

The purpose of the Medicines Management newsletter is to deliver succinct, evidence-based advice and information on primary care prescribing issues. Aimed at busy prescribers wanting to know key messages from the many publications in the previous month.

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1. Round up of what's in the news

Sulfonylureas as second line drugs in type 2 diabetes and the risk of cardiovascular and hypoglycaemic events: population based cohort study.

Douros A, Dell'Aniello S, et al. *BMJ* 2018;362:k2693

This was a population based cohort study, to assess whether adding or switching to sulfonylureas is associated with an increased risk of myocardial infarction, ischaemic stroke, cardiovascular death, all-cause mortality, and severe hypoglycaemia, compared with remaining on metformin monotherapy in patients with type 2 diabetes.

The study showed an increased risk of myocardial infarction, all-cause mortality, and severe hypoglycaemia associated with the use of second line sulfonylureas compared with remaining on metformin monotherapy. The associations with myocardial infarction and all-cause mortality were driven by the switching to sulfonylureas and not the addition of sulfonylureas. Thus, in line with current recommendations on the treatment of type 2 diabetes, continuing metformin when introducing sulfonylureas is safer than switching.

Current local type 2 diabetes guidance - metformin remains first line recommended treatment and second line therapy should be added to existing metformin treatment at first intensification.

Omega-3 fatty acids for the primary and secondary prevention of cardiovascular disease.

Abdelhamid AS, Brown TJ, et al. *Cochrane Database of Systematic Reviews* 2018, Issue 7. Art. No.: CD003177.

To assess effects of increased intake of fish- and plant-based omega-3 for all-cause mortality, cardiovascular (CVD) events, adiposity and lipids. The review included 79 trials involving over 112,000 people. These studies assessed effects of greater omega-3 intake versus lower or no omega-3 intake for heart and circulatory disease.

The main types of omega-3 fats are alpha-linolenic acid (ALA), a fat found in plant foods, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), both found in fish.

Key results

Increasing EPA and DHA has little or no effect on all-cause deaths and cardiovascular events (high-quality evidence) and probably makes little or no difference to cardiovascular death, coronary deaths or events, stroke, or heart irregularities (moderate-quality evidence, coronary events are illnesses of the arteries which supply the heart). EPA and DHA slightly reduce serum triglycerides and raise HDL (high-quality evidence).

Eating more ALA (for example, by increasing walnuts or enriched margarine) probably makes little or no difference to all-cause or cardiovascular deaths or coronary events but probably slightly reduce cardiovascular events, coronary mortality and heart irregularities (moderate/low-quality evidence). Effects of ALA on stroke are unclear as the evidence was of very low quality.

There is evidence that taking omega-3 capsules does not reduce heart disease, stroke or death. There is little evidence of effects of eating fish. Although EPA and DHA reduce triglycerides, supplementary omega-3 fats are probably not useful for preventing or treating heart and circulatory diseases. However, increasing plant-based ALA may be slightly protective for some heart and circulatory diseases.

Locally the traffic light status of omega-3 is BROWN after consultant lipid specialist recommendation in patients with severe hypertriglyceridaemia (triglycerides >10mmol/L) after trial of fibrates +/- statins.

Evidence and tips on the use of medication compliance aids

Furmedge DS, Stevenson JM, et al BMJ 2018;362:k2801

Medication compliance aids (MCAs) such as Dossett boxes are used to support people taking medication who may find it difficult because of cognitive impairment or the complexity of their regimen.

There is little evidence to say whether these devices improve compliance, safety, satisfaction, or convenience taking medication.

Many commonly prescribed medicines may not be suitable for long term storage in a multi-compartment MCA because they can break down or expire when outside the standard sealed packaging. Drugs that are taken only when needed or those subject to frequent changes in dosage schedule are also unsuitable for multi-compartment MCAs.

Multi-compartment MCAs are often prepared in advance—make sure any changes in the medication regimen are clearly communicated to the pharmacist preparing the MCA.

