

Lincolnshire Prescribing and Clinical Effectiveness Bulletin

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What's new this month?

- **Sukkarto** is a new lower cost sustained release tablet formulation of metformin and is approved for use in those intolerant to standard release metformin (see page 4).
- Venlafaxine should be prescribed as a low cost immediate release twice daily generic formulation wherever possible. Where a modified release product is required, a branded prescription for either *Venlablue XL* capsules or *Vensir XL* capsules should be issued (see page 5).
- Ropinirole modified release tablets 2mg, 3mg, 4mg, 6mg and 8mg (*Ippinia XL*) are designated AMBER without shared care and approved for inclusion in the *Lincolnshire Joint Formulary*. Both the *Repinex XL* brand (2mg, 4mg and 8mg MR tablets) and the *Spiroco XL* brand are also approved for use (see page 6).
- All modified release galantamine should be prescribed as a lower cost brand such as *Consion XL*, *Galantex XL*, *Gatalin XL*, *Gazylan XL* or *Luventa XL*. All of these products are designated AMBER with shared care and are approved for inclusion in the *Lincolnshire Joint Formulary*. Prescribers are urged to review all patients currently prescribed galantamine modified release capsules generically or as *Acumor XL*, *Elmino XL*, *Galsya XL*, *Lotprosin XL* and the originator brand *Requip XL* with a view to switching to their preferred low cost brand (see page 8).
- In moderate to severe Alzheimer's disease, patients taking memantine who develop swallowing difficulties should be considered for either: memantine 10mg and 20mg orodispersible tablets (*Valios*) or memantine oral solution 10mg/ml. Both oral solution and orodispersible tablets are similarly priced; both are designated AMBER with shared care and approved for inclusion in the *Lincolnshire Joint Formulary* (see page 9).
- In mild to moderate dementia in Alzheimer's disease, patients taking rivastigmine who develop or experience swallowing difficulties should be considered for low cost rivastigmine transdermal patches (*Alzest*); designated AMBER with shared care (see page 10).
- The recommended starting dose of etoricoxib for the treatment of rheumatoid arthritis and ankylosing spondylitis has been reduced to 60 mg once daily, with the option to increase to a maximum of 90 mg once daily if necessary (see page 11).
- Some patients may have exacerbation or rebound symptoms of rosacea following initiation of treatment with brimonidine 3mg/g gel (*Mirvaso*). It is important to initiate treatment with a small amount of gel and increase the dose gradually, based on tolerability and treatment response (see page 12).

CONTENTS

Page 4	Rapid Cost Comparison: <i>Metformin modified release tablets 500mg and 1 gram (Sukkarto)</i>
Page 5	Rapid Cost Comparison: <i>Venlafaxine modified release capsules (VenlaBlue XL and Vensir XL)</i>
Page 6	Rapid Cost Comparison: <i>Ropinirole modified release tablets 2mg, 3mg, 4mg, 6mg and 8mg (Ippinia XL)</i>

Page 8	Rapid Cost Comparison: <i>Galantamine sustained release 8mg, 16mg and 24mg (Conson XL, Gazylan XL, Luventa XL)</i>
Page 9	Rapid Cost Comparison: <i>Memantine hydrochloride 20mg orodispersible tablet (Valios)</i>
Page 10	Rapid Cost Comparison: <i>Rivastigmine transdermal patches 4.6mg/24hour, 9.5mg/24hour (Alzest/Prometax/Voleze) and 13.3mg/24 hour patch (Erastig)</i>
Page 11	Medicines and Healthcare Products Regulatory Agency (MHRA) <i>Drug Safety Update (October 2016): Etoricoxib (Arcoxia): revised dose recommendation for rheumatoid arthritis and ankylosing spondylitis</i>
Page 12	Medicines and Healthcare Products Regulatory Agency (MHRA) <i>Drug Safety Update (November 2016): Brimonidine gel (Mirvaso): Risk of exacerbation of rosacea.</i>

