

# Minutes of the Lancashire Medicines Management Group Meeting Held on Thursday 12<sup>th</sup> March 2015 at Preston Business Centre

#### PRESENT:

Dr Kamlesh Sidhu (KS)	Chair of LMMG	NHS Lancashire North CCG
Dr Emile Li Kam Wa (LKW)	Consultant Physician	Blackpool Teaching Hospitals NHS Foundation Trust
Christine Woffindin (CW)	Medicines Information Manager	East Lancashire Hospitals NHS Trust
Dr Catherine Fewster (CF)	Chief Pharmacist	Lancashire Care NHS Foundation Trust
David Jones (DJ)	Assistant Chief Pharmacist	Lancashire Teaching Hospitals NHS Foundation Trust
Julie Kenyon (JK)	Senior Operating Officer Primary Care, Community & Medicines	NHS Blackburn with Darwen CCG
Melanie Preston (MP)	Assistant Director - Medicines Optimisation	NHS Blackpool CCG
Dr Lisa Rogan (LR)	Head of Medicines Commissioning	NHS East Lancashire CCG
Clare Moss (CM)	Head of Medicines Optimisation	NHS Greater Preston CCG, NHS Chorley and South Ribble CCG
Kenny Li (KL)	Senior Manager – Medicines Optimisation	NHS Lancashire North CCG
Nicola Baxter (NB)	Head of Medicines Optimisation	NHS West Lancashire CCG
Pauline Bourne (PB)	Senior Pharmacist, Medicines Management, Deputy Chief Pharmacist	University Hospitals of Morecambe Bay NHS Foundation Trust
Julie Lonsdale (JL)	Head of Medicines Optimisation	NHS Fylde and Wyre CCG

### IN ATTENDANCE:

Elaine Johnstone (EJ)	Senior Executive – Medicines Management	NHS Midlands and Lancashire CSU
Brent Horrell (BH)	Head of Medicines Commissioning	NHS Midlands and Lancashire CSU
Susan McKernan (SM)	Senior Medicines Performance Pharmacist	NHS Midlands and Lancashire CSU
Suzanne Penrose (SP)	Medicines Optimisation Pharmacist	NHS Midlands and Lancashire CSU
Jane Johnstone (Minutes)	Medicines Management Administrator	NHS Midlands and Lancashire CSU

ITEM	SUMMARY OF DISCUSSION	ACTION
2015/046	Welcome & apologies for absence	
	The chair welcomed everyone to the meeting. Apologies for absence were received on behalf of Dr Tony Naughton, Dr David Shakespeare, Alastair Gibson and Cassandra Edgar.	
	It was noted that Suzanne Penrose, Medicines Optimisation Pharmacist from M&LCSU was in attendance to observe the meeting.	

ITEM	SUMMARY OF DISCUSSION	ACTION
2015/047	Declaration of any other urgent business	
	None.	
2015/048	Declarations of interest pertinent to agenda	
	None.	
2015/049	Minutes of the last meeting (12 <sup>th</sup> February 2015)	
	The minutes of the meeting dated 12 <sup>th</sup> February 2015 were agreed as a true and accurate record.	
	All LMMG members agreed with the amendment made in these minutes to agenda item 2015/008 SSRIs FOR PREMATURE EJACULATION - 2015/008b - Dapoxetine (Priligy <sup>®</sup> ▼) For the treatment of premature ejaculation (PE) in men 18 to 64 years of age.	
2015/050	Matters arising (not on the agenda)	
	There were no matters arising.	
NEW MEDIC	INES REVIEWS	
2015/051	Olodaterol in the treatment of COPD	
	BH presented the paper, summarising the evidence review and the draft recommendation which had been consulted on, as follows:-	
	Olodaterol (Striverdi® Respimat®) is recommended as a maintenance bronchodilator treatment in adult patients with chronic obstructive pulmonary disease (COPD).	
	Olodaterol is an alternative to other long-acting beta2 agonists (LABAs).	
	6 of 8 CCGs and 3 of 4 acute trusts responded by the closing date.	
	5 consultation responses agreed with the recommendation while 4 consultation responses disagreed with the recommendation.	
	A detailed discussion on the comparative evidence base available for olodaterol versus other available once daily Long Acting Beta Agonists (LABAs) took place.	

