	No	Yes	Yes
GlucoRx Nexus	Fully compliant	Yes	No	Yes	No	Yes	Yes
GlucoRx Nexus Mini	Fully compliant	Yes	No	Yes	No	Yes	Yes

GlucoRx Nexus Voice	Fully compliant	Yes	No	Yes	No	Yes	Yes
iCare Advanced	Fully compliant	Yes	No	Yes	No	Yes	Yes
Microdot +	Fully compliant	Yes	No	Yes	No	Yes	Yes
MyLife Pura	Fully compliant	Yes	No	Yes	No	Yes	Yes
Omnitest 3	**Fully compliant**	**Yes**	**No**	**Yes**	**No**	**Yes**	**Yes**
TRUEyou	Fully compliant	Yes	No	Yes	No	Yes	Yes
WaveSense JAZZ	Fully compliant	Yes	No	Yes	No	Yes	Yes

PACEF Recommendation:
Omnitest 3 **is confirmed as fully compliant with PACEF criteria and is designated GREEN within defined prescribing criteria; it is also approved for inclusion in the** ***Lincolnshire Joint Formulary.*** **The online version of the** ***PACE Bulletin*** **evaluating lower cost BGTS (Vol 8 No 2 (February 2014)) has been updated to include this product and provides detailed information on the context within which a lower cost product might be preferred or a switch from a higher cost product advocated.**

REVIEW OF EXPIRY DATES OF BLOOD GLUCOSE TESTING STRIPS

Following the publication of PACEF advice on the use of the lower cost blood glucose meters and test strips, we have been asked to publish further information on the expiry dates of each of the strips. This information is tabulated below:

Blood glucose strip	**Pack size**	**Shelf life of strips once opened.**	**Cost**
Accu-Chek Active	50	Approximately 18 months post production	£9.95
Element	2 x 25	Pot has 3 month expiry once opened; 2 x 25 will last 6 months if used consecutively	£9.89
Glucolab	2 x25	Pot has 3 month expiry once opened; 2 x 25 will last 6 months if used consecutively	£9.89
GlucoRX Nexus	2x25	Pot has 6 month expiry. 2 x 25 will last 12 months if used consecutively	£9.95
Icare Advanced	50	6 months	£9.70
Microdot +	50	6 months	£10.00
Mylife Pura	2 x 25	Pot has 6 month expiry. 2 x 25 will last 12 months if used consecutively	£9.50
Omnitest 3	2x25	6 months	£9.89
TRUEyou	50	4 months	£9.92
WaveSense JAZZ	1 x 50	6 months	£9.87
WaveSense JAZZ Duo+	2 x 25	Pot has 6 month expiry. 2 x 25 will last 12 months if used consecutively	£9.95

PACEF Comment:
For very infrequent testers, the most cost effective options in terms of the avoidance of unnecessary expired stock are: *Accu-Chek Active*, *GlucoRx Nexus*, *Mylife Pura*, *Omnitest 3* or *WaveSense JAZZ*.

NICE UPDATE

NICE TECHNOLOGY APPRAISAL 304: *TOTAL HIP REPLACEMENT AND RESURFACING ARTHROPLASTY FOR END-STAGE ARTHRITIS OF THE HIP* (FEBRUARY 2014)

Prostheses for total hip replacement and resurfacing arthroplasty are recommended as treatment options for people with end-stage arthritis of the hip only if the prostheses have rates (or projected rates) of revision of 5% or less at 10 years.

NICE TECHNOLOGY APPRAISAL 305: *AFLIBERCEPT FOR TREATING VISUAL IMPAIRMENT CAUSED BY MACULAR OEDEMA SECONDARY TO CENTRAL VEIN OCCLUSION* (FEBRUARY 2014)

Aflibercept solution for injection is recommended as an option for treating visual impairment caused by macular oedema secondary to central retinal vein occlusion only if the manufacturer provides aflibercept solution for injection with the discount agreed in the patient access scheme.

PACEF Recommendation:
Aflibercept solution for injection (*Eylea*) is designated RED for adults for the treatment of visual impairment caused by macular oedema secondary to central retinal vein occlusion. It has been approved for inclusion in the *Lincolnshire Joint Formulary* for this indication.

NICE TECHNOLOGY APPRAISAL 306: *PIXANTRONE MONOTHERAPY FOR TREATING MULTIPLY RELAPSED OR REFRACTORY AGGRESSIVE NON-HODGKINS'S B-CELL LYMPHOMA* (FEBRUARY 2014)

Pixantrone monotherapy is recommended as an option for treating adults with multiply relapsed or refractory aggressive non-Hodgkin's B-cell lymphoma only if:

- the person has previously been treated with rituximab **and**
- the person is receiving third- or fourth-line treatment **and**
- the manufacturer provides pixantrone with the discount agreed in the patient access scheme.