SUMMARY OF PACEF DECISIONS: NOVEMBER 2016 UPDATE

Device, Dressing or Drug	Indication(s)	Traffic Light and Joint Formulary Status
Galantamine modified release capsules (Conson XL) (Dr Reddy's Laboratories UK Ltd)	For the treatment of mild to moderate dementia in Alzheimer's disease	AMBER with shared care. Approved for inclusion in the <i>Lincolnshire Joint Formulary</i> . Preferred lower cost brand.
Galantamine sustained release capsules (<i>Galantex XL</i>) (Creo Pharma Ltd)	For the treatment of mild to moderate dementia in Alzheimer's disease	AMBER with shared care. Approved for inclusion in the <i>Lincolnshire Joint Formulary</i> . Preferred lower cost brand.
Galantamine sustained release capsules (<i>Gatalin XL</i>) (Aspire)	For the treatment of mild to moderate dementia in Alzheimer's disease	AMBER with shared care. Approved for inclusion in the <i>Lincolnshire Joint Formulary</i> . Preferred lower cost brand.
Galantamine sustained release capsules (<i>Gazylan XL</i>) (Teva UK Ltd)	For the treatment of mild to moderate dementia in Alzheimer's disease	AMBER with shared care. Approved for inclusion in the <i>Lincolnshire Joint Formulary</i> . Preferred lower cost brand.
Galantamine sustained release capsules (<i>Luventa XL</i>) (Fontus Health Ltd)	For the treatment of mild to moderate dementia in Alzheimer's disease	AMBER with shared care. Approved for inclusion in the <i>Lincolnshire Joint Formulary</i> . Preferred lower cost brand.
Memantine hydrochloride 10mg and 20mg orodispersible tablet (<i>Valios</i>) (Dr Reddy's Laboratories UK Ltd)	For the treatment of moderate to severe Alzheimer's dementia.	AMBER with shared care. Approved for inclusion in the <i>Lincolnshire Joint Formulary</i> . Standard 10mg and 20mg tablets remain the preferred memantine formulation.
Metformin modified release tablets 500mg and 1 gram (<i>Sukkarto</i>) (Morningside)	For the treatment of type 2 diabetes mellitus in adult patients who are intolerant of standard release metformin and in whom prolonged release tablets allow the use of a dose not previously tolerated.	GREEN Approved for inclusion in the <i>Lincolnshire Joint Formulary</i> .
Rivastigmine transdermal patches 4.6mg/24hour, 9.5mg/24hour (<i>Alzest</i>) (Dr Reddy's Laboratories UK Ltd)	Licensed for the treatment of mild to moderate dementia in Alzheimer's disease	AMBER Specialist initiation; shared care guideline is required. Approved for inclusion in the <i>Lincolnshire Joint Formulary</i> . The use of the patch should be restricted to those for whom rivastigmine is considered an appropriate therapy and the patch an appropriate formulation.
Rivastigmine transdermal patches 4.6mg/24hour, 9.5mg/24hour and 13.3mg/24 hour (<i>Erastig</i>) (Teva UK Ltd)	Licensed for the treatment of mild to moderate dementia in Alzheimer's disease	RED-RED Not approved for inclusion in the <i>Lincolnshire Joint Formulary</i> .

Rivastigmine transdermal patches 4.6mg/24hour, 9.5mg/24hour and 13.3mg/24 hour (Exelon) (Novartis)	Licensed for the treatment of mild to moderate dementia in Alzheimer's disease or in Parkinson's disease	RED-RED 4.6mg/24hour, 9.5mg/24hour. Removed from the <i>Lincolnshire Joint Formulary</i> AMBER 13.3mg/24 hour Specialist initiation; shared care guideline is required. The use of the patch should be restricted to those for whom rivastigmine is considered an appropriate therapy and the patch an appropriate formulation. Remains of the <i>Lincolnshire Joint Formulary</i> .
Rivastigmine transdermal patches 4.6mg/24hour, 9.5mg/24hour (<i>Prometax</i>) (Novartis)	Licensed for the treatment of mild to moderate dementia in Alzheimer's disease	RED-RED Not approved for inclusion in the <i>Lincolnshire Joint Formulary</i> .
Rivastigmine transdermal patches 4.6mg/24hour, 9.5mg/24hour (<i>Voleze</i>) (Focus Pharmaceuticals)	Licensed for the treatment of mild to moderate dementia in Alzheimer's disease	RED-RED Not approved for inclusion in the <i>Lincolnshire Joint Formulary</i> .
Ropinirole modified release tablets 2mg, 3mg, 4mg, 6mg and 8mg (<i>Ipinnia XL</i>) (Ethypharm UK Ltd)	For use as monotherapy or as an adjunct to levodopa in Parkinson's disease.	AMBER without shared care. Approved for inclusion in the <i>Lincolnshire Joint Formulary</i> .
Ropinirole modified release tablets 2mg, 4mg, and 8mg (<i>Repinex XL</i>) (Aspire Pharma)	For use as monotherapy or as an adjunct to levodopa in Parkinson's disease.	AMBER without shared care. Included in the <i>Lincolnshire Joint Formulary</i> .
Ropinirole modified release tablets 2mg, 4mg, and 8mg (<i>Spiroco XL</i>) (Teva UK Ltd)	For use as monotherapy or as an adjunct to levodopa in Parkinson's disease.	AMBER without shared care. Included in the <i>Lincolnshire Joint Formulary</i> .
Venlafaxine modified release capsules 37.5mg, 75mg, 150mg (<i>VenlaBlue XL</i>) (Creo Pharma)	For major depression, generalised anxiety disorder and social anxiety disorder.	GREEN. Approved for inclusion in the <i>Lincolnshire Joint Formulary</i> .
Venlafaxine modified release capsules 75mg, 150mg, 225mg (<i>Vensir XL</i>) (Morningside)	For major depression, generalised anxiety disorder and social anxiety disorder.	GREEN. Approved for inclusion in the <i>Lincolnshire Joint Formulary</i> .

