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DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)

Minutes of the meeting held on 13th July 2021

CONFIRMED MINUTES

Summary Points

Traffic lights

Drug	Decision
Bempedoic acid & bempedoic acid/ezetimibe	GREY for primary hypercholesterolaemia or mixed dyslipidaemia: when a statin is contraindicated or not tolerated, and ezetimibe alone does not control low-density lipoprotein cholesterol well enough. (For primary prevention)
Ondansetron	GREY specialist initiation for IBS associated diarrhoea
SGLT2i (including empagliflozin, canagliflozin, dapagliflozin)	GREEN specialist initiation for adults with CKD in addition to an ACEi or an ARB if they have type 2 diabetes, and an ACR of 30mg/mmol or more Subject to NICE approval
Onasemnogene abeparvovec (Zolgensma)	RED (as per NHS England commissioning intentions)
Ibrutinib with Obinutuzumab	DNP (NHS England as per NICE TA702) for untreated chronic lymphocytic leukaemia and small lymphocytic lymphoma (terminated appraisal)
Ibrutinib with rituximab	DNP (NHS England as per NICE TA703) for untreated chronic lymphocytic leukaemia (terminated appraisal)
Trastuzumab deruxtecan	RED (NHS England as per NICE TA704) for treating HER2-positive unresectable or metastatic breast cancer after 2 or more anti-HER2 therapies
Atezolizumab monotherapy	RED (NHS England as per NICE TA705) for untreated advanced non-small-cell lung cancer
Ozanimod	DNP (NHS England as per NICE TA706) for treating relapsing–remitting multiple sclerosis
Nivolumab	RED (NHS England as per NICE TA707) for previously treated unresectable advanced or recurrent oesophageal cancer
Budesonide orodispersible tabs	RED (as per NICE TA708) for inducing remission of eosinophilic oesophagitis.
Pembrolizumab	RED (NHS England as per NICE TA709) for untreated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency
Ravulizumab	RED (NHS England as per NICE TA710) for treating atypical haemolytic uraemic syndrome
Guselkumab	RED (as per NICE TA711) for treating active psoriatic arthritis after inadequate response to DMARDs

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Derbyshire Medicines Management Shared Care and Guideline Group Traffic Lights

Drug	Decision
Budesonide + Formoterol + glycopyrronium (Trixeo aerosphere)	GREY for the maintenance treatment of moderate to severe COPD. Triple therapy is reserved for exceptional use in severe disease in the presence of persistent exacerbations despite other treatments
Glycopyrronium + formoterol (Bevespi Aerosphere)	GREEN as per local COPD guidance. Choice should be based on patient ability to tolerate and use inhaler device
Potassium dihydrogen phosphate	RED as per UHDBFT/CRHFT formularies. Hospital to prescribe and supply
Thuasne Action Reliever osteoarthritis knee brace	DNP medical device (appliance). Awaiting national review
Delafloxacin	DNP
Pizotifen	GREY review existing patients when appropriate. Not for new patients.
Rifampicin	RED for all indications, including TB
Clomipramine MR (Anafranil SR)	Removed as discontinued
Sodium chloride 5% eye drops (Aeon)	Removed entry for specific brand

Clinical Guidelines

Identification and Management of Familial Hypercholesterolaemia – partial update
Adult Lipid Modification Therapy in Non-Familial Hyperlipidaemia – partial update
Primary Care management of Irritable Bowel Syndrome (IBS) guideline – partial update
Management of Low back pain and Sciatica (New Guideline)

Patient Group Directions (PHE)

Rotavirus vaccine v5.00
Meningococcal group A, C, W and Y (MenACWY) conjugate vaccine v4.00

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Present:	
Derby and Derbyshire CCG	
Dr R Gooch	GP (Chair)
Mr S Dhadli	Assistant Director of Clinical Policies and Decisions (Professional Secretary)
Mr S Hulme	Director of Medicines Management and Clinical Policies
Mrs K Needham	Assistant Director of Medicine Optimisation and Delivery
Mrs S Qureshi	Head of Medicines Management, Clinical Policies and High Cost Interventions
Dr R Dills	GP
Dr A Mott	GP
Ms J Savoury	Assistant Chief Finance Officer
Ms A Reddish	Clinical Quality Manager – Primary Care
Derby City Council	
Derbyshire County Council	
University Hospitals of Derby and Burton NHS Foundation Trust	
Dr W Goddard	Chair – Drugs and Therapeutic Committee
Mr D Moore	Lead Pharmacist Commissioning & High Cost Medication
Derbyshire Healthcare NHS Foundation Trust	
Mr S Jones	Chief Pharmacist
Dr M Broadhurst	Consultant Psychiatrist/Deputy Medical Director
Chesterfield Royal Hospital NHS Foundation Trust	
Derbyshire Community Health Services NHS Foundation Trust	
Mr B Dorward	Advanced Pharmacist
Derby and Derbyshire Local Medical Committee	
Dr K Markus	Chief Executive Officer
Derbyshire Health United	
Staffordshire and Stoke-on-Trent CCG's	
Ms E Bryant	Pharmacist
In Attendance:	
Ms E Evans	Chief Pharmacy Technician (Interface)
Mr A Brownlee	Chief Pharmacy Technician (Interface)
Mrs K Rogers	Derby and Derbyshire CCG Senior Administrator (minutes)