ITEM	SUMMARY OF DISCUSSION	ACTION
	<b>Decision</b> Due to a lack of evidence base supporting the superiority of Olodaterol over other available LABAs, it was agreed that Olodaterol will be made Grey on the LMMG website. It was further agreed that the place in therapy of olodaterol would be defined as part of the review of inhalers which is due to take place imminently, the review of inhalers will start with LABA/LAMA combination products and devices.	
	As a starting point for a Lancashire wide approach to Respiratory drugs, LR will share the EL Respiratory pathway with CCG MM Leads. The CSU MM Team will coordinate a meeting to agree the scope and timescales for the review. A decision about the way forward will be brought to the April LMMG.	
	Action The website will be amended to show Grey colour classification.	JJ
	LR will share the existing East Lancs Respiratory pathway with CCG MM Leads.	LR
	CE to coordinate a meeting to agree the scope and timescales for the inhaler review. An update will be provided at the next meeting.	CE
2015/052	LMMG – New Medicine Reviews Work Plan update	
	BH discussed this paper; updating LMMG on the current status of the work plan, as follows:-	
	<u>Medications for discussion at the March LMMG</u> Tiotropium Respimat – the website will be updated for the Respimat and HandiHaler devices in light of the newly published MHRA Guidance.	LL
	Infliximab Biosimilar – BH has had discussions with UKMI; clarification is awaited regarding the Procurement of this. MP will forward an email trail regarding the North West Contract to the CSU for cascading. LMMG members will discuss this internally and Infliximab Biosimilar will be added as an agenda item to the May LMMG for discussion.	MP BH
	Liothyronine – Acute Trusts to provide the contact details of appropriate specialists; CSU will then contact Specialists to see if there is a requirement for its use and in which indications. A review of Liothyronine will be carried out dependent upon the feedback from the Specialists.	Acute Trust Leads
	<u>Medications for Recommendation from April LMMG</u> Insulin degludec & liraglutide (Xultophy®) – this is currently out to consultation.	

ITEM	SUMMARY OF DISCUSSION	ACTION
	<u>Medications for future review</u> Testosterone Peristeen Co-trimoxazole Renavit/Ketovit LABA/LAMA combinations	
	<u>Individual Funding Request - Botox</u> In light of a recent Individual Funding Request for Botox which has been received from an out of area provider it was decided that the following actions would be taken:-	
	CSU will look at the evidence base and the commissioning policy position for the requested indication.	ВН
	A financial analysis on current costs by CCG will be undertaken.	JL
	SM will liaise with NWCSU, Manchester regarding details of their approach to this issue	SM
2015/053	Aripiprazole Long Acting Injection	
	CF discussed the ongoing issues with Aripiprazole Long Acting Injection. As part of the business planning process a bid was submitted by LCFT to Lead Commissioners at BwD where it was suggested that this should initially be discussed at LMMG then brought back to the Lead Commissioners.	
	Following discussions at the D&T Committee meeting, CF is working on a paper reviewing 2 <sup>nd</sup> generation antipsychotics, which is based on the SMC/AWSMG evidence review. CF will forward this paper to the CSU.	
	CF informed the LMMG that at a recent Chief Pharmacists' meeting the same issue was highlighted; CF informed LMMG that a paper will be put to NETAG in April which considers the evidence base and place in therapy of 2 <sup>nd</sup> generation antipsychotics.	
	<b>Decision</b> The group decided that the CSU will review the NETAG and LCFT evidence reviews as a starting point for a consultation on behalf of the LMMG. This work will be prioritised.	
	Action CF will forward the LCFT and the SMC/AWMSG evidence reviews to the CSU.	CF
	CSU to liaise with NETAG requesting sight of their evidence review.	ВН

