







Information on Managing ADHD Medicines Shortages

The following guidance is designed for primary and secondary care prescribers to provide assistance in maintaining supply of ADHD medicines for their patients during periods where there are supply issues. This guidance relates to prescribing in adults, children and adolescents. The nature and severity of the shortages is constantly changing and therefore the guidance aims to address all possible shortages and scenarios that could arise.

Switches are in order of preference, with those listed first being the most likely to provide similar symptom control to current treatment.

Prescribers should always act within their scope of competence and should refer to specialist teams when they feel appropriate. The guidance below has been reviewed by specialists in this field, and considered safe for primary care prescribers to undertake in times of shortages.

Choice and Medication[©] has a wide range of leaflets for individual ADHD medicines as well as comparison charts:

ADHD – Switching Methylphenidate Products

ADHD Formulations

ADHD Medicines and Side effects

Individual medicine leaflets are available here by selecting 'Patient Information Leaflets' from the drop down menu









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1. General Advice

- Patients should be advised to contact different community pharmacies to try to obtain their supply of ADHD medicine Different pharmacy multiples (i.e. Boots, Superdrug, Rowlands etc) and independents will use different suppliers, so it is always worth trying a few different pharmacies to obtain medicines.
- **Consider short treatment breaks to prolong supply** For patients taking stimulant medicines (methylphenidate, lisdexamfetamine and dexamfetamine), treatment breaks on weekends / non-working / non-school days could be considered. Functioning on these days is likely to be impacted and breaks may not be suitable for everyone. Those who have managed treatment breaks in the past could be asked to consider doing this again. Treatment breaks help prolong supply and reduce the risk of long-term tolerance to medicines. Breaks of 1-2 days do not require re-titration of dose, and patients should continue on their regular dose when they restart.
- Prescribers should not prescribe more than 30 days of these medicines at a time Access to medicines needs to remain fair, and issuing large quantities at a time could further exacerbate supply issues and goes against controlled drug prescribing best practice.
- Switching to shorter acting preparations can cause re-emergence of side effects Shorter acting formulations release the medicine into the blood stream faster, resulting in higher plasma peaks than their longer-acting alternatives. When switching to shorter-acting preparations, patients should be counselled on the possible risk of side effects and that these should usually reduce with time.
- Not all products are licensed in adults Check product licensing in the SmPC (available at <u>www.medicines.org.uk</u>) to see if a product is licensed for intended use. Where it is not licensed, it is considered 'off label' and the patient should be informed and best practice applied. Prescribing 'off label' is common practice in adults with ADHD since many of the standard medicines have no licence for initiation in adulthood.
- Patients should be given non-pharmacological support and signposted as appropriate below is a list of useful resources:
 - The Royal College of Psychiatrists provides information about ADHD, in the form of a leaflet http://www.rcpsych.ac.uk/healthadvice/problemsdisorders/adhdinadults.aspx
 - http://www.aadduk.org- This is a website for, and created by, adults with ADHD including information on University and College issues for students with ADHD
 - o http://www.addiss.co.uk- National Attention Deficit Disorder Information and Support Service
 - www.additudemag.com An American website with a wealth of information about living with ADHD









- o www.howtoadhd.com A website and YouTube channel dedicated to helping people with ADHD live and work effectively
- o https://www.nhs.uk/conditions/stress-anxiety-depression/mindfulness/
- o https://www.nhs.uk/apps-library/be-mindful/
- o <u>https://www.mind.org.uk/information-support/drugs-and-treatments/mindfulness/how-to-learn-mindfulness/</u>
- o <u>https://www.youngminds.org.uk/young-person/mental-health-conditions/adhd-and-mental-health/</u>

2. Managing Unavailability of Methylphenidate Products – General Advice

• Methylphenidate products are divided into three categories according to their duration of action. These categories are listed below and are mentioned in further detail in the relevant sections.