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Item		Action
1.	**APOLOGIES**	
	Dr H Hill, Ms A Brailey, Ms S Bamford, Ms A Braithwaite, Ms J Shaw	
2.	**DECLARATIONS OF CONFLICTS OF INTEREST**	
	Dr Gooch reminded committee members of their obligation to declare any interest they may have on any issues arising at committee meetings which might conflict with the business of JAPC. No conflicts of interest were declared in relation to this agenda; in addition to the existing register of interests.	
3.	**DECLARATIONS OF ANY OTHER BUSINESS**	
	It was noted that there would be no representation for Chesterfield Royal Hospital NHS Foundation Trust (CRHFT) at this month's JAPC meeting. For quoracy purposes, a summary of proposed recommendations would be sent to Ms A Brailey for comment and agreement, following the meeting.	
4.	**JAPC ACTION SUMMARY**	
a.	**Cannabis based medicine (Sativex)** Mr Dhadli advised that Sativex was previously discussed at a JAPC meeting in June 2020. It was recommended that it be bought back to a future meeting in 12 months' time, to consider the current RED traffic light classification. Data is expected from University Hospitals of Derby and Burton NHS Foundation Trust (UHDBFT) to show how many patients could potentially be taking Sativex as a long-term treatment option and how efficacious the drug is. Mr Moore informed the committee that he is expecting to bring this information to the JAPC meeting in August 2021.	**DM**
b.	**Hydroxychloroquine** Mr Dhadli reported that the work surrounding hydroxychloroquine is still ongoing. Comments are awaited from the Commissioning team at NHS Derby and Derbyshire CCG (DDCCG) regarding how the service delivery will be carried out, in line with the latest Royal College of Ophthalmologists (RCO) guidance.	
c.	**Acute Coronary Syndrome (ACS)** Mr Dhadli informed the committee that guidance for ACS Dual antiplatelet has been drafted in line with NICE NG185 and circulated to cardiologists for comment.	
d.	**Mycophenolate** Mr Dhadli advised that a draft shared care agreement for mycophenolate has been received from CRHFT. However a shared care agreement for mycophenolate is also awaited from the Regional Medicines Optimisation Committee (RMOC), who are currently in the process of producing this.	
e.	**Chronic pain** Mr Dhadli stated that the chronic pain update is being drafted as per NICE NG193, it is expected to be tabled at the JAPC meeting in October 2021.	

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f.	**Atrial Fibrillation** Mr Dhadli advised that the Atrial Fibrillation guidance is in the process of being updated. Consideration will be made as to the JAPC positioning of NOAC over warfarin in AF, in line with NICE NG196. A review will be carried out to look at whether Orbit is on clinical systems.	
5.	**NEW DRUG ASSESSMENT/TRAFFIC LIGHT ADDITION**	
a.	**Bempedoic acid with ezetimibe** Mr Dhadli reported that bempedoic acid is a new drug, it is recommended with or without ezetimibe. NICE TA694 (April 2021) states that bempedoic acid with ezetimibe is recommended as an option for treating primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia as an adjunct to diet in adults. It is recommended by NICE only if statins are contraindicated or not tolerated, or ezetimibe alone does not control low-density lipoprotein cholesterol well enough. Bempedoic acid is a novel oral lipid-lowering medicine. It is a prodrug that is activated in the liver to ETC 1002-Coenzyme A (ETC-1002-CoA), which subsequently inhibits adenosine triphosphate citrate lyase (ACL), an enzyme upstream of 3-hydroxyl-3-methylglutaryl Coenzyme A (HMG-CoA) reductase in the cholesterol synthesis pathway. Inhibition of cholesterol synthesis triggers the upregulation of low-density lipoprotein (LDL) receptor (LDLR) expression in the liver resulting in increased clearance of LDL particles and lowering of LDL-C in the blood. Additionally, inhibition of ACL by ETC-1002-CoA results in concomitant suppression of hepatic fatty acid biosynthesis. The percentage reduction in LDL-C was statistically significantly larger with bempedoic acid compared with placebo across all four key CLEAR studies and this was supported by significantly greater improvements in secondary outcomes. The primary efficacy outcome, mean percentage change in LDL-C is accepted as a surrogate endpoint for the reduction of cardiovascular events but published CLEAR studies have not assessed the effect of bempedoic acid on cardiovascular outcomes. An ongoing CLEAR OUTCOMES study will assess a composite of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke or coronary revascularisation in more than 14,000 patients with a history or high risk of cardiovascular disease, who were statin-intolerant and fasting LDL-C of ≥100 mg/dL (2.6mmol/L). This study is not expected to be completed until December 2022. Mr Moore advised that until data from this study is available, UHDBFT lipidologists do not recommend bempedoic acid for secondary prevention, only for primary prevention. Lipidologists have requested consideration to a change to the current traffic light classification from RED to GREY, thereby transferring the care of these patients to primary care. This would mean that GPs offer bempedoic acid before referral into the lipidology service at UHDBFT. If bempedoic acid fails to have the desired effect, the patient would be considered for PCKS9-inhibitors at the UHDBFT lipid clinic. Forecast patient numbers to receive bempedoic acid are estimated at 60-70 per year for UHDBFT and 20 per year for CRHFT. Mr Dhadli discussed the cost effectiveness of using bempedoic acid/ezetimibe ahead of PCSK9-inhibitors and it was agreed that this could result in cost savings for Derbyshire, taking also into account any patient access scheme	