ITEM	SUMMARY OF DISCUSSION	ACTION
	CSU will send this out to consultation once the reviews have been considered and an appropriate consultation document / evidence review developed.	вн
GUIDELINE	S and INFORMATION LEAFLETS	
2015/054	Psychotropic Formulary	
	SM discussed the Joint Formulary for Psychotropic Medicines paper.	
	Responses were received from 7 CCGs and 2 provider trusts.	
	<u>The following drugs were deferred; CF will discuss these within</u> <u>LCFT; they will be brought to a future LMMG meeting:</u> Clonazepam - Insomnia/Rapid Eye Movement sleep behaviour disorder in Lewy Body Dementia or Parkinson's Disease Dementia.	
	Melatonin - Insomnia in patients over 55yrs.	
	Promethazine – Insomnia.	
	Levomepromazine – Schizophrenia.	
	Carbamazepine/Semisodium Valproate (Depakote)/Sodium Valproate - behavioural disturbance in autistic spectrum disorder or severe learning disability.	
	Escitalopram – Depression and Generalised Anxiety Disorder	
	SSRIs - Social anxiety and obsessional rigidity in autistic spectrum disorder and/or learning disability.	
	Procyclidine tablets - drug induced EPSE.	
	Trihexyphenidyl - drug induced EPSE.	
	Hyoscine Hydrobromide – hypersalivation.	
	Orphenadrine - drug induced EPSE.	
	<u>The following drugs were discussed and agreed by the group</u> :- All second generation antipsychotics – Psychosis – LMMG agreed that these should stay with shared care.	

ITEM	SUMMARY OF DISCUSSION	ACTION
	Drugs for Dementia (all) – Dementia – LMMG agreed that these will be changed from Amber1 to Amber0 colour classification on the LMMG website. SM will liaise with LCFT regarding the rebranding of the Shared Care Guideline to an information sheet; this will then be circulated for comments.	SM
	Triclofos Sodium – Insomnia – as this drug is no longer available LMMG agreed that this should be removed from the joint formulary and the LMMG website.	All website updates JJ
	Sodium Oxybate – Narcolepsy/cataplexy off label use, this is listed as black on the LMMG website – LMMG agreed that no action was required and agreed to it being added to the formulary as black	
	Chlordiazepoxide – Anxiety – LMMG agreed this should be added to the joint formulary as 'non formulary' and Black colour classification for primary care, LMMG website to be updated with the recommendation.	
	Chlordiazepoxide – Adjunct in acute alcohol withdrawal - LMMG agreed this should be added to the joint formulary as Red for primary care, this will be added to the website.	
	Propranolol – Anxiety - LMMG agreed this should be added to the joint formulary and will be added to the LMMG website as Green colour classification.	
	Promazine Injection – Schizophrenia - as this drug is no longer available LMMG agreed that this should be removed from the joint formulary and will be removed from the LMMG website.	
	Risperidone – Conduct disorder with autistic spectrum disorder or severe learning disability – LMMG agreed that this indication should be added to the joint formulary and will be added to the website as Amber1 colour classification recommendation	
	Paliperidone palmitate – Schizophrenia - LMMG agreed this should be added to the joint formulary as restricted use in LCFT and this will be added to the LMMG website as Red colour classification.	
	Amoxapine – Depression – as this drug is no longer available LMMG agreed that it should be removed from the joint formulary and it will be removed from the website.	
	Duloxetine – Depression – LMMG noted the proposed change from restricted use to consultant initiation only in LCFT; no action was required as this will remain as Amber0	

ITEM	SUMMARY OF DISCUSSION	ACTION
	Atomoxetine, Dexamfetamine & Methylphenidte – ADHD – LMMG agreed to the additions to the joint formulary; no action was required as these were already on the LMMG website as Amber1	
	Lisdexamfetamine – ADHD – LMMG agreed to the addition, no action required as this is already on the LMMG website as Red.	
	Clonidine – ADHD – LMMG agreed this should be added to the formulary and it will be added to the website at Red colour classification.	
	Pirenzepine – Hypersalivation (unlicensed) – LMMG agreed this should be added to the formulary and it will be added to the website at Red colour classification.	SM
	All above recommendations will be fed back to the LCFT joint formulary working group	SM
2015/055	RAG list Annual Review – List 2	
	SM presented the paper, summarising the consultation responses for the review of the colour classification list 2. Responses were received from 7 CCGs and 4 provider trusts.	
	The following were discussed and agreed by the group:-	
	Pindolol for hypertension/Angina – LMMG agreed that this will be removed from the LMMG website.	All website updates JJ
	Buprenorphine patches for pain – the CSU will look at its proposed place in therapy, patient numbers and its costs locally. This will then be sent out to consultation as part of the non-cancer pain guidelines work. Buprenorphine patches will be added to the website as Grey colour classification pending the outcome of the consultation.	SM
	Rifampicin - Non-TB, Licensed indications – LMMG agreed that this will be added to the website as Amber0 colour classification recommendation	
	Raloxifene for secondary prevention of osteoporotic fragility fractures in postmenopausal women - LMMG agreed that this will be added to the website as Green colour classification.	
	Alendronate and etidronate for primary and secondary prevention of osteoporotic fragility fractures in postmenopausal women - LMMG agreed that these will also be added to the website as Green colour classification recommendation under the NICE technology appraisal.	