Offer an annual medication review to all patients who are dispensed their medications in a multi-compartment MCA to minimise the chance that people continue inappropriate medication

Consider recording on the electronic records all patients that have their medicines dispensed in a MCA, so that all prescribers including locums are aware when making changes to prescriptions for patients.

NOACs and Antidepressants - What are the risks of using these together and how should these risks be managed?

<https://www.sps.nhs.uk/articles/noacs-and-antidepressants-what-are-the-risks-of-using-these-together-and-how-should-these-risks-be-managed/>

This review highlights potential drug interactions between NOACs and antidepressant agents that are known inhibitors/inducers of CYP3A4 or P-gp and also those that affect haemostasis.

- Co-administration of NOACs (novel oral anticoagulants) with drugs that affect haemostasis, such as SSRIs (Selective serotonin re-uptake inhibitors) or SNRIs (serotonin and noradrenaline re-uptake inhibitors), increases the risk of bleeding and the manufacturers of SSRIs and SNRIs advise caution when these agents are used concomitantly.
- See individual drug sections within the main text of this Q&A for NOAC manufacturers' comments regarding their concomitant use with an SSRI or SNRI.

When prescribing NOAC's for patients on either an SSRI or SNRI, clinicians are reminded to take this potential interaction into account and seek alternative oral anticoagulant if possible.

Deleted products 2018 | MIMS online for June 2018

AllStar (insulin pen)	Angiox (bivalirudin)	Electrolade
Fisio Chamber Vision	Floxapen (flucloxacillin)	Nuvelle Continuous (estradiol/norethisterone)
Salipraneb (salbutamol/ipratropium)	Tiloryth (erythromycin)	Vitaquick

2. Drug safety update primarily relating to primary care prescribing

(For more information see [Drug Safety Update](#)) Volume 11 Issue 10 May 2018

None relevant for primary care.

3. Local news and GP/pharmacist queries

Incorrect Ranitidine doses prescribed and dispensed for Paediatric patients

We have had reported to us 2 local medication incidents by a GP practice involving the prescribing and dispensing of incorrect doses of Ranitidine oral solution (75mg/5ml) in paediatric patients.

In one case a 6 week old was prescribed a dose of 2mls instead of the correct dose of 0.26mls according to patient weight.

In the second case, a 10 week old child was prescribed a dose of 5mls instead of the correct dose of 0.3ml according to patient weight. The same community pharmacy was involved in dispensing these prescriptions and it appears that in both cases, the dose prescribed was not appropriately checked against the patient weight.

Prescribing in Paediatrics - Advice from the BNF

Children, and particularly neonates, differ from adults in their response to drugs. Special care is needed in the neonatal period (first 28 days of life) and doses should always be calculated with care. At this age, the risk of toxicity is increased by reduced drug clearance and differing target organ sensitivity. When a prescription for a liquid oral preparation is written and the dose ordered is smaller than 5ml an oral syringe should be supplied.

Please be extra vigilant when prescribing and dispensing medicines for paediatric patients, ensuring that doses are calculated carefully and according to the patients most recent weight (check with parent/carer where needed)- or refer to mean weight values per age in the BNF where a weight is not available. Further information about the recognition, diagnosis and management of gastro-oesophageal reflux disease (GORD) in children and young children (including paediatric doses for Ranitidine) can be found in our local Derbyshire Medicines Management [guidelines](#). Our local guidelines state that when prescribing Ranitidine oral solution for paediatric patients, the 75mg/5ml strength should be used to allow for small volumes to be administered to the neonate/child.

