Information to support primary care in managing patients affected by the shortages of methylphenidate prolonged-release capsules and tablets, lisdexamfetamine capsules, and guanfacine prolonged-release tablets

Background

There are supply disruptions affecting the following medications:

Methylphenidate

- Equasym XL® 10, 20, and 30mg capsules
- Xaggitin XL® 18 and 36mg prolonged-release tablets
- Concerta XL® 54mg prolonged-release tablets
- Xenidate XL® 27mg prolonged-release tablets

Lisdexamphetamine

- Elvanse® 20, 30, 40, 50, 60 and 70mg capsules
- Elvanse® Adult 30, 50 and 70mg capsules

Guanfacine

- Intuniv® 1, 2, 3 and 4mg prolonged-release tablets

The supply disruption is caused by a combination of manufacturing issues and increased global demand. An NPSA alert was issued on the 27th September 2023.
Other ADHD products remain available but stocks are not sufficient to meet the increased demand caused by other shortages.
Supply disruption is expected to resolve at various dates between October and December 2023.
The advice in this document is recommendations from SLAM/Oxleas and will not invalidate any NHS Shared Care Agreement in place if followed.

Action:

- **No new patients may be initiated on products affected by this shortage until the supply issues resolve**.
- Patients calling for advice should be informed of current stock situation and a management plan should be agreed with the patient and prescriber.
- For patients identified with insufficient supply remaining, work with the patient's usual pharmacy to find out which products/strengths are currently available and prescribe if appropriate. For some products the patient's community pharmacy may be able to obtain an unlicensed imported alternative, which can be considered (supply is likely to take 2-4 weeks). Please see the Specialist Pharmacy Service (SPS) Medicines Supply Tool for further information.
- Where prescriptions cannot be fulfilled, Community pharmacy colleagues will ask patients to contact their GP practice via econsults, telephone or face to face.
- If the patient is unable to access supply of their medication and the primary care clinician requires further guidance on a management plan, please contact the relevant mental health team. Please ensure specialist colleagues can be provided with all the necessary background information relating to the patient so they can advise/refer appropriately.
- Clinical information on switching between products is given below. Further information can be sought from:
  - **Maudsley Pharmacy Medicines Advice -** on 0203 228 2317
  - **Oxleas** – refer to local team (Children and Young People, and adults with a current referral),

Mental Health Hub (adults no longer under a CMHT) or call Oxleas Medicines Line for clinicians Tel: 01322 625002

- **For adults with sleep disorders under the care of Guy's and St Thomas' Sleep Centre**: Medicines advice (for patients with narcolepsy or idiopathic hypersomnia) - Tel: 0207 188 3430 Email: gst-tr.thesleeppharmacistgstt@nhs.net
- **For children and young people with sleep disorders under the care of Evelina London Children's Hospital:** Medicines Helpline – Tel: 020 7188 3003 (For urgent enquiries) Email: gst-tr.Evelinapharmacy@nhs.net

Clinical Information on switching between products

Methylphenidate

- All long-acting methylphenidate (MPH) preparations include an immediate-release component as well as a modified-release component.
- Preparations differ in their immediate release (IR) and extended release (ER) release profiles.
- Data from head-to head studies comparing long-acting MPH formulations[1, 2] suggest that clinical equivalence is most closely related to the IR component of the release mechanism, rather than the ER component.
- Therefore, the IR component should be used as a reference when switching between long-acting MPH formulations.
- Note that switching between formulations can result in changes in symptom management at different time periods during the day. Patients should be reviewed after the switch and doses adjusted if required.

How to switch between preparations:

1. Identify the new preparation to switch to, using table 1.
2. Select the dose to switch to by matching (as closely as possible) the IR component of the old and new preparations, using table 2 - 4.

Table 1. MPH preparations affected by the shortage, and options for switching:

Preparation affected by shortage	Switch options
Equasym XL® 10, 20, and 30mg capsules	Medikinet XL® MPH IR
Xaggitin XL® 18 and 36mg prolonged-release tablets	Affenid XL® Concerta XL® Delmosart XL® Matoride XL® Xenidate XL®
Concerta XL® 54mg prolonged-release tablets	Affenid XL® Delmosart XL® Matoride XL® Xaggitin XL® Xenidate XL®
Xenidate XL® 27mg prolonged-release tablets	Affenid XL® Concerta XL® Delmosart XL® Xaggitin XL®

Table 2. Equasym XL® release characteristics[1]

Equasym XL®		
Total daily dose	Immediate release component	Slow release component
	0 - 4 hours	4 - 8hours
10mg/day	3mg	7mg
20mg/day	6mg	14mg
30mg/day	9mg	21mg
40mg/day	12mg	28mg
50mg/day	15mg	35mg
60mg/day	18mg	42mg

Table 3. Concerta XL® and bioequivalent generic preparations release characteristics[1]

Affenid XL®, Concerta XL®, Delmosart XL®, Matoride XL®, Xaggitin XL®, Xenidate XL®		
Total daily dose	Immediate release component	Slow release component
	0 - 4 hours	4 - 12hours
18mg/day	4mg	14mg
27mg/day	6mg	21mg
36mg/day	8mg	28mg
45mg/day	10mg	35mg
54mg/day	12mg	42mg
63mg/day	14mg	49mg
72mg/day	16mg	56mg

Table 4. Medikinet XL® release characteristics1

Medikinet XL®		
Total daily dose	Immediate release component	Slow release component
	0 - 4 hours	4 - 8hours
5mg/day	2.5mg	2.5mg
10mg/day	5mg	5mg
20mg/day	10mg	10mg
30mg/day	15mg	15mg
40mg/day	20mg	20mg
50mg/day	25mg	25mg
60mg/day	30mg	30mg

Worked example:

- Current preparation: Equasym XL® 20mg/day
- Using table 1, switching to: Medikinet XL®
- Using table 2, IR component of current preparation = 6mg
- Using table 4, closest match for current IR component = 5mg, contained in Medikinet XL® 10mg preparation.