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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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**.

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RAPID COST COMPARISON: METFORMIN SUSTAINED RELEASE TABLETS 500MG AND 1G (SUKKARTO SR)

Sukkarto SR is a new lower cost sustained release tablet formulation of metformin and is approved for use in those intolerant to standard release metformin.

The United Kingdom Prospective Diabetes Study (UKPDS) established metformin as the first line drug of choice for the treatment type 2 diabetes. In the study, metformin was shown to reduce the rates of myocardial infarction, diabetes related death and all-cause mortality. Unfortunately, the drug is commonly associated with gastrointestinal side effects, including nausea, vomiting and diarrhoea; these effects are often transient and can be minimised by taking the drug with meals and slowly titrating the dose up over several weeks. Approximately 5% of patients will be forced to discontinue therapy as a result of gastrointestinal intolerance. Standard *BNF* advice is to initiate on 500mg with breakfast for at least a week, increasing to 500mg with breakfast and evening meal for at least another week and then increasing to 500mg with breakfast, lunch and evening meal. The usual maximum dose is 2g daily in divided doses. Judicious use of modified release metformin in those experiencing gastric intolerance to standard release metformin can help to maximise the number of patients able to benefit.

Sukkarto SR is a new lower cost sustained release formulation of metformin. A cost comparison reveals the following:

Drug	Dose	Cost
Metformin 500mg tablets (generic)	500mg twice daily	£1.72
	500mg three times daily	£2.58
Metformin 500mg sustained release tablets (<i>Bolamyn SR</i>) (Teva UK Ltd)	500mg once daily	£3.20
Metformin 1g sustained release tablets (<i>Bolamyn SR</i>) (Teva UK Ltd)	1g once daily	£5.06
Metformin 500mg sustained release tablets (<i>Diagemet XL</i>) (Genus Pharmaceuticals Ltd)	500mg once daily	£1.49
Metformin 500mg sustained release tablets (<i>Diagemet XL</i>) (Genus Pharmaceuticals Ltd)	1g once daily	£2.97
Metformin 500mg sustained release tablets (<i>Glucient SR</i>) (Consilient Health)	500mg once daily	£2.51
Metformin 1g sustained release tablets (<i>Glucient SR</i>) (Consilient Health)	1g once daily	£4.26
Metformin 500mg sustained release tablets (<i>Glucophage SR</i>) (Merck Serono Ltd)	500mg once daily	£2.66
Metformin 1g sustained release tablets (<i>Glucophage SR</i>) (Merck Serono Ltd)	1g once daily	£4.26
Metformin 500mg sustained release tablets (<i>Metabet SR</i>) (Morningside)	500mg once daily	£3.07
Metformin 1g sustained release tablets (<i>Metabet SR</i>) (Morningside)	1g once daily	£5.33
Metformin 500mg sustained release tablets (<i>Sukkarto SR</i>) (Morningside)	500mg once daily	£1.73

Metformin 1g sustained release tablets (<i>Sukkarto SR</i>) (Morningside)	1g once daily	£2.77
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If all metformin sustained release tablets were prescribed as *Sukkarto SR* the potential annual saving to the Lincolnshire CCGs would be as follows:

	Annual Saving
Lincolnshire East CCG	£112,956
Lincolnshire West CCG	£63,361
South Lincolnshire CCG	£40,785
South West Lincolnshire CCG	£51,783

PACEF Recommendation:

Where low cost generic standard release metformin is tolerated it should always be preferred first line. In patients experiencing intolerance to standard release metformin, low cost sustained release metformin should be considered as an alternative. Sustained release metformin is indicated for the treatment of type 2 diabetes mellitus in adult patients who are intolerant of standard release metformin and in whom prolonged release tablets allow the use of a dose not previously tolerated. Sustained release metformin tablets should always be prescribed as a low cost brand such as *Sukkarto SR*. Metformin 500mg and 1g sustained release tablets (*Sukkarto SR*) are designated GREEN and approved for inclusion in the *Lincolnshire Joint Formulary*.