Prescribing note:**1. Blood glucose test strips - type 1 diabetics**

Type 1 Diabetes in adults NICE NG 17, recommends routine self-monitoring of blood glucose levels for all adults with type 1 diabetes at least 4 times a day, including before each meal and before bed. This may be increased up to 10 times a day if any of the following apply:

- Desired target HbA1c level is not achieved
- Frequency of hypoglycaemic episodes increases
- There is a legal requirement to do so e.g. driving in line with DVLA
- During periods of illness
- Before, during or after sport
- When planning pregnancy, during pregnancy and while breastfeeding
- If needed for another reason e.g. impaired hypoglycaemia awareness, high risk activities, occupation or travel

Ketone monitoring NICE NG17 & 18, recommends considering monitoring of ketones in children, young people and adults as part of “sick-day rules” for managing type 1 diabetes during intercurrent illness or episodes of hyperglycaemia.

Prescribers are reminded preferred blood glucose test strip brands are for type 2 diabetic patients.

2. Insulin aspart brands - remember to prescribe by brand

Currently two different brands of insulin aspart are available on the market for prescribing and they are not interchangeable due to differences in the mechanism of action:

- Novo Rapid (**GREEN**)
- Fiasp (**GREEN after specialist recommendation**)

There are subtle differences between the onset of action time and the timing of the injections, as shown in the table below.

	Timing of injection	Onset of action	Peak	Duration of action
Rapid-acting analogues				
Insulin aspart (Fiasp) (After specialist recommendation) <i>-an option for type 1 diabetes (NG17) in new adult patients</i>	Within 0-15 mins of meal	4 mins	1-3 hrs	3-5 hrs
Insulin aspart (Novo Rapid) <i>-an option for children and type 1 diabetes in patients already on treatment (NG17)</i>	Immediately before meal	10-20 mins	1-3 hrs.	3-5 hrs

Prescribers are reminded that insulin aspart should be prescribed by brand name, as the two brands are not interchangeable. Community pharmacists should check which brand the patient uses if presented with a generic prescription.

Valproate medicines – further information & advice about the Pregnancy Prevention Programme

In light of recent MHRA advice (April 2018 edition of [Drug Safety Update](#)) regarding use of Valproate medicines in women and girls of childbearing potential and requirement for conditions of the Pregnancy Prevention Programme to be met, Derbyshire CCGs have produced a primary care pathway to support prescribers in prioritising patient referrals to specialists for immediate and ongoing review. See Appendix 1 for a copy of this pathway

GPs are reminded that they must identify and recall all women and girls, who may be of childbearing potential, provide the Patient Guide and check they have been reviewed by a specialist in the last year and are on highly effective contraception. Please ensure that these patients are referred to the relevant specialist, using the primary care pathway to support this process.

Specialists must book in review appointments at least annually with women and girls under the Pregnancy Prevention Programme and re-evaluate treatment as necessary; explain clearly the conditions as outlined in the supporting materials and complete and sign the Risk Acknowledgement Form – copies of the form must be given to the patient or patient/caregiver/responsible person and sent to their GP. Further information and all the resources are available on the [MHRA Valproate Toolkit](#).

Graseby Syringe Drivers – actions following the Gosport Inquiry

You may be aware of recent media interest in relation to the Gosport Inquiry (<https://www.gosportpanel.independent.gov.uk/>) and use of the older Graseby MS16/MS26 syringe drivers across the NHS. As a result of this, we are seeking assurances that there are no Graseby ambulatory syringe drivers, of the type that worked by millimetres of syringe length (e.g. MS16, MS16A, MS26), still in use.

We are aware that some pumps may have historically been purchased by individual organisations/businesses or from charitable funds and may therefore not have come through formal organisational routes. If any of these types of pumps are found to be in use they should be withdrawn as soon as possible; ensuring patient care is not compromised. For further information please contact Jaskiran Dhamrait, Medicines Safety and Quality Pharmacist, Southern Derbyshire CCG at Jaskiran.dhamrait@nhs.net

4. Quality, Innovation, Productivity and Prevention (QIPP)

Fobumix inhaler – cost effective budesonide/formoterol inhaler.