Lisdexamphetamine

- Lisdexamphetamine is a prodrug of dexamphetamine. It is broken down in red blood cells so that dexamphetamine is gradually made available.
- The dexamphetamine portion of lisdexamphetamine is complexed with the amino acid lysine, and in this form is inactive until activated by red blood cells. It is therefore unlikely to be abused for recreational or dependency-driven purposes, compared with dexamphetamine.
- In the event of unavailability of lisdexamphetamine, patients may be switched to dexamphetamine. However, if there is a risk of abuse or diversion of dexamphetamine, an alternative medication (eg. MPH XL) may be considered instead.
- Patients on Dexamphetamine should be switched back to Lisdexamphetamine (Elvanse®) when the product is back in stock.

Table 5. Suggested switches from lisdexamphetamine to dexamphetamine

Preparation affected	Switch to dexamphetamine
Elvanse® 20mg capsules	Dexamfetamine sulphate 5mg in divided doses
Elvanse® 30mg capsules	Dexamfetamine sulphate 7.5mg in divided doses
Elvanse® 40mg capsules	Dexamfetamine sulphate 10mg in divided doses
Elvanse® 50mg capsules	Dexamfetamine sulphate 15mg in divided doses
Elvanse® 60mg capsules	Dexamfetamine sulphate 17.5mg in divided doses
Elvanse® 70mg capsules	Dexamfetamine sulphate 20mg in divided doses and monitor for need to adjust dose further (maximum daily dose in children and adolescents is usually 20mg, although doses of 40mg may be necessary in rare cases)
Elvanse® Adult 30, 50 and 70mg capsules	As above, but note the need to enquire for current or history of substance misuse and assess risk of diversion

Worked example:

- Current preparation: Elvanse® 20mg capsules once daily
- Using table 5, switching to: Dexamfetamine
- 20mg lisdexamphetamine (Elvanse®) is equivalent to 5mg dexamphetamine.
- Therefore dose to be prescribed is dexamphetamine 2.5mg twice daily. Please note the 5mg dexamphetamine tablets are scored.

Guanfacine:

- Seek advice from a Specialist using contact details above as a different treatment will need to be sought based on the patient's ADHD medication history and medical history.
- Guanfacine is an alpha-2-agonist, and sometimes used as an alternative non-stimulant medication to atomoxetine.
- There are no alternative to guanfacine preparations..
- Guanfacine should not be stopped abruptly because of the risk of rebound hypertension. Hypertensive encephalopathy has been very rarely reported on abrupt cessation of treatment. Contact patients prescribed guanfacine and advise them to reduce their dose gradually if their stock of medication at home allows. Ideal tapering is to reduce in decrements of 1mg every 3 – 7 days. For example, for a patient prescribed 4mg Intuniv® tablets, with a stock of 3mg and 1mg tablets at home: reduce the dose to 3mg, then 2mg, then 1mg. Intuniv® tablets cannot be split.
- If it is not possible to reduce slowly, monitor BP and HR on stopping. The hypotensive effect of guanfacine may take about 2 – 4 days to resolve[3,4], but increased blood pressure has been reported

to persist in some cases[5]. This is usually asymptomatic and clinically insignificant[5,6]. Monitor BP and HR at day 2, and again at day 4. If blood pressure is raised at day 4, measure again at weekly intervals until normal. If there are signs of clinically significant rebound hypertension, seek medical advice.

Clonidine:

- **Seek advice from a specialist using the contact details above**.
- Clonidine is also an alpha-2-agonist and may be considered as an alternative to guanfacine.
- Note this is an unlicensed use of clonidine.
- If a switch to clonidine is considered necessary, start at 25mcg once daily at bedtime. Increase in 25mcg increments weekly if required, up to a maximum of 150mcg/day. Doses above 25mcg are usually given in divided doses (25mcg BD, or TDS for higher doses).

Further information

- National Patient Safety Alert
- Extended-release methylphenidate: a review of the pharmacokinetic profiles of available products, Specialist Pharmacy Service
- Attention deficit hyperactivity disorder: diagnosis and management, NICE
- Manufacturer's information about individual products, electronic medicines compendium

Patient/parents/carers - education and counselling

- Services to agree what information should be shared with patients/parents/carers re: shortages
- Patients/parents/carers should be provided age/cognitively appropriate verbal and written medication on medication. This should include any specific additional monitoring which may be needed for specific patients.
- Patients/parents/carers should avoid abrupt withdrawal of medication
- Patients/parents/carers can be signposted to the information on ADHD in adults available from the Royal College of Psychiatrists (adults) and to Medicines in Children leaflets (children/ parents/carers)
- Signpost to appropriate websites which can provide additional information/ support:
  - ADHD and You: https://www.adhdandyou.co.uk/
  - ADHD Foundation: https://www.adhdfoundation.org.uk/
  - ADDiSS: http://www.addiss.co.uk/
  - Mind- ADHD and mental health: https://www.mind.org.uk/information-support/tips-for-everyday-living/adhd-and-mental-health/
  - NHS- Living with ADHD: https://www.nhs.uk/conditions/attention-deficit-hyperactivity-disorder-adhd/living-with/
  - Young Minds: https://www.youngminds.org.uk/parent/parents-a-z-mental-health-guide/adhd/
  - ADHD in Adults https://www.rcpsych.ac.uk/mental-health/problems-disorders/adhd-in-adults

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