	Darifenacin for Urinary frequency, urgency and incontinence – LMMG agreed this this will be added to the website as Green colour classification. KL will forward the LNCCG pathway to other CCG Leads.	KL
	Cyclosphosphamide for Rheumatic Disease – LMMG agreed that this will be added to the website as Red colour classification.	
	Mycophenolate (Myfortic brand) – all agreed that this will be listed as Red colour classification with the same background wording and in line with the other Renal transplant medicines.	
	The following drugs are deferred and will be brought back to the April LMMG after local CCG discussions:	
	LMWHs for the treatment of VTE (excluding pregnancy and patients with cancer).	
	LMWHs for the treatment of VTE in cancer patients.	
	LMWHs for the treatment of VTE in pregnancy.	
	LMWHs for VTE prophylaxis in pregnancy.	
2015/056	Oral Anticoagulant Consensus Statement	
	SM discussed the amendments made to the Oral Anticoagulant Consensus Statement which were made in light of newly published figures from larger scale studies around the percentage risk of stroke or VTE Risk assessment scores and feedback received from Professor Lip.	
	<b>Decision</b> The Oral Anticoagulant Consensus Statement was approved by the LMMG.	
	Action Upload the current version of the Consensus Statement to the website.	JJ
2015/057	LMMG – Guidelines Work Plan update	
	JL discussed this paper, updating LMMG on the current status of the work plan, as follows:-	
	Due for approval at the April LMMG meeting Ivabradine information sheet - this information sheet is currently out for consultation.	

ITEM	SUMMARY OF DISCUSSION	ACTION
	<u>Due for approval at future LMMG meetings</u> Non Cancer pain guidelines – undergoing further work with Task and Finish Group. The chronic pain section will go out for consultation soon for discussion at a future meeting of LMMG.	
	Apomorphine shared care guidelines – LTHT are producing a shared care and will send for comments/approval to LMMG once complete.	
	Treatment of Juvenile Idiopathic Arthritis – Policy to continue prescribing into adulthood, as per BSR and BSPAR consensus statement, is being finalised and will be sent out for consultation shortly.	
	Erectile Dysfunction – the first draft is being developed, and will be consulted on in April, for discussion at the June LMMG.	
	ADHD shared care guidelines for children – this has been added to the work plan.	
	Gout prescribing guidance - a scoping exercise is currently being undertaken which will be consulted on in April 2015.	
	Secondary prevention of stroke post TIA – a scoping exercise is currently being undertaken which will be consulted on in April 2015	
	Joint Palliative Care Guideline – SM updated the LMMG in relation to the joint Lancashire and Cumbria guideline. SM has spoken with Susan Salt, Consultant from Trinity Hospital Blackpool. Future updates to this document will be circulated to LMMG for comment and Susan Salt will be included in any work around palliative care that LMMG undertake. The CSU will send the current document out to LMMG members and a joint LMMG response will be submitted	SM
NATIONAL	DECISIONS FOR IMPLEMENTATION	
2015/058	New NICE Technology Appraisal Guidance for Medicines (February 2015)	
	TA329 - Infliximab, Adalimumab and Golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy (including a review of TA140 and TA262) – LMMG agreed that this will be put on the website as Red colour classification. The CSU will look at the use of $2^{nd}$ and $3^{rd}$ line biologics as this was not clear from the NICETA. BlueTeq forms will be updated accordingly.	SM