PACEF Recommendation:
Pixantrone infusion (*Pixuvri)* is designated RED as monotherapy for treating multiply relapsed or refractory aggressive non-Hodgkin's B-cell lymphoma for patients who meet the criteria stipulated by NICE. It is approved for inclusion in the *Lincolnshire Joint Formulary* for this indication.

NICE TECHNOLOGY APPRAISAL 307: *AFLIBERCEPT IN COMBINATION WITH IRINOTECAN AND FLUOROURACIL-BASED THERAPY FOR TREATING METASTATIC COLORECTAL CANCER THAT HAS PROGRESSED FOLLOWING PRIOR OXALIPLATIN-BASED CHEMOTHERAPY* (MARCH 2014)

Aflibercept in combination with irinotecan and fluorouracil-based therapy is not recommended within its marketing authorisation for treating metastatic

colorectal cancer that is resistant to or has progressed after an oxaliplatin containing regimen.

Afibercept (*Zaltrap*) is licensed for use in combination with irinotecan/5-fluorouracil/folinic acid (FOLFIRI) chemotherapy for adults with metastatic colorectal cancer (MCRC) that is resistant to or has progressed after an oxaliplatin-containing regimen.

PACEF Recommendation:
Aflibercept intravenous infusion (*Zaltrap*) is designated RED-RED for this indication and is not recommended for inclusion in the *Lincolnshire Joint Formulary.*

MEDICINES AND HEALTHCARE REGULATORY AGENCY: *DRUG SAFETY UPDATE* (APRIL 2014)

TUMOUR NECROSIS FACTOR ALPHA INHIBITORS: RISK OF TUBERCULOSIS – SCREEN ALL PATIENTS BEFORE STARTING TREATMENT AND MONITOR THEM CLOSELY

As reported in *PACE Bulletin* Vol 8 No 7 (April 2014), there is an increased risk of tuberculosis or reactivation of latent tuberculosis during treatment with tumour necrosis factor alpha (TNF-alpha) inhibitors. Tuberculosis in patients receiving TNF-alpha inhibitors can be life-threatening, and deaths from tuberculosis have occurred in these patients. TNF-alpha inhibitors are therefore contraindicated in patients with active tuberculosis or other severe infections. Patients should be screened for active and latent tuberculosis before starting treatment with a TNF-alpha inhibitor. Patients should be monitored closely for infectious diseases, including tuberculosis before, during, and after treatment

Advice for healthcare professionals:

- TNF-alpha inhibitors are contraindicated in patients with active tuberculosis or other severe infections.

Pretreatment screening

- Assess all patients for active and latent tuberculosis before starting treatment with a TNF-alpha inhibitor and record the results on the patient's alert card. This assessment should include:
    - a detailed medical history of possible previous contact with tuberculosis and any history of immunosuppressive therapy;
    - tuberculin skin test;
    - chest radiograph
- Be aware of the risk of false-negative tuberculin skin-test results, especially in patients who are severely ill or immunocompromised.

Diagnosis of tuberculosis

Active infection

- If active tuberculosis is diagnosed, do not start treatment with a TNF-alpha inhibitor.

Latent infection

- If latent tuberculosis is diagnosed, start treatment for this infection before treatment with a TNF-alpha inhibitor
- If latent tuberculosis is suspected, consider antituberculous therapy before starting treatment with a TNF-alpha inhibitor
- In these situations, consult a physician with expertise in tuberculosis treatment, and carefully consider the balance of benefits and risk for TNF-alpha inhibitor treatment.

Monitoring

- Closely monitor patients for infectious diseases, including tuberculosis, before, during, and after treatment with a TNF-alpha inhibitor.

Advice to give to patients

- Inform all patients that they should seek medical advice if symptoms of tuberculosis develop during or after treatment with a TNF-alpha inhibitor (eg, persistent cough, weight loss, low-grade fever).
- Give patients being treated with a TNF-alpha inhibitor a patient alert card, which includes information on the risk of tuberculosis and other infectious diseases.

PACEF Comment

***PACE Bulletin* Vol 8 No 7 (April 2014) highlighted the potentially fatal link between anti-TNF alpha drugs and infectious diseases like TB. The MHRA guidance adds to the advice PACEF has already issued. Particular reference is drawn to the use of patient alert cards which are provided within the patient information leaflets provided by the manufacturers of these products. The patient alert card for infliximab (*Remicade*) instructs the patients that this card should be shown to any doctor involved in their treatment. The card allows for contact details to be recorded for the specialist and for details of pre-treatment screening, allergies and current medication to be recorded. It also provides the patient with detailed information on the management of infections and heart failure.**

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