Туре 1	Concerta XL®, Xaggitin XL®, Affenid XL®, Xenidate XL®,
Duration of action: 12 hours*	Delmosart XL®, Matoride XL®
Release profile: An early boost and a second bigger one	
Туре 2	Equasym XL®
Duration of action: 8 hours*	
Release profile: More evenly spread throughout the day	
Туре 3	Medikinet XL®, Metyrol XL® and Meflynate XL®
Duration of action: 8 hours*	
Release profile: A big boost early and less later on	

* Duration of action taken from <u>SPS</u> however, experience shows that symptom control experienced by the patient is often shorter than the listed durations of action. Type 3 products provide a shorter duration of symptom control compared to the Type 2, likely due to their release profile.

• Guidance from the MHRA states that methylphenidate must be prescribed according to brand. In times of medicine shortages, prescribers may prefer to prescribe generically to minimise inconvenience and delays in treatment for the patient. **Generic prescribing only applies to Type 1 products**, as they have different tablet strengths to Type 2 and Type 3 products.









- Type 3 products (Medikinet XL[®], Metyrol XL[®] and Meflynate XL[®]) are equivalent to each other, however, the strength of these capsules is the same as Equasym XL[®] (Type 2 product). Therefore, generic prescribing of Type 3 products is not possible as it could result in the supply of Equasym XL[®] which has a different release profile.
- Experience shows that most patients are able to switch between methylphenidate formulations within the same product group without any significant issues. The differences that could arise include: slightly different experience of side effects, slight difference in symptom control or differences in the duration of action. Patients should be advised to report any problems arising from brand switches to their prescriber.
- Where doses are changed from once daily to twice daily, consideration should be given to the practicality of taking the second dose, particularly for children who need to take their second dose in school time.
- In the appendix are the approximate release profiles of the different methylphenidate products and of lisdexamfetamine.









2.1 Managing Unavailability of Type 1 Methylphenidate Products

If a patient is having trouble obtaining their prescription of Methylphenidate XL, the prescriber may consider prescribing generically for a short period of time so that the pharmacy can supply whichever brand is available, however this is not recommended as a long term course of action.

Type 1 Products	Type 1 Products		
Product and IR:MR ratio	Strengths	Appearance	Practical information
Concerta XL [®] 22% IR : 78% MR	18mg 27mg 36mg 54mg	atzo 18 atza 27 atza 36 atza 36	 Can be taken with or without food Swallow whole – do not chew, break, divide or crush
Xenidate XL [®] 22% IR : 78% MR	18mg 27mg 36mg 54mg		 Take with or without food All tablet strengths except 18mg can be divided
Matoride XL [®] 22% IR : 78% MR	18mg 36mg 54mg		 Take with or without food Swallow whole – do not chew, break, divide or crush
Affenid XL [®] 22% IR : 78% MR	18mg 27mg 36mg 54mg		 Take with or without food Swallow whole – do not chew, break, divide or crush









Delmosart [®] Xaggitin [®] 25% IR : 75% MR	18mg 27mg 36mg 54mg	2392 2391 2394 2395	 Take with or after breakfast Swallow whole – do not chew, break, divide or critical divide divide or critical divide divide or critical divide di di	ush
Switching Advice treatment)	(Switches are in order of p	preference, with the	ose listed first being the most likely to provide similar symp	tom control to current
Type 1 to a different type 1	 switching can ca If there is product Switching between otice subtle difficult report ba 	use differences in ct unavailability, the en Type 1 products erences in control ck to the prescribe	e the same brand of methylphenidate as there are subtle c symptom control and side effects. en type 1 products can be interchanged. s is unlikely to affect most patients. Patients should be adv of symptoms, duration the medicine lasts for and side effect r any issues with brand switches. ered as per section above.	ised that they may
Type 1 to Type 2	wear off sooner in the d	ay, whilst their effe lvised to alter the ti	action than the Type 1 products; this means the benefits of cts may be more noticeable in the first few hours. Patients ming of their morning dose if they feel this will better optim	should be informed
		Type 1 dose	Equivalent Type 2 dose	
		18mg	10mg*	
		27mg	20mg*	
		36mg	30mg	
		45mg	40mg*	
		54mg	50mg*	
		63mg		