ITEM	SUMMARY OF DISCUSSION	ACTION
	TA330 - Sofosbuvir for treating chronic hepatitis C - LMMG agreed that this will be put on the website as Red colour classification.	
	TA331 - Simeprevir in combination with Peginterferon Alfa and Ribavirin for treating genotypes 1 and 4 chronic hepatitis C - LMMG agreed that this will be put on the website as Red colour classification.	All website updates JJ
	TA332 - Sipuleucel-T for treating asymptomatic or minimally symptomatic metastatic hormone-relapsed prostate cancer - LMMG agreed that this will be put on the website as Black colour classification.	
	TA333 Axitinib for treating advanced renal cell carcinoma after failure of prior systemic treatment - LMMG agreed that this will be put on the website as Red colour classification.	
	TA334 - Regorafenib for metastatic colorectal cancer after treatment for metastatic disease (terminated appraisal) – NICE is unable to make a recommendation of this TA because no evidence submission was received; therefore no action will be taken by LMMG.	
	NB left the meeting at 1110 hours.	
2015/059	New NHS England medicines commissioning policies (February 2015)	
	None published in February 2015.	
2015/060	Evidence reviews published by SMC or AWMSG	
	BH discussed the SMC and AWMSG published medicines from February 2015.	
	978/14 Umeclidinium/Vilanterol (Anoro) - As a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease.	
	A decision was made at the February 2015 LMMG to prioritise a review of LABA/LAMA combinations therefore LMMG agreed that no action would be taken.	
	It was agreed that the remaining SMC/AWMSG recommendations in the paper did not meet LMMG criteria; therefore LMMG agreed that no further action would be taken with regards to them.	

ITEM	SUMMARY OF DISCUSSION	ACTION
PROCESS	PROPOSALS	
2015/061	Rebate Scheme Assessment Process	
	EJ discussed this paper which was brought to the meeting in light of a recent offer of a rebate scheme in primary care by a pharmaceutical company for one of its products.	
	<b>Decision/Action</b> LMMG agreed that the CSU will progress the work on the primary care rebate scheme policy document on behalf of the CCGs. CCG Leads will discuss further requirements outside of this meeting.	EJ CCG Leads
OTHER PR	OPOSALS	
2015/062	LMMG Annual Report	
	BH informed the group that the 2015 LMMG Annual Report is currently being updated. CCG Leads were reminded to send in their local decisions to the CSU.	
	Action CCG Leads to send their local decisions to the CSU.	CCG Leads (open action item 2015/022)
	An updated Annual Report will be brought to the next LMMG meeting.	ВН
ITEMS FOR		
2015/063	Lancashire Care FT Drug and Therapeutic Committee	
	No meeting in February.	
2015/064	Minutes of the Lancashire CCG Network minutes (29 <sup>th</sup> January 2015)	
	The group noted these minutes.	

**Date and time of the next meeting** Thursday 9<sup>th</sup> April 2015, 9.30 am to 11.30 am, Meeting Room 253, Preston Business Centre

## ACTION SHEET FROM THE LANCASHIRE MEDICINES MANAGEMENT GROUP 12 March 2015

MINUTE NUMBER	DESCRIPTION	ACTION	DATE	STATUS AT 02.04.15
	FROM THE 13 NOVEMBER 2014 MEETING			
2014/167	Melatonin Action: Melatonin (Circadin®) – LR to inform the CSU of the outcome of local discussions at ELMMB. Update: LR is working with ELHT; the financial impact and patient numbers are being looked at; the discussions are ongoing in the EL health economy, it was agreed to close this as an LMMG action. FROM THE 13 DECEMBER 2014 MEETING	LR	05.03.15	Closed
2015/201	LMMG engagement with the			
2013/201	<b>pharmaceutical</b> <b>Action:</b> Discuss with Comms regarding adding the work plan to the website <b>Update:</b> There is now a section on the website for the work plan to be added. The work plan will be uploaded on a monthly basis following the LMMG meetings.	ВН	05.03.15	Closed
ACTION SHEET	FROM THE 8 <sup>th</sup> JANUARY 2015 MEETING			
2015/022	Updating of LMMG Annual report All CCGs to check that websites are up to date with decisions on new medicines to support refreshing of the LMMG annual report. Update: Feedback is awaited from 1 CCG; an updated Annual Report will be brought to the April meeting.	All CCG Leads	02.04.2015	Closed
ACTION SHEET	FROM THE 12 <sup>th</sup> FEBRUARY 2015 MEETING			
2015/027	<ul> <li>RAG list review – immunosuppressants post renal transplant.</li> <li>Action: JL to contact Specialised Commissioning / NHS England to determine timescales for the repatriation plan.</li> <li>Update: JL has contacted Specialised</li> </ul>			
	Commissioning/NHS England; there are ongoing discussions with LTH, however the timescales for the repatriation plan have not been determined at this time. LTH to inform LMMG of timescales once agreed.	DJ	02.04.2015	Open