Current Traffic light status for Derbyshire:

- Fobumix (80/4.5, 160/4.5, 320/9 DPI):
 - **GREEN:** alternative ICS/LABA to 1st line Fostair for adult asthma
 - **GREEN:** 2nd line option for COPD

	80/4.5 (=100/6)	160/4.5 (=200/6)	320/9 (=400/12)
Fobumix Breath-actuated dry powder inhaler	£21.50 x120	£16.99 x 60 £21.50 x120	£21.50 x 60
Symbicort Turbohaler	£28.00 x 120	£28.00 x 120	£28.00 x 60
DuoResp Breath-actuated dry powder inhaler	NA	£27.97 x 120	£27.97 x 60

Total spend on Symbicort over the last 12 months = £1.7m

Total spend on DuoResp over the last 12 months = £600k

Switching to Fobumix could potentially generate savings of approx. £500k over 12 month period.

June – price concessions

Prescribers should note that the re-imburement price on FP10 may not necessarily reflect the Drug Tariff price as a result of a drug shortage. These concessionary prices are set by the Department of Health to reflect actual market prices.

A concession only lasts until the end of the month in which it was granted. If there is an on-going supply problem, it is possible that a new concession will be granted by the Department of Health the following month, however this is not guaranteed

Drug	Pack size	Price concession	Drug tariff price
Amisulpride 50mg tablets	60	£7.52	£1.61
Amisulpride 100mg tablets	60	£9.95	£3.24
Amisulpride 200mg tablets	60	£14.98	£5.59
Aripiprazole 10mg tablets	28	£2.86	£1.99
Bicalutamide 50mg tablets	28	£14.75	£2.20
Bicalutamide 150mg tablets	28	£16.00	£5.72
Buprenorphine 2mg sublingual tablets sugar free	7	£5.24	£0.93
Buprenorphine 8mg sublingual tablets sugar free	7	£10.90	£1.81
Chlorpromazine 50mg tablets	28	£31.46	£28.09
Co-codamol 30mg/500mg capsules	100	£4.50	£3.88
Diamorphine 10mg powder for solution for injection ampoules	5	£16.56	£12.95
Digoxin 62.5microgram tablets	28	£1.50	£1.23
Digoxin 125microgram tablets	28	£1.50	£1.22
Digoxin 250microgram tablets	28	£1.50	£1.22
Doxazosin 1mg tablets	28	£0.80	£0.44
Doxazosin 2mg tablets	28	£0.70	£0.50
Doxazosin 4mg tablets	28	£0.78	£0.60
Glimepiride 3mg tablets	30	£4.00	£3.65
Irbesartan 75mg tablets	28	£2.35	£0.80
Irbesartan 150mg tablets	28	£3.99	£1.08
Irbesartan 300mg tablets	28	£5.49	£1.77
Lacidipine 2mg tablets	28	£2.95	£2.71
Lamotrigine 25mg tablets	56	£6.42	£1.08
Lamotrigine 50mg tablets	56	£7.97	£1.22
Lamotrigine 100mg tablets	56	£26.58	£1.76
Lamotrigine 200mg tablets	56	£36.20	£2.55
Latanoprost 50micrograms/ml eye drops	2.5	£12.48	£1.53
Latanoprost 50micrograms/ml/timolol 5mg/ml eye drops	2.5	£6.90	£2.44
Levetiracetam 100mg/ml Oral Solution	300	£6.95	£6.76
Mirtazapine 15mg orodispersible tablets	30	£1.27	£1.00
Mirtazapine 45mg orodispersible tablets	30	£1.76	£1.68
Mometasone 0.10% ointment	100	£7.19	£5.23
Nebivolol 5mg tablets	28	£1.14	£0.89
Nicorandil 10mg tablets	60	£2.50	£1.60
Nicorandil 20mg tablets	60	£4.65	£3.88
Orlistat 120mg capsules	84	£20.00	£15.90
Oxybutynin 2.5mg tablets	56	£2.23	£0.84
Oxybutynin 5mg tablets	56	£3.89	£1.19
Perindopril erbumine 4mg tablets	30	£2.42	£1.91