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	price. Bempedoic acid has been placed in the Derbyshire familial and non-familial lipid modification guidelines as an option for patients who are intolerant or contra-indicated to statins as per NICE TA. A discussion took place, and it was noted that bempedoic acid is not a familiar drug amongst GP's in primary care. As a result of this, initiation of bempedoic acid in primary care may be low. It was highlighted that GP practices in Chesterfield and Dronfield areas may see a slight increase in the use of bempedoic acid, as a review is currently underway of lipid management in patients. It was agreed that monitoring of appropriate use of statins should be carried out, prior to initiation of bempedoic acid. **Agreed:** JAPC reclassified bempedoic acid and bempedoic acid/ezetimibe from RED to **GREY**, for primary hypercholesterolaemia or mixed dyslipidaemia: when a statin is contraindicated or not tolerated, and ezetimibe alone does not control low-density lipoprotein cholesterol well enough. (For primary prevention).	**SD**
	Agreed: JAPC ratified the partial update to the Identification and Management of Familial Hypercholesterolaemia and Adult Lipid Modification Therapy in Non-Familial Hyperlipidaemia.	**SD**
b.	**<u>Canagliflozin and dapagliflozin</u>** Mr Moore informed the committee that in May 2021, diabetologists and renal clinicians submitted an application to the UHDBFT Drugs and Therapeutics committee for the use of canagliflozin, for the treatment of chronic kidney disease (CKD) in type 2 diabetes. An updated draft CKD guideline has been published by NICE in January 2021 which recommends that for diabetic patients who are already on an ACE-I/ARB, the addition of an SGLT-2 inhibitor (as a drug class) would be a cost-effective treatment option. Evidence is based on the CREDENCE trial, which was an event-driven trial designed to formally test whether canagliflozin lowers the risk of kidney failure and cardiovascular outcomes in people with type 2 diabetes monitoring and established diabetic nephropathy. A total of 4401 people were enrolled in the CREDENCE trial and randomized (1:1) to canagliflozin 100mg or placebo. The CREDENCE trial was initiated in 2014 before the conclusion of the cardiovascular outcome trial (CVOTs) and its initiation was motivated by renal data measured in phase 3 studies of canagliflozin. The study population included adults at least 30 years of age with T2DM (HbA1c ≥ 6.5% and ≤ 12.0%), eGFR ≥ 30 and < 90 mL/min/1.73 m2, and UACR > 300 and ≤ 5000 mg/g. People were also required to be receiving a maximally tolerated dose of an ACE inhibitor or ARB for at least 4 weeks prior to randomization. The trial was stopped 2 years early on the advice of an independent data monitoring committee, based on the efficacy and safety findings observed in an interim analysis conducted in July 2018, after a planned 405 primary endpoint events had occurred. A post hoc analysis in participants with baseline eGFR <30 mL/min/1.73 m2 (n = 174) also demonstrated consistent effects of canagliflozin on renal, cardiovascular, and mortality outcomes as those seen in the overall population, with no differences in the risk of renal-related	