2015/031	Horizon Scanning 2015/16			
	<ul> <li>Action: LMMG members to consult internally with Specialists discussing the prioritisation for new medicines reviews for the 2015/16 financial year.</li> <li>Update: BH has received feedback from 2 CCGs, LCFT and 1 Acute Trust. BH reminded LMMG members to consult internally with Specialists and to forward feedback to CSU. Upon receipt of these a list of the drugs which have been prioritised will be brought to the next meeting.</li> </ul>	LMMG members	02.04.15	Open
2015/037	Rheumatology Alliance – UpdateAction: TN to update LMMG once formal feedback has been received from the rheumatology alliance meetingUpdate: TN will bring an update to the April meeting.	TN	02.04.15	Open
2015/045	<ul> <li>Minutes of the Lancashire Care FT Drug and Therapeutic Committee (20th January 2015)</li> <li>DT/08/15 NHS England Misuse of Pregabalin and Gabapentin Action: CF will forward the NHS England document to the CSU Medicines Management Team for forwarding to CCGs.</li> <li>Update: NHS England has been working on their Pain Guidelines for Prisons on the use of Pregabalin and Gabapentin. CF will forward both documents to the CSU; this will be brought to a future LMMG meeting.</li> </ul>	CF	02.04.15	Open
2015/046	Ticagrelor         Action         In light of recent requests for the use of Ticagrelor for a period longer than 12 months         – CCG Medicines Management leads to carry out an audit of Ticagrelor prescribing in Primary Care.         Update: A summary will be brought back to the April LMMG meeting.	CCG MM Leads	02.04.15	Open
	ET FROM THE 12 MARCH MEETING			
2015/051	Oladaterol in the treatment of COPD LR will share the existing East Lancs Respiratory pathway with CCG MM Leads.	LR	02.04.15	Open
	CE to coordinate a meeting to agree the scope and timescales for the inhaler review. An update will be provided at the next meeting.	CE	09.04.15	Open

2015/052	LMMG – New Medicine Reviews Work Plan update			
	Infliximab Biosimilar - MP will forward an email trail regarding the North West Contract to the CSU for cascading. Infliximab Biosimilar will be added as an agenda item for the May	MP BH	02.04.15 07.05.15	Open Open
	LMMG meeting.			<b>O</b> pon
	Liothyronine - Acute Trusts to provide the contact details of appropriate specialists; the CSU will then contact specialists to see if there is a requirement for its use and in which indications. A review of Liothyronine will be carried out dependent upon the feedback from the Specialists.	Acute Trust Leads	02.04.15	Open
	Botox – Individual Funding Request CSU will look at the evidence base and the commissioning policy position for the requested indication.	ВН	07.05.15	Open
	A financial analysis on current costs by CCG will be undertaken.	JL	02.04.15	Open
	SM will liaise with NWCSU, Manchester regarding details of their approach to this issue	SM	02.04.15	Open
2015/053	Aripiprazole Long Acting Injection			
	CF will forward the LCFT and the SMC/AWMSG evidence reviews to CSU.	CF	02.04.15	Open
	CSU will send this out to consultation once the reviews have been considered and an appropriate consultation document / evidence review developed.	ВН	In line with agreed work plan	Open
2015/054	Drugs for Dementia			
	SM will liaise with LCFT regarding the rebranding of the Shared Care Guideline to an information sheet; this will then be circulated for comments.	SM	02.04.15	Open
2015/055	RAG list Annual Review – List 2			
	Darifenacin for Urinary frequency, urgency and incontinence – KL will forward the LNCCG pathway to CCG Leads	KL	02.04.15	Open

2015/057	Joint Palliative Care Guideline			
	The CSU will send the current document out to LMMG members and a joint LMMG response will be submitted	SM	02.04.15	Open
2015/061	Rebate Scheme Assessment Process			
	Decision making group - CCG Leads will discuss further requirements outside of this meeting.	CCG Leads	02.04.15	Open