RAPID COST COMPARISON: VENLAFAXINE MODIFIED RELEASE CAPSULES (VENLABLUE XL/VENSIR XL)

Venlafaxine should be prescribed as a low cost immediate release twice daily generic formulation wherever possible. Where a modified release product is required, a branded prescription for either *Venlablue XL* capsules or *Vensir XL* capsules should be issued.

Two modified release venlafaxine capsule formulations have recently reduced their prices, *Venlablue XL* and *Vensir XL*. An updated cost comparison of venlafaxine modified release preparations reveals that *Venlablue XL* capsules and *Vensir XL* capsules are now significantly lower in cost than any other modified release venlafaxine formulations:

Cost (28 days' supply)	37.5mg	75mg	150mg	225mg
<i>Alventa XL</i> caps (Consilient Health Ltd)	-	£19.12	£31.88	-
<i>Amphero XL</i> caps (Mylan Ltd)	-	£15.46	£25.77	-
<i>Depefex XL</i> caps (Chiesi Ltd)	-	£10.40	£17.40	-
<i>Efexor XL</i> caps (Pfizer) (also <i>Tariff</i> reimbursement rate for modified release capsules)	-	£22.08	£36.81	£47.11
<i>Politid XL</i> capsules (Actavis UK Ltd)	-	£23.41	£39.03	-
<i>Rodomel XL</i> caps (Teva UK Ltd)	-	£17.91	£29.85	-
<i>Sunveniz XL</i> tabs (Sun Pharmaceuticals UK Ltd)	-	£11.14	£18.64	-
<i>Tonpular XL</i> cap (Wockhardt UK Ltd)	-	£7.00	£12.00	-
<i>Venaxx XL</i> caps (Concordia)	-	£10.40	£17.40	-
<i>Venlablue XL</i> caps (Creo Pharma)	£5.25	£6.95	£9.95	-
<i>Venladex XL</i> tabs (Dexcel-Pharma Ltd)	-	£11.20	£18.70	-
<i>Venlalic XL</i> tabs (DB Ashbourne Ltd) (also <i>Tariff</i>)	£6.60	£11.20	£18.70	-

reimbursement rate for generic venlafaxine modified release tablets)				£33.60
<i>Venlaneo XL caps</i> (Kent Pharmaceuticals)	-	£22.08	£36.81	-
<i>Vensir XL caps (Morningside)</i>	-	£2.60	£3.90	£21.90
<i>ViePax XL tabs</i> (Dexcel-Pharma Ltd)	-	£10.44	£17.44	-

Immediate release venlafaxine products are available generically and are still significantly lower in cost than modified release preparations:

<u>Drug</u>	<u>Dose</u>	<u>Cost (28 days' supply)</u>
Venlafaxine 37.5mg tablets (generic)	37.5mg twice daily	£1.92
Venlafaxine 75mg tablets (generic)	75mg twice daily	£2.19

PACEF Recommendations:

Wherever possible, venlafaxine should be prescribed as a low cost immediate release twice daily generic formulation. Where a modified release product is required, a branded prescription for either *Venlablue XL capsules* or *Vensir XL capsules* should be issued. Both of these products in all strengths are designated GREEN and included in the *Lincolnshire Joint Formulary*. Specifically, modified release venlafaxine capsules should not be prescribed generically as the *Tariff* reimbursement price is set at the price of the premium price originator brand, *Efexor XL*.

Notes

If all modified release venlafaxine capsules were prescribed as a preferred low cost brand rather than generically or as *Efexor XL* the saving for the Lincolnshire CCGs would be as follows:

	Annual Saving
Lincolnshire East CCG	£52,487
Lincolnshire West CCG	£66,921
South Lincolnshire CCG	£204,371
South West Lincolnshire CCG	£30,014

RAPID COST COMPARISON: ROPINIROLE MODIFIED RELEASE TABLETS 2MG, 3MG, 4MG, 6MG AND 8MG (IPINNIA XL)

Ropinirole modified release tablets 2mg, 3mg, 4mg, 6mg and 8mg (*Ippinia XL*) are designated AMBER without shared care and approved for inclusion in the *Lincolnshire Joint Formulary*. Both the *Repinex XL* brand (2mg, 4mg and 8mg MR tablets) and the *Spiroco XL* brand are also approved for use.