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	adverse events or other safety outcomes compared to the overall population. The NNT to prevent one event from the primary composite outcome over 2.5 years was 22 (95% CI 15–38). NNTs for other outcomes were 28 (95% CI 19–54) for the composite renal outcomes of ESKD, doubling of the serum creatinine level, or renal death; 43 (95% CI 26–121) for ESKD events; and 46 (95% CI 29–124) for hospitalization for heart failure. NICE final appraisal determination (FAD) included data for canagliflozin and dapagliflozin in the CKD update. Empagliflozin was not included, however the on-going trial (EMPA-KIDNEY) has been passed to the NICE surveillance team to follow-up once the trial is published. It is anticipated that approximately 150 patients at UHDBFT and 50 patients at CRHFT per year might receive this treatment. Use of an SGLT2i in type 2 diabetics with CKD is cost effective if successful in preventing the use of dialysis in these patients. The recommendation is to classify canagliflozin and dapagliflozin GREEN specialist initiation, for adults with CKD in addition to an ACEi or an ARB if they have type 2 diabetes, and an ACR of 30mg/mmol or more. A discussion took place, and the committee supported the recommendation in principle, however the decision was taken to wait for the NICE guidance to be published, which is due mid-August, to ensure that the criteria remain unchanged, before formally agreeing this. A query was raised as to whether prescribing canagliflozin/dapagliflozin /empagliflozin for the treatment of CKD in type 2 diabetes should be initiated in primary care as well as secondary care. It was agreed for this to be discussed further with the clinicians at UHDBFT and CRHFT, and to understand their long-term plans.	**DM**
	It was noted that empagliflozin is the preferred choice for diabetes in Derbyshire. This will continue to be recommended as the most cost-effective option due to the outcome data, including for the treatment of CKD in type 2 diabetes, providing this is in line with the NICE guidance when published. **Action:** JAPC members to agree the classification of GREEN specialist initiation for SGLT2s (canagliflozin, empaglflozin and dapagliflozin, for adults with CKD in addition to an ACEi or an ARB if they have type 2 diabetes, and an ACR of 30mg/mmol or more, following the publication of the NICE guidance in August 2021. Agreement will take place virtually via email. JAPC made this decision based upon the strong evidence from the studies and to prevent delay in uptake for agreement during the pandemic.	**ALL**
c.	**<u>Ondansetron</u>** Mr Dhadli reported that a paper for the use of ondansetron for IBS with diarrhoea was sent out for consultation to gastroenterologists at both UHDBFT and CRHFT, and to the Derbyshire Medicines Management Shared Care and Guideline Group (MMSCGG). UHDBFT would like JAPC to consider assigning a traffic light classification for ondansetron for the management of irritable bowel syndrome with diarrhoea (IBS-D); and to update the IBS guideline accordingly. The current management of IBS-D involves the use of loperamide alongside	

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	mebeverine (or hyoscine). If the antispasmodics fail to control pain, then a tricyclic antidepressant can be added to help relieve symptoms. After these agents have been tried there is currently limited other options available for the management of IBS-D. Serotonin (5-HT), acting particularly through the 5-HT3 and 5- HT4 receptors, plays a significant role in the control of gastrointestinal motility, sensation, and secretion. Furthermore, recent observations that plasma 5-HT concentrations are reduced in IBS patients with constipation, but raised in those with diarrhoea, especially those showing postprandial symptoms, provide further support for its involvement in the motor and sensory dysfunction associated with this condition. The British Society of Gastroenterology (BSG) guidelines on the management of irritable bowel syndrome, were updated in April 2021. This has also been published in the British Medical Journal (BMJ). The BSG guidelines state how 5-Hydroxytryptamine 3 receptor antagonists are efficacious second-line drugs for IBS with diarrhoea in secondary care. Alosetron and ramosetron are unavailable in many countries; ondansetron titrated from a dose of 4mg once a day to a maximum of 8mg three times a day is a reasonable alternative. Randomised Controlled Trials (RCT) of ondansetron, a widely available 5-HT3 receptor antagonist with a robust safety profile, have been conducted. Mr Dhadli advised that requests to use ondansetron have been made previously, however at that time there was no specific mention of 5HT3 antagonists in the updated NICE guidance in 2017. There were also questions around the safety and efficacy of the drug, and whether it was appropriate for primary care. Evidence was taken from a 2014 publication, which examined 120 patients meeting Rome III criteria for IBS-D. They entered a randomised, double-blind, placebo-controlled crossover study of 5 weeks of ondansetron 4mg versus placebo with dose titration allowed, up to two tablets three times daily in the first 3 weeks. UHDBFT are proposing that ondansetron is used in those IBS-D patients who have been referred to secondary care, with symptoms resistant to other IBS therapies. It would potentially be used long term, dependent on the patient's response and symptoms over time, and would be specialist initiated by secondary care. QTc interval check in appropriate patients would be carried out by secondary care prior to handing over to primary care. The MMSCGG previously raised queries on the duration of treatment, monitoring requirements and safety in pregnancy/QT prolongation. MHRA warnings for ondansetron include small increased risk of oral clefts following use in the first 12 weeks of pregnancy, and dose-dependent QT interval prolongation (mostly ondansetron for intravenous use). UHDBFT recommended that female patients who take ondansetron for IBS-D/functional GI disease would be advised to stop ondansetron during their first trimester, to avoid the small increased risk of oral clefts. In regard to QT interval prolongation, the 2014 RTC suggests that a baseline ECG would only be required in those patients with known significant cardiac disease and/or those on other medications that prolong the QTc. Estimated patient numbers to receive ondansetron for the management of IBS-D, are up to 75 per year for UHDBFT and <5 for CRHFT. Cost effectiveness is based on patients taking 4mg TDS, however patients taking part in the RTC often found 4mg daily to be just as effective in managing	