Pioglitazone 15mg tablets	28	£4.80	£0.50
Pioglitazone 30mg tablets	28	£6.50	£0.92
Pioglitazone 45mg tablets	28	£6.00	£0.66
Ramipril 2.5mg tablets	28	£2.82	£0.60
Sodium Valproate 200mg gastro-resistant tablets	100	£6.00	£4.04
Sodium Valproate SF Liquid 200mg/5ml	300	£5.94	£4.46
Tadalafil 5mg tablets	28	£38.59	£8.55
Telmisartan 20mg tablets	28	£0.95	£0.63
Tolterodine 1mg tablets	56	£3.16	£1.79
Tolterodine 2mg tablets	56	£2.46	£2.09
Topiramate 25mg tablets	60	£5.75	£1.01
Topiramate 50mg tablets	60	£8.50	£1.40
Topiramate 100mg tablets	60	£15.75	£2.29
Trimethoprim 200mg tablets	6	£0.40	£0.31
Trimethoprim 50mg/5ml oral suspension SF	100	£3.52	£2.30
Venlafaxine 37.5mg tablets	56	£2.96	£1.97
Venlafaxine 75mg tablets	56	£4.69	£1.94

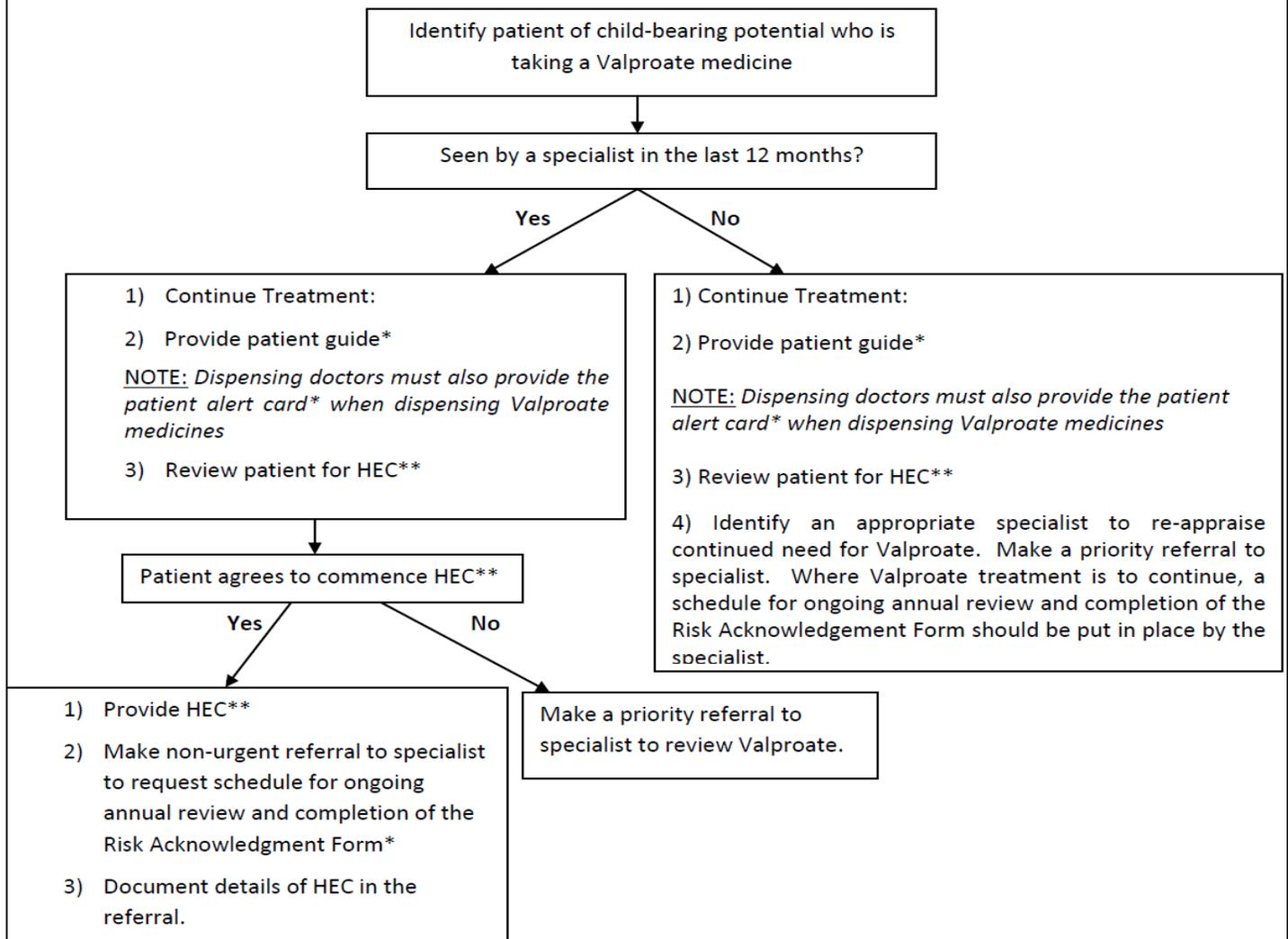
5. NICE summaries: New medicines (relating to primary care prescribing)