Ippinia XL is a modified release tablet formulation of ropinirole indicated as monotherapy or as an adjunct to levodopa in the treatment of Parkinson's disease. The marketing authorisation and dose titration regimen are the same as for the original sustained release ropinirole formulation, *Requip XL*. *Ippinia XL* is a rebranding of a previously available product known as *Eppinix XL*.

A cost comparison between the currently available modified release ropinirole formulations reveals that *Ippinia XL* and *Spiroco XL* are currently the lowest cost products; *Repinex XL*

tablets are marginally higher in price but remain low cost in comparison to *Requip XL*, the originator brand:

	Dose	Cost (£) (28 days)
Ropinirole modified release tablets 2mg (Ippinia XL) (Ethypharm UK Ltd)	2mg once daily	£5.64
Ropinirole modified release tablets 3mg (Ippinia XL) (Ethypharm UK Ltd)	3mg once daily	£8.46
Ropinirole modified release tablets 4mg (Ippinia XL) (Ethypharm UK Ltd)	4mg once daily	£11.29
Ropinirole modified release tablets 6mg (Ippinia XL) (Ethypharm UK Ltd)	6mg once daily	£15.32
Ropinirole modified release tablets 8mg (Ippinia XL) (Ethypharm UK Ltd)	8mg once daily	£18.95
Ropinirole modified release tablets 2mg (<i>Ralnea XL</i>) (Consilient Health Ltd)	2mg once daily	£10.65
Ropinirole modified release tablets 4mg (<i>Ralnea XL</i>) (Consilient Health Ltd)	4mg once daily	£21.32
Ropinirole modified release tablets 8mg (<i>Ralnea XL</i>) (Consilient Health Ltd)	8mg once daily	£35.79
Ropinirole modified release tablets 2mg (<i>Raponer XL</i>) (Actavis UK Ltd)	2mg once daily	£12.54
Ropinirole modified release tablets 4mg (<i>Raponer XL</i>) (Actavis UK Ltd)	4mg once daily	£25.09
Ropinirole modified release tablets 8mg (<i>Raponer XL</i>) (Actavis UK Ltd)	8mg once daily	£42.11
Ropinirole modified release tablets 2mg (<i>Requip XL</i>) (GlaxoSmithKline) (also Tariff generic reimbursement rate)	2mg once daily	£12.54
Ropinirole modified release tablets 4mg (<i>Requip XL</i>) (GlaxoSmithKline) (also Tariff generic reimbursement rate)	4mg once daily	£25.09
Ropinirole modified release tablets 8mg (<i>Requip XL</i>) (GlaxoSmithKline) (also Tariff generic reimbursement rate)	8mg once daily	£42.11
Ropinirole modified release tablets 2mg (<i>Repinex XL</i>) (Aspire Pharma)	2mg once daily	£6.20
Ropinirole modified release tablets 4mg (<i>Repinex XL</i>) (Aspire Pharma)	4mg once daily	£12.50
Ropinirole modified release tablets 8mg (<i>Repinex XL</i>) (Aspire Pharma)	8mg once daily	£21.00
Ropinirole modified release tablets 2mg (<i>Spiroco XL</i>) (Teva UK Ltd)	2mg once daily	£5.63
Ropinirole modified release tablets 4mg (<i>Spiroco XL</i>) (Teva UK Ltd)	4mg once daily	£11.28
Ropinirole modified release tablets 8mg (<i>Spiroco XL</i>) (Teva UK Ltd)	8mg once daily	£18.94

Preferred products are highlighted in bold.

PACEF Recommendation:

Ropinirole modified release tablets 2mg, 3mg, 4mg, 6mg and 8mg (*Ippinia XL*) are designated AMBER without shared care and approved for inclusion in the *Lincolnshire Joint Formulary*. Both the *Repinex XL* brand (2mg, 4mg and 8mg MR tablets) and the *Spiroco XL* brand are also approved for use. Prescribers are urged to review all patients currently prescribed ropinirole modified release tablets generically or as *Requip XL* with a view to switching to their preferred low cost brand.