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	symptoms. Mr Dhadli highlighted that one of the concerns was the high failure rates on treatment and questions on cost effectiveness. For this reason, the specialist will assess efficacy before GPs will be asked to continue to prescribe. JAPC approved the use of ondansetron for IBS associated diarrhoea. **Agreed:** JAPC classified ondansetron as **GREY specialist initiation** for IBS associated diarrhoea. **Agreed:** JAPC ratified the partial update of Primary Care Management of Irritable Bowel Syndrome (IBS) guideline.	**SD** **SD**
6.	**CLINICAL GUIDELINES**	
a.	**<u>Low back pain and sciatica</u>** Mr Dhadli advised that a new local guideline has been developed, based on NICE NG59 low back pain and sciatica in over 16s. NICE partially updated NG59 low back pain and sciatica in 2020, making 'do not' recommendations on several pharmacological treatments, including the use of gabapentinoids & antiepileptics for sciatica, and the use of opioids for chronic sciatica. There were subsequently specialist consultant concerns which were raised through feedback and the British Pain Society. These concerns and the lack of local resources to implement the guidance have been taken into consideration within the guideline, with the suggestion to pragmatically enable limited gabapentinoids/antiepileptics usage in individuals if recommended by a specialist. The draft guideline has been sent out for consultation to pain consultants and anaesthetists at UHDBFT and Dr. D Farquharson at CRHFT, no comments have been received to date. The guideline is aimed at primary care clinicians with specific recommendations on prescribed medication. It includes NICE's recommendation on risk stratification, self-management advice, as well as recommendations on non-pharmacological and pharmacological management. Pharmacological management for treatments of minor, short-term back pain, encourages patients to self-care with lifestyle changes and over-the-counter painkillers e.g. paracetamol, ibuprofen. If oral NSAIDs are to be used, recommendations are Ibuprofen up to 1200mg daily as first line; alternatively naproxen up to 1000mg daily. The lowest effective dose should be used for the shortest possible time. If opioids are needed, codeine is recommended as first line, with or without paracetamol for managing acute low back pain, only if an NSAID is contraindicated, not tolerated or has been ineffective. Opioids should not be offered for managing chronic (≥3 months) low back pain or chronic sciatica. NICE does not recommend gabapentinoids or antiepileptics for managing low back pain or sciatica, as there is no overall evidence of benefit and there is evidence of harm. Local pain specialists recognise the potential issues in the long-term use of these medications for back pain and sciatica, however, they reserve the option to use gabapentinoids and some antiepiliptics e.g. carbamazepine, oxcarbazepine for a small number of selected individuals after considering all other options. These should be	

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	started on specialist recommendation on a trial basis with a clear plan to review/stop. The guideline also advises other medications that should not be recommended/offered. NICE recommends that if a person is already taking opioids, gabapentinoids or benzodiazepines for sciatica, clinicians should explain the risks of continuing these medicines, and as part of shared decision making about whether to stop these medications for sciatica, discuss the problems associated with withdrawal. JAPC recognises that withdrawing these medications may not be feasible/appropriate, especially for stable patients, following FPM/BPS concerns, and also partly due to current limitations in capacity and service provision for alternative non-pharmacological treatment options. A discussion took place, and concern was raised as to whether there are enough pain management services to refer these patients into and if there is appropriate support in place for existing patients taking opioids, gabapentinoids or benzodiazepines, where treatment will be stopped. JAPC agreed that there is a non-drug therapy commissioning gap, this has previously been raised through clinicians within Joined Up Care Derbyshire (JUCD). It will continue to be raised as a priority via DDCCG Clinical and Lay Commissioning Committee (CLCC), the Strategic Intent Group and Long-Term Conditions Group. The committee discussed the aspiration of the guideline and the challenge for practical implementation of it. The difficulties primary care clinicians face is acknowledged, with limited local specialist capacity/services in place currently for alternative treatment options. JAPC recognise that withdrawal of existing (pharmacological) treatments may not be feasible/appropriate at present and that implementation of this guideline may take some time. **Agreed:** JAPC ratified the Management of Low back pain and Sciatica in primary care with a review date of 3 years.	**SD** **SD**
7.	**PATIENT GROUP DIRECTIONS**	
	The following Public Health England (PHE) PGD's were noted at JAPC: • Rotavirus vaccine v5.00 Administration of rotavirus vaccine (live) to infants aged 6 weeks to 23 weeks and 6 days for active immunisation against rotavirus. This is an update to the existing PHE PGD Rotavirus vaccine template (v4.00), which will take effect from 1st July 2021. • Meningococcal group A, C, W and Y (MenACWY) conjugate vaccine v4.00 Administration of meningococcal group A, C, W and Y (MenACWY) conjugate vaccine to individuals eligible for the national routine MenACWY vaccination programme; university freshers (catch-up); outbreak control and contacts of confirmed cases, for active immunisation against Neisseria meningitidis. This is an update to the existing PHE PGD Meningococcal group A, C, W and Y (MenACWY) conjugate vaccine template (v3.00), which will take effect from 1st July 2021.	