		72mg	60mg			
	Where Type 2 product	* not directly equivalent, represents nearest equivalent dose Where Type 2 products do not provide long enough relief, wearing off too early in the day, a short acting immediate				
	release dose can be a	dded in the afternoon. Alternatively	contact the patient's specialist for further	r advice.		
Type 1 to Type 3	medicine will w	ear off sooner in the day.	than Type 1 and Type 2 products; this m			
		Type 1 dose	Equivalent Type 3 dose]		
		18mg	10mg*			
		27mg	20mg*			
		36mg	30mg			
		45mg	40mg*			
		54mg	50mg*			
		63mg				
		72mg	60mg			
	 * not directly equivalent, represents nearest equivalent dose Where Type 3 products do not provide long enough relief, wearing off too early in the day, a short acting immediate release dose can be added in the afternoon. Alternatively contact the patient's specialist for further advice. Alternatively, the dose could be split across the day. For example, Concerta XL[®] 45mg could be converted to Medikinet XL[®] 20mg in the morning and 20mg at lunch. Switching to twice daily will give a duration of action similar to the Type 1 products. 					









	 The use of twice daily dosing may lead to potential side effects in the evening, including effects on sleep appetite. If sleep is affected, then the second dose is being taken too late in the day and consideration sh given to taking it earlier or switching to a once daily regimen. 				
Type 1 to IR	Fou	rth Choice - Switc	h to be undertaken or advis	ed by specialist team	
	are i	more likely to requi	-	oviding symptom relief into the e	ed duration of effect. Adult patients evening, while some children or
		Type 1 dose	Equivalent IR dose	Suggested BD Dosing	Suggested TDS dosing
		18mg	15mg as a split dose	7.5mg BD	5mg TDS
		27mg			
		36mg	30mg as a split dose	15mg BD	10mg TDS
		45mg			
		54mg	45mg as a split dose	25mg OM and 20mg	15mg TDS
		J		afternoon	
		63mg		afternoon	









2.2 Managing Unavailability of Type 2 Methylphenidate Products

Type 2 Products			
Product	Strengths	Appearance	Practical information
Equasym XL [®] 30% IR : 70% MR	10mg 20mg 30mg	5544 10mg 20mg 30mg	 Take before breakfast Swallow whole, or sprinkle contents onto apple sauce and swallow straight away. Therapeutic plasma levels for approximately 8 hours The capsule contents must not be crushed or chewed
Switching Advice (treatment.)	Switches are in order of pre	eference, with tho	se listed first being the most likely to provide similar symptom control to current
Type 2 to a Type 3	Type 3 products will have wear off earlier in the day. These preparations are le If switching from a For patients on twi would switch to Me	a shorter duration ss likely to affect Type 2 to a Type ce daily Equasyn edikinet XL [®] 20m n of action is too	e 3, the dose is the same/equivalent. n XL [®] , switch to the same dose of Type 3 twice daily, e.g. Equasym XL [®] 20mg BD g BD. short, consider splitting the dose so it is taken morning and lunchtime or consider
Type 2 to a type 1	 First Choice - Preferable switch where a longer duration of action is preferred Type 1 products have a longer duration of action than Type 2 and as a result, the effects of the medication will last longer. Patients should be informed the effects of the medication will last longer and asked to report any effects on sleep If sleep is affected then consider switching to a Type 3 product or the dose could be taken earlier, where possible. 		