Notes

The potential annual savings for all four of the Lincolnshire CCGs if ropinirole modified release tablets were prescribed entirely as the *Ippinia XL* brand are as follows:

	Potential annual saving
Lincolnshire East CCG	£18,376
Lincolnshire West CCG	£15,910
South Lincolnshire CCG	£18,320
South West Lincolnshire CCG	£15,248

UPDATED RAPID COST COMPARISON: LOWER COST GALANTAMINE MODIFIED RELEASE FORMULATIONS (CONSION XL/ GAZYLAN XL/ LUVENTA XL)

This is an updated version of a *PACE Bulletin* feature that originally appeared in *PACE Bulletin* Vol 8 No 19 (December 2014).

Galantamine is a reversible inhibitor of acetylcholinesterase originally marketed as *Reminyl* and licensed for the treatment of mild to moderate Alzheimer's disease. A number of lower cost modified release formulations are now available; a cost comparison is provided below:

Product	Strength	Cost (£) (28 days)
Galantamine modified release capsules (<i>Acumor XL</i>) (Mylan Ltd)	8mg	£49.26
	16mg	£61.65
	24mg	£75.81
Galantamine modified release capsules (<i>ConSION XL</i>) (Dr Reddy's Laboratories UK Ltd)	8mg	£25.94
	16mg	£32.45
	24mg	£39.90
Galantamine modified release capsules (<i>Elmino XL</i>) (Zentiva)	8mg	£51.88
	16mg	£64.90
	24mg	£79.80
Galantamine modified release capsules (<i>Galantex XL</i>) (Creo Pharma Ltd)	8mg	£25.42
	16mg	£31.80
	24mg	£39.10
Galantamine modified release capsules (<i>Galsya XL</i>) (Consilient Health Ltd)	8mg	£44.09
	16mg	£55.16
	24mg	£67.83
Galantamine modified release capsules (<i>Gatalin XL</i>) (Aspire)	8mg	£25.94
	16mg	£32.45
	24mg	£39.90
Galantamine modified release capsules (<i>Gazylan XL</i>) (Teva UK Ltd)	8mg	£25.41
	16mg	£31.79
	24mg	£39.09
Galantamine modified release capsules (<i>Lotprosin XL</i>) (Actavis)	8mg	£51.88
	16mg	£64.90
	24mg	£79.80
Galantamine modified release capsules (<i>Luventa XL</i>) (Fontus Health Ltd)	8mg	£25.42
	16mg	£31.80
	24mg	£39.10

Galantamine modified release capsules (<i>Reminyl XL</i>) (originator brand) (Shire)	8mg	£51.88
	16mg	£64.90
	24mg	£79.80
Galantamine modified release capsules (Category C generic reimbursement price)	8mg	£51.88
	16mg	£64.90
	24mg	£79.80

Lowest cost products are highlighted in bold.

Potential savings in each of the Lincolnshire Clinical Commissioning Groups (CCGs) if all sustained release galantamine was prescribed as a low cost brand (*Consion XL*, *Galantex XL*, *Gatalin XL*, *Gazylan XL* or *Luventa XL*) are as follows:

	Annual saving
Lincolnshire East CCG	£14,260
Lincolnshire West CCG	£13,891
South Lincolnshire CCG	£9,185
South West Lincolnshire CCG	£5,652

PACEF Recommendation:

The availability of a wider range of lower cost branded modified release formulations of galantamine offers further savings opportunities for CCGs in the coming months. All modified release galantamine should be prescribed as a lower cost brand such as *Consion XL*, *Galantex XL*, *Gatalin XL*, *Gazylan XL* or *Luventa XL*. All of these products are designated AMBER with shared care and are approved for inclusion in the *Lincolnshire Joint Formulary*. Prescribers are urged to review all patients currently prescribed galantamine modified release capsules generically or as *Acumor XL*, *Elmino XL*, *Galsya XL*, *Lotprosin XL* and the originator brand *Requip XL* with a view to switching to their preferred low cost brand.

RAPID COST COMPARISON: MEMANTINE HYDROCHLORIDE 10MG AND 20MG ORODISPERSIBLE TABLET (VALIOS)

In moderate to severe Alzheimer's disease, patients taking memantine who develop swallowing difficulties should be considered for either memantine 10mg and 20mg orodispersible tablets (*Valios*) or memantine oral solution 10mg/ml. Both oral solution and orodispersible tablets are similarly priced; both are designated AMBER with shared care.

Valios is a new orodispersible formulation of memantine available as 10mg and 20mg tablets and licensed for the treatment of moderate to severe Alzheimer's disease.