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Item		Action
8.	**MISCELLANEOUS**	
a.	**Moderate Rheumatoid Arthritis** Mr Moore reported that a request to enable the prescribing of Adalimumab, Etanercept and Infliximab for patients with Rheumatoid Arthritis (RA) defined as moderate (DAS28 score of 3.2-5.1) has been received from UHDBFT in consultation with CRHFT. In February 2021 NICE approved Filgotinib for the treatment of moderate to severe RA (DAS 28 score >3.2) in patients who have failed on at least 2 csDMARDs. Following this there is a more pronounced unmet clinical need for more therapies to be available for prescribing for patients with moderate RA. NICE TA375 recommends Adalimumab, Etanercept and Infliximab for the treatment of severe RA defined as a DAS28 sore of >5.1 after the failure of at least 2 csDMARDs. NICE are currently in the process of a partial update to TA375, which will cover the use of these drugs for patients with moderate RA, who have failed at least 2 csDMARDs. The TA is expected to be published on 15th July 2021. NICE reviewed the clinical evidence during the approval process for TA375 severe RA and have stated that the clinical evidence suggests that Adalimumab, Etanercept and Infliximab are likely to be similarly effective in both moderate and severe disease. In the current update NICE have deemed Adalimumab, Etanercept and Infliximab as cost-effective options based on the principle of price reduction through the availability of biosimilars. (Abatacept has not been deemed cost-effective so is not recommended). A discussion took place with respect to sequential switching of drugs and whether the moderate RA pathway should reflect the severe RA pathway in regard to this. Both pathways will be reviewed and taken to the MMSCGG meeting. **Action:** JAPC supported the proposal to utilise adalimumab, etanercept and infliximab for moderate RA, subject to the publication of NICE TA375 updated guidance. Following this, the moderate RA pathway will be updated and agreed virtually by JAPC members presenting the most cost effective options in order. Mr Dhadli suggested that the issue of sequential use should follow the same principles previously agreed at JAPC for severe RA.	**SQ/DM**
9.	**GUIDELINE GROUP ACTION TRACKER**	
	The summary of key messages from the Derbyshire Medicines Management Shared Care and Guideline Group meeting held in June 2021 was noted. Mr Dhadli highlighted the following: Traffic Lights: • Budesonide + Formoterol + glycopyrronium (Trixeo aerosphere) – classified as GREY for the maintenance treatment of moderate to severe COPD. Triple therapy is reserved for exceptional use in severe disease in the presence of persistent exacerbations despite other treatments. • Glycopyrronium + formoterol (Bevespi Aerosphere) – classified as GREEN, as per local COPD guidance. Choice should be based on patient ability to tolerate and use inhaler device.	

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	• Potassium dihydrogen phosphate – classified as RED, as per UHDBFT/CRHFT formularies. Hospital to prescribe and supply. • Thuasne Action Reliever osteoarthritis knee brace – classified as DNP, medical device (appliance). Awaiting national review. • Delafloxacin – reclassified as DNP from RED, this decision was based on secondary care clinician's preference. • Pizotifen – reclassified as GREY from GREEN. Review existing patients when appropriate. Not available for new patients. • Rifampicin (clarification of existing) – classified as RED for all indications, including TB. • Clomipramine MR (Anafranil SR) – removed as discontinued. • Sodium chloride 5% eye drops (Aeon) – removed entry for specific brand. Formulary/Clinical Guideline Update: • CNS chapter – replaced diamorphine with morphine injections as per End-of-Life pathway. Long-term supply issue with diamorphine. Link to SPS memo added. • Endocrine chapter – removed advice to use betamethasone soluble instead of soluble prednisolone due to cost effectiveness. • Skin chapter/Acne guideline – removed Dalacin T solution due to discontinuation. • Type 2 diabetes guideline – cross referenced dapagliflozin use in heart failure. • Respiratory chapter, COPD guideline, summary of common inhalers document – updated to include Trixeo and Bevespi. Guideline Timetable: • The guideline table action summary and progress were noted by JAPC.	
10.	**BIOSIMILAR REPORT**	
	Mr Dhadli advised that the biosimilar report has been tabled for information.	
11.	**REGIONAL MEDICINES OPTIMISATION COMMITTEE (RMOC)**	
a.	**<u>RMOC Shared Care Agreement consultation</u>** Mr Dhadli stated that RMOC (North) have been commissioned to review a series of shared care protocols over the following months. The second and third set of shared care protocols are currently open for consultation. The documents are intended to represent the minimum information required to support safe, effective sharing of prescribing of the specified drugs. The shared care protocols have been drafted in line with the agreed RMOC process using key sources such as the BNF, relevant Summaries of Product Characteristics, MHRA safety warnings, national guidance and specialist input. RMOC shared care agreements (SCA) will be medicine-specific and not condition-specific, this will have implications for the Derbyshire local ADHD shared care agreement. Children are not currently included in the RMOC SCA'S, the ask from NHS England was to focus upon adults as the initial phase. Children's SCA should follow, most probably in 2022. Narcolepsy is to be included to the RMOC SCA as a licenced indication.	