NG97: Dementia: assessment, management and support for people living with dementia and their carers. Local guidance is currently under review.

6. Useful resources

BMJ	www.thebmj.com
JAMA: The Journal of the American Medical Association	http://jama.ama-assn.org/
The Lancet	www.thelancet.com
The New England Journal of Medicine	http://content.nejm.org/
BMJ, JAMA and NEJM can be accessed in full-text directly through your NHS Athens Account via: National Library for Health: search via My Journals MyAthens: Via National Library for Health Resources or Local Resources. Current Lancet articles are sometimes available with free registration from http://www.thelancet.com/content/register . Print copies of The Lancet are available at DCGH library.	www.library.nhs.uk or www.athens.ac.uk
If you have not already registered for an NHS Athens Account, please register at: NB: It is recommended that you register on a Trust (NHS) PC for speedy confirmation of your username a password. Once registered, your account can be accessed from any computer with online access.	https://register.athensams.net/nhs/nhseng/
UKMI Nathnac NHS evidence Electronic medicines compendium Clinical Knowledge Summaries Medicines Prescribing Centre (Formerly NPC) Medicines for children (patient information leaflets) Drugs in lactation	http://www.ukmi.nhs.uk/ https://www.evidence.nhs.uk/search?om=%5B%7B%22srn%22%3A%5B%22%20ukmi%20%22%5D%7D%5D http://www.nathnac.org/ http://www.evidence.nhs.uk/ http://www.medicines.org.uk/emc/ www.cks.nhs.uk http://www.nice.org.uk/mpc/ http://www.medicinesforchildren.org.uk/ http://www.midlandsmedicines.nhs.uk/content.asp?section=6&subsection=17&pageIdx=1
UK teratology services	http://www.uktis.org/index.html
Vaccine update- Vaccination newsletter for health professionals and immunisation practitioners	https://www.gov.uk/government/organisations/public-health-england/series/vaccine-update

Primary Care pathway for patient referrals to specialists for review in line with the MHRA Valproate medicines Pregnancy Prevention Programme (PPP)



*Supporting information and resources can be found in the MHRA Valproate Toolkit available at this [link](#).

**HEC = Highly Effective Contraception: is considered for regulatory purposes to be those user independent methods such as the long acting reversible contraceptives (LARC), copper intrauterine device (Cu-IUD), levonorgestrel intrauterine system (LNG-IUS) and progestogen-only implant (IMP) and female sterilisation. Where user independent contraception is not used, then two complementary forms of contraception including a barrier method should be used.

Adapted and produced by Jaskiran Dhamrait, Medicines Safety and Quality Pharmacist, Southern Derbyshire CCG – July 2018. With thanks and acknowledgement to James Hooley, Medicines Safety Officer at University Hospitals of Derby and Burton.