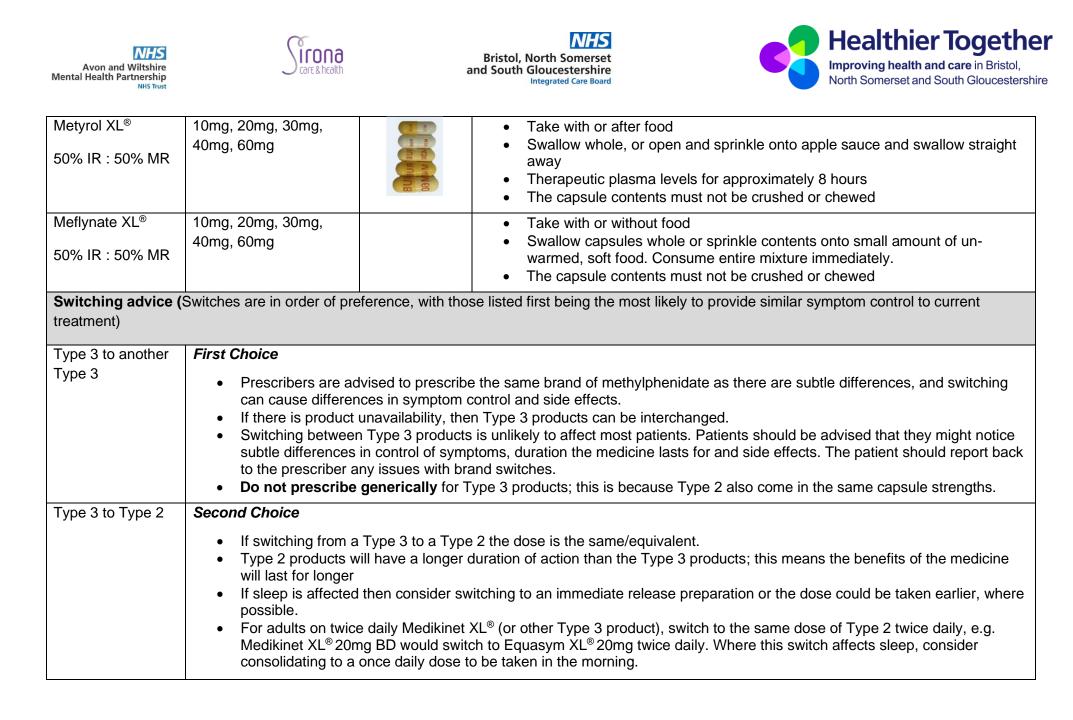


		Type 2 Dose	Equivalent Type 1 Dose	
		10mg	18mg*	
		20mg	27mg*	
		30mg	36mg	
		40mg	45mg*	
	* not directly	50mg	54mg*	equivalent, represents
	nearest equivalent	60mg	72mg	dose
Type 2 to IR	Third Choice - Switch	n to be undertaken or advise	d by specialist team	
	 Third Choice - Switch to be undertaken or advised by specialist team Total daily dose is the same / equivalent however, the dose should be split. The dose can be split either twice daily or three times daily, depending on the required duration of effect. Adult patients are more likely to require three times daily dosing, providing symptom relief into the evening, while some children or adolescents may prefer twice daily to minimise impact on sleep and appetite. e.g. Equasym XL[®] 30mg would be switched to methylphenidate 15mg twice daily, or methylphenidate 10mg three times daily. 		ire three times daily dosing, e daily to minimise impact on sleep	

2.3 Managing Unavailability of Type 3 Methylphenidate Products

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Type 3 Products			
Product	Strengths	Appearance	Practical information
Medikinet XL®	5mg, 10mg, 20mg, 30mg, 40mg, 50mg, 60mg	HILL	 Take with or after food Swallow whole, or open and sprinkle onto apple sauce and swallow straight away Therapeutic plasma levels for approximately 8 hours
50% IR : 50% MR			The capsule contents must not be crushed or chewed