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	Currently narcolepsy is not included in the local SCA, and methylphenidate and dexamphetamine do not have narcolepsy as an indication in the Derbyshire traffic light classifications. Following feedback from the first set of shared care protocols from JAPC members, amendments to the local SCA templates are being made to reflect the RMOC SCA's for consistency.	
12.	**JAPC BULLETIN**	
	The June 2021 bulletin was ratified.	**SD**
13.	**MHRA DRUG SAFETY UPDATE**	
	The MHRA Drug Safety Alert for June and July 2021 was noted. Mr Dhadli highlighted the following MHRA advice: <u>June 2021</u> • CDK4/6 inhibitors (abemaciclib▼, palbociclib▼, ribociclib▼): reports of interstitial lung disease and pneumonitis, including severe cases – cases of interstitial lung disease and pneumonitis have been reported in patients receiving CDK4/6 inhibitors indicated for some breast cancers. **Ensure that patients taking these medicines are aware of the need to seek advice right away if they develop new or worsening respiratory symptoms**. • Atezolizumab (Tecentriq▼) and other immune-stimulatory anti-cancer drugs: risk of severe cutaneous adverse reactions (SCARs) – cases of severe cutaneous adverse reactions, including Stevens-Johnsons syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in patients treated with immune-stimulatory anti-cancer drugs, including atezolizumab. **Advise patients to be vigilant for the signs of severe skin reactions and to seek urgent medical advice if they occur.** • COVID-19 vaccines: updates for June 2021 – MHRA continue to publish the summaries of the Yellow Card reporting for the COVID-19 vaccines being used in the UK. Information about a review of reports of menstrual disorders and unexpected vaginal bleeding with the three COVID-19 vaccines currently being used in the UK has been included in the weekly summary. The current evidence does not suggest an increased risk of either menstrual disorders or unexpected vaginal bleeding following vaccination with the vaccines reviewed (Pfizer/BioNTech, COVID-19 Vaccine AstraZeneca or COVID-19 Vaccine Moderna). The advice remains that the benefits of the vaccine outweigh the risks for most people. Reports of suspected menstrual disorders and vaginal bleeding with COVID-19 vaccines will continue to be closely monitored. <u>July 2021 (noted a month earlier because of the chloramphenicol advice)</u> • Chloramphenicol eye drops containing borax or boric acid buffers: use in children younger than 2 years – following a review of the available toxicological data and a calculation of daily exposure to boron from a typical dosing regimen, MHRA have concluded that the **balance between the benefits and risks of chloramphenicol eye drops containing borax or boric acid remains positive for children aged 0 to 2 years. Chloramphenicol eye drops can be safely administered to children aged 0 to 2 years where antibiotic eye drop treatment is indicated.**	

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Item		Action
	• Herbal and homeopathic medicines: reminder to be vigilant for suspected adverse reactions and to report them to the Yellow Card scheme – if an adverse drug reaction is suspected, ask patients if they are taking any herbal or homeopathic medicines and report any suspicions to the Yellow Card scheme. Remind patients to check that a herbal or homeopathic medicine is licensed and to follow the advice included in the patient information. • Oral retinoid medicines (isotretinoin▼, alitretinoin▼, and acitretin▼): temporary monitoring advice during coronavirus (COVID-19) pandemic – guidance has been published about the use of remote consultations for pregnancy prevention in women of childbearing potential and monitoring for signs of psychiatric reactions (especially depression) and other safety risks in all patients taking oral retinoid medicines during the COVID-19 pandemic. • COVID-19 vaccines: updates for July 2021 – revisions have been made to the information for healthcare professionals and information for UK vaccine recipients for the COVID-19 Vaccine Moderna and Pfizer/BioNTech COVID-19 vaccine following a thorough review of extremely rare reports of myocarditis and pericarditis after COVID-19 vaccination. These events are extremely rare and tend to be mild when they do occur. The advice remains that the benefits of getting vaccinated outweigh the risks in the majority of people. **Varenicline (Champix) supply issues** Pfizer are currently facing an issue with the supply of varenicline (Champix) across all doses and presentations. Pfizer anticipate this supply disruption will last for at least several weeks. The current recommendation is that until the Champix shortage is resolved, patients will need to consult with their healthcare professional to choose an alternative treatment option. For those who have already started a course of Champix, there isn't a lot of evidence on switching from Champix to an alternative stop smoking medication like combination NRT, but that would seem a reasonable option.	
14.	**HORIZON SCAN**	
a.	**Monthly Horizon Scan** Mr Dhadli advised JAPC of the following new drug launches, new drug formulations, licence extensions and drug discontinuations: New drug launches in the UK: • Onasemnogene abeparvovec (Zolgensma) – classified as **RED** (as per NHS England commissioning intentions) Licence extensions: • Atezolizumab (Tecentriq) – previously classified as **DNP/RED** • Daratumumab (Darzalex) – previously classified as **DNP/RED** • Elexacaftor+ ivacaftor + tezacaftor (Kaftrio) – previously classified as **RED** • Enzalutamide (Xtandi) – previously classified as **DNP/RED** • Osimertinib (Tagrisso) – previously classified as **DNP/RED** • Pembrolizumab (Keytruda) – previously classified as **DNP/RED**	