A cost comparison with alternative options is provided below:

Preparation	Dose	Cost (28 days)
Memantine 10mg tablets (generic)	10mg daily	£1.36
Memantine 20mg tablets (generic)	20mg daily	£1.50
Memantine oral solution 10mg/ml (generic)	1ml daily	£31.77
	2ml daily	£63.55
Memantine 10mg orodispersible tablets (<i>Valios</i>) (Dr Reddy's Laboratories UK Ltd)	10mg daily	£32.78
Memantine 20mg orodispersible tablets (<i>Valios</i>)	20mg daily	£65.56

PACEF Recommendation:

Standard memantine tablets 10mg and 20mg are preferred first line. Where the patient has swallowing difficulties, memantine 10mg and 20mg orodispersible tablets (*Valios*) are similarly priced to memantine 10mg/ml oral solution and can be considered as an alternative. The *NEWT Guidelines 2015* recommend memantine 10mg/ml oral solution in preference to crushing memantine tablets. While the tablets can be crushed and dispersed in a little water, they are film coated and need to be crushed very thoroughly. All three formulations of memantine are designated AMBER with shared care; all of them are approved for inclusion in the *Lincolnshire Joint Formulary*.

RAPID COST COMPARISON: RIVASTIGMINE TRANSDERMAL PATCHES
(ALZEST/PROMETAX/VOLEZE/ERASTIG)

In mild to moderate dementia in Alzheimer's disease, patients taking rivastigmine who develop or experience swallowing difficulties should be considered for low cost rivastigmine transdermal patches (*Alzest*); designated AMBER with shared care.

Alzest is a new lower cost rivastigmine transdermal patch launched for the treatment of mild to moderate dementia in Alzheimer's disease. A cost comparison with alternative products reveals that it is currently the lowest cost rivastigmine transdermal patch by a significant margin:

Product	4.6mg/24hours	9.5mg/24hours	13.3mg/24hours
Rivastigmine patch (<i>Alzest</i>) (Dr Reddy's Laboratories UK Ltd)	£35.10 (30)	£19.97 (30)	-
Rivastigmine patch (<i>Eluden</i>) (Mylan Ltd)	£74.07 (30)	£74.07 (30)	-
Rivastigmine patch (<i>Erastig</i>) (Teva UK Ltd))	£74.07 (30)	£74.07 (30)	£73.90 (30)
Rivastigmine patch (<i>Exelon Transdermal Patch</i>) (Novartis)	£77.97 (30)	£77.97 (30)	£77.97 (30)
Rivastigmine patch (<i>Prometax</i>) (Novartis)	£77.97 (30)	£77.97 (30)	-
Rivastigmine patch (<i>Voleze</i>) (Focus Pharmaceuticals Ltd))	£77.97 (30)	£77.97 (30)	£77.97 (30)

The lowest cost product is highlighted in bold.

A cost comparison of the available AChE inhibitors for the treatment of dementia in Alzheimer's disease reveals the importance of utilizing low cost generic oral therapy first line:

	Daily maintenance dose	Cost / 28 days
Donepezil 10mg tablets (generic)	10mg	£1.11
Donepezil 10mg orodispersible tablets (<i>Aricept Evess</i>) (Eisai)	10mg	£83.89
Galantamine 8mg and 10mg tablets (generic)	8 - 12mg twice daily	£61.13 - £74.10
Galantamine 16mg and 24mg modified release capsules (<i>Conson XL/Galantex XL/Gatalin</i>)	16 - 24mg daily	£32.00 - £39.00

<i>XL/Gazylan XL/Luventa XL</i>		
Rivastigmine 3mg and 6mg capsules (generic)	3 - 6mg twice daily	£5.22 - £35.50
Rivastigmine oral solution 2mg/ml (generic)	3 - 6mg twice daily (1.5ml to 3ml twice daily)	£67.77 - £135.55
Rivastigmine patches (<i>Alzest</i>) (Dr Reddy's Laboratories UK Ltd)	4.6mg - 9.5mg once every 24 hours	£19.97 - £35.10
Memantine 10mg and 20mg tablets (generic)	10mg - 20mg	£1.36 – £1.50
Memantine 10mg orodispersible tablets (<i>Valios</i>) (Dr Reddy's Laboratories UK Ltd)	10mg – 20mg	£32.78 - £65.56

Potential savings in each of the Lincolnshire CCGs if all rivastigmine patches were prescribed as *Alzest* are as follows:

	Annual saving
Lincolnshire East CCG	£45,244
Lincolnshire West CCG	£29,884
South Lincolnshire CCG	£25,038
South West Lincolnshire CCG	£13,263

PACEF Recommendations:

In mild to moderate dementia in Alzheimer's disease, patients taking rivastigmine who develop or experience swallowing difficulties should be considered for low cost rivastigmine transdermal patches (*Alzest*); designated AMBER with shared care and approved for inclusion in the *Lincolnshire Joint Formulary*. Rivastigmine oral solution 2mg/ml is a more expensive alternative. The *NEWT Guidelines 2015* recommend rivastigmine transdermal patches as the preferred choice in patients experiencing long-term swallowing difficulties. Oral solution is recommended second line. Only if both of these options prove unsuccessful should consideration be given to opening the capsules and dispersing in water prior to administration. High cost rivastigmine transdermal patches are no longer recommended for use. Examples include: *Eluden*, *Erastig*, *Exelon*, *Prometax* and *Voleze* patches; designation RED-RED.

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

ETORICOXIB (ARCOXIA): REVISED DOSE RECOMMENDATIONS FOR RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS

The recommended starting dose of etoricoxib for the treatment of rheumatoid arthritis and ankylosing spondylitis has been reduced to 60 mg once daily, with the option to increase to a maximum of 90 mg once daily if necessary.

Etoricoxib is a selective COX-2 inhibitor and may be associated with an increased risk of coronary and cerebrovascular thrombotic events, heart failure, hypertension, and oedema (compared with placebo and other non-steroidal anti-inflammatory drugs).

Following an EU-wide review in 2008 of the benefits and risks of etoricoxib, the marketing authorisation holder was required to do clinical trials to assess the efficacy and safety of etoricoxib 60 mg once daily for the treatment of rheumatoid arthritis (RA) and ankylosing spondylitis (AS) including comparison with etoricoxib 90 mg. From these trials, there is

evidence that 60mg is effective in RA and AS in some patients, although others may require the 90mg dose; it is not possible to predict which patients might benefit from the higher dose.

As a result of this the recommended starting dose of etoricoxib for the treatment of RA or AS has been reduced to 60 mg once daily, with the option to increase to a maximum of 90 mg once daily if necessary.

Advice for healthcare professionals:

- The cardiovascular and other important risks of etoricoxib (*Arcoxia*) may increase with dose and duration of exposure. Therefore, the lowest effective daily dose should be used, and the need for treatment should be regularly reassessed
- The recommended dose is 60 mg once daily
- In patients with insufficient relief from symptoms, an increased dose of 90 mg once daily may improve efficacy
- Once the patient is clinically stabilised, down-titration to 60 mg once daily may be appropriate
- In the absence of therapeutic benefit, other treatment options should be considered

The 30mg once daily dose is specifically indicated for treatment of patients with osteoarthritis, although the dose can be increased to 60mg if the patient receives insufficient relief of symptoms.

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

BRIMONIDINE GEL (MIRVASO): RISK OF EXACERBATION OF ROSACEA

Some patients may have exacerbation or rebound symptoms of rosacea following initiation of treatment with brimonidine 3mg/g gel (*Mirvaso*). It is important to initiate treatment with a small amount of gel and increase the dose gradually, based on tolerability and treatment response.

Brimonidine 3mg/g gel (*Mirvaso*) is indicated for the symptomatic treatment of facial erythema of rosacea in adults. Symptom exacerbation has been reported very commonly in patients treated with brimonidine gel, including cases of a rebound effect after the therapeutic effect wears off (approximately 8–12 hours after application) and cases in which exacerbation of symptoms (particularly erythema and flushing) occurred during treatment soon after it was applied. Across all clinical studies, 16% of patients who were receiving brimonidine gel had symptom exacerbation with most patients recovering on cessation of treatment.

Following an EU-wide review, prescribing advice has been updated. Patients should start treatment with a small amount of gel (less than the maximum dose) for at least 1 week and increase the dose gradually, based on tolerability and response to treatment. This will help enable patients to find the best balance between therapeutic and adverse effects. Before prescribing, healthcare professionals should carefully advise patients on how to apply the gel and build up the dose gradually. They should be informed not to exceed the maximum daily dose (1 g of gel in total weight, approximately 5 pea-sized amounts). Patients should be warned to stop treatment and see their doctor if worsening of rosacea symptoms occurs.

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Stephen Gibson
Head of Medicines Management & Optimisation
Optum Commissioning Support Unit

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