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Item		Action
	Drug discontinuations: May 2021 • Acnecide Wash (Benzoyl peroxide) • Elleste Solo MX 80 (Estradiol) • Esbriet Capsules (Pirfenidone) • Evista (Raloxifene) • Fentalis (Fentanyl) • Fluor-a-day (Sodium fluoride) • Gardasil (HPV vaccine) • Glytactin Restore Powder 5 • Linc Gel (Lidocaine/chlorhexidine) • Losinate (Tamsulosin) • Neofordex (Dexamethasone (as acetate)) • Onexila XL (Oxycodone) • Perfalgan (Paracetamol) • Physeptone (Methadone) • Promixin (Colistimethate sodium) • Santizor XL (Tolterodine) • Seractil (Dexibuprofen) • Solian Liquid (Amisulpride) • Telzir Oral Suspension (Fosamprenavir) • Xatral (Alfuzosin hydrochlor.) • Zydol XL (Tramadol) June 2021 • Bleo-Kyowa (Bleomycin sulf.) • Galactomin 17 • GlucoMen LX Ketone • GlucoMen LX Sensors • Linc Pure Gel • Psoriderm Emulsion Bath Additive • Vertab SR (Verapamil) • Xeloda (Capecitabine)	
15.	**NICE SUMMARY**	
	Mrs Qureshi informed JAPC of the comments for the CCG which had been made for the following NICE guidance in June 2021: TA702 Ibrutinib with obinutuzumab for untreated chronic lymphocytic leukaemia and small lymphocytic lymphoma (terminated appraisal) – classified as **DNP** (NHS England as per NICE TA702) TA703 Ibrutinib with rituximab for untreated chronic lymphocytic leukaemia (terminated appraisal) – classified as **DNP** (NHS England as per NICE TA703) TA704 Trastuzumab deruxtecan for treating HER2-positive unresectable or metastatic breast cancer after 2 or more anti-HER2 therapies – classified as **RED** (NHS England as per NICE TA704)	

Item		Action
	TA705 Atezolizumab monotherapy for untreated advanced non-small-cell lung cancer – classified as **RED** (NHS England as per NICE TA705) TA706 Ozanimod for treating relapsing–remitting multiple sclerosis – classified as **DNP** (NHS England as per NICE TA706) TA707 Nivolumab for previously treated unresectable advanced or recurrent oesophageal cancer – classified as **RED** (NHS England as per NICE TA707) TA708 Budesonide orodispersible tablet for inducing remission of eosinophilic oesophagitis – to remain classified as **RED** (as per NICE TA708) TA709 Pembrolizumab for untreated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency – classified as **RED** (NHS England as per NICE TA709) TA710 Ravulizumab for treating atypical haemolytic uraemic syndrome – classified as **RED** (NHS England as per NICE TA710) TA711 Guselkumab for treating active psoriatic arthritis after inadequate response to DMARDs – classified as **RED** (as per NICE TA711)	
16.	**MINUTES OF OTHER PRESCRIBING GROUPS**	
a.	• Chesterfield Drugs and Therapeutics Committee 18/05/2021 • UHDBFT Drugs and Therapeutics Group 18/05/2021 • Sheffield Area Prescribing Group 18/02/2021 • Sheffield Area Prescribing Group 15/04/2021 • Sheffield Area Prescribing Group 20/05/2021	
17.	**TRAFFIC LIGHTS – ANY CHANGES?**	
	Classifications Bempedoic acid & bempedoic acid/ezetimibe – GREY for primary hypercholesterolaemia or mixed dyslipidaemia: when a statin is contraindicated or not tolerated, and ezetimibe alone does not control low-density lipoprotein cholesterol well enough (for primary prevention) Ondansetron – GREY specialist initiation for IBS associated diarrhoea SGLT2i (including empagliflozin, canagliflozin, dapagliflozin) – GREEN specialist initiation, for adults with CKD in addition to an ACEi or an ARB if they have type 2 diabetes, and an ACR of 30mg/mmol or more **subject to NICE approval** Onasemnogene abeparvovec (Zolgensma) – RED (as per NHS England commissioning intentions) Ibrutinib with Obinutuzumab – DNP (NHS England as per NICE TA702) Ibrutinib with rituximab – DNP (NHS England as per NICE TA703) Trastuzumab deruxtecan – RED (NHS England as per NICE TA704) Atezolizumab monotherapy – RED (NHS England as per NICE TA705) Ozanimod – DNP (NHS England as per NICE TA706) Nivolumab – RED (NHS England as per NICE TA707) Budesonide orodispersible tablet – to remain classified as RED (as per NICE TA708)	

Item		Action
	Pembrolizumab – RED (NHS England as per NICE TA709) Ravulizumab – RED (NHS England as per NICE TA710) Guselkumab – RED (as per NICE TA711)	
18.	**ANY OTHER BUSINESS**	
a.	There were no items of any other business.	
19.	**DATE OF NEXT MEETING**	
	Tuesday, 10th August 2021, papers are to be circulated and agreed virtually as per JAPC interim Terms of Reference, which is effective during the COVID-19 pandemic.	