Type 3 to Type 1	Third Choice				
	will last for longerIf sleep is affected then consider s	r duration of action than the Type 3 products; this switching to a Type 2 product. e option for those patients on a Type 3 product tw			
	Type 3 Dose	Equivalent Type 1 Dose			
	10mg	18mg*			
	20mg	27mg*			
	30mg	36mg			
	40mg	45mg*			
	50mg	54mg*			
	60mg	72mg			
	* not directly equivalent, represents nearest equivalent dose				
Type 3 to IR	Fourth Choice - Switch to be undertaken or advised by specialist team				
	times daily, depending on the required du	however the dose should be split. The dose can iration of effect. Adult patients are more likely to , while some children or adolescents may prefer	require three times daily dosing,		
	e.g. Equasym XL [®] 30mg could be switche	ed to methylphenidate 15mg twice daily or methy	Iphenidate 10mg three times daily		









3. Managing Unavailability of Lisdexamfetamine

Lisdexamfetamine	Products		
Product	Strengths	Appearance	Practical information
Elvanse [®] Elvanse adult [®]	20mg 30mg 40mg 50mg 60mg 70mg 20mg 30mg 40mg 50mg 60mg 70mg	S489 20 mg 30 mg S489 50 mg S689 50 mg S689 70 mg S689 50 mg S489 50 mg S489	 Swallow whole or empty into liquid and swallow straight away Capsules can be opened and the contents added to yoghurt Take with or after food Avoid large doses of Vitamin C in the morning, (e.g. orange juice and some supplements such as Berocca[®]) as these can reduce the absorption and efficacy of lisdexamfetamine
Switching Advice (S treatment.)	witches are in order o	f preference, with those listed first	being the most likely to provide similar symptom control to current
Switching to another	First Choice		
brand	Where possible, pa children and adole	-	and that is licensed for them. Elvanse adult $^{\ensuremath{\mathbb{B}}}$ for adults and Elvanse $^{\ensuremath{\mathbb{B}}}$ for
		hortage of brands, a generic presc might be 'off label' and take appro	ription for "Lisdexamfetamine" can be issued and prescribers should opriate action.
Lisdexamfetamine to dexamfetamine	Second Choice		

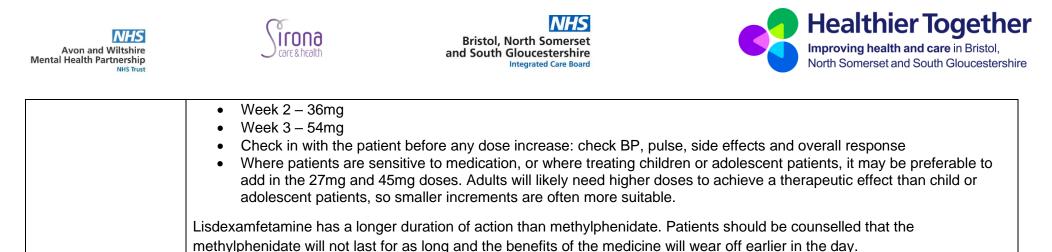








	 Lisdexamfetamine 30mg → Dexamfetamine 5 - 7.5mg BD Lisdexamfetamine 40mg → Dexamfetamine 7.5 - 10mg BD Lisdexamfetamine 50mg → Dexamfetamine 10 - 12.5mg BD
	 Lisdexamfetamine 50mg → Dexamfetamine 10 – 12.5mg BD Lisdexamfetamine 60mg → Dexamfetamine 12.5 – 15mg BD Lisdexamfetamine 70mg → Dexamfetamine 15 – 17.5mg BD
	Both the generic and Amfexa [®] preparations have a score line, however halving Amfexa® is considered 'off-label' use as the manufacturer states: "The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses".
	Twice daily dosing should be taken morning and lunchtime. Some patients will require the total dose to be divided into three times daily dosing.
	Further dose adjustments are subject to patient feedback (including adverse events) and monitoring (BP, pulse), again bearing in mind this is a holding arrangement.
	Dexamfetamine is not licensed in adults and therefore its use would be 'off label'.
	Dexamfetamine is more likely to cause agitation, anxiety and irritability than lisdexamfetamine. These side effects are likely to subside with time but may be experienced during the first few days after switching.
	Switching recommendations are based on expert specialist opinion and information courtesy of Oxford Health NHS Foundation Trust.
Switching to	Third Choice
methylphenidate	Lisdexamfetamine can be switched to long-acting methylphenidate, provided that the patient has not already had an ineffective trial of methylphenidate. This switch is preferred if there was previously a good response to methylphenidate, or where there are abuse/misuse concerns. The following titration regimen for a switch to a methylphenidate XL type 1 product can be started after stopping lisdexamfetamine:



4. Managing Unavailability of Dexamfetamine

Product	Strengths	Appearance	Practical information
Dexamfetamine (generic)	5mg		 Tablets have a score line Take with or after food
Amfexa®	5mg 10mg 20mg		 Both the generic and Amfexa[®] preparations have a score line however halving Amfexa[®] is considered 'off-label' use as the manufacturer states: "The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses". Amfexa[®] is halved in practice and it is safe to advise this. Take with or after food









Switching to another brand	<i>First Choice</i> The dexamfetamine products are interchangeable and no problems are expected when changing between the above two products.		
Dexamfetamine to	Second Choice		
Lisdexamfetamine	The guiding principle is to start conservatively with the lower end of the dose range, increasing if necessary. Please consider the switch as a holding arrangement rather than a perfect replacement.		
	 Dexamfetamine 5 - 7.5mg BD → Lisdexamfetamine 30mg Dexamfetamine 7.5 - 10mg BD → Lisdexamfetamine 40mg Dexamfetamine 10 - 12.5mg BD → Lisdexamfetamine 50mg Dexamfetamine 12.5 - 15mg BD → Lisdexamfetamine 60mg Dexamfetamine 15 - 17.5mg BD → Lisdexamfetamine 70mg Switching recommendations are based on expert specialist opinion and information courtesy of Oxford Health NHS Foundation Trust.		
Switching to	Third Choice		
methylphenidate	Switch to be undertaken or advised by specialist team		

5. Managing Unavailability of Guanfacine

- GP surgeries and specialist teams should promptly and proactively identify patients prescribed guanfacine and refer them back to their specialist team These patients should be referred to the specialist team outlined on the shared care agreement. Abrupt cessation of guanfacine can result in rebound hypertension, therefore patients need to be weaned off the medicine where possible, and will require specialist input.
- Where abrupt cessation of guanfacine occurs, any rebound hypertension typically resolves within 2 4 days^{2,3} and is usually asymptomatic and clinically insignificant ^{4,5}. There have been rare reports of hypertensive encephalopathy. Patients should be advised to check their blood pressure 2 and 4 days after abrupt cessation. If their BP remains raised then they should check weekly until it









returns to normal. Blood pressure readings can be done at their GP surgery or local community pharmacy. If there are signs of clinically significant rebound hypertension then this should be managed appropriately.

• **Do not switch to other medicines without advice from a specialist service** – Guanfacine is recommended after other medicines have failed. Switching to alternative medicines requires specialist input.

6. Managing Unavailability of Atomoxetine

Do not switch to other medicines without advice from a specialist service – Normally atomoxetine is recommended where stimulants are not suitable, meaning switching options are extremely limited.

7. Monitoring After Switches

- No additional baseline monitoring is needed when undertaking switches within the stimulant family, unless there has been any recent change to the patient's physical health.
- Patients should be advised to have their blood pressure and pulse checked after any product type or medicine switch. Monitoring is not
 required when switching between Type 1 products or Type 3 products, e.g. Concerta XL[®] to Xaggitin XL[®]. This can be done at home if
 they have a machine, at their local pharmacy, or at their GP surgery. If either of these measurements are abnormal then they should
 contact their GP, and the GP should refer to the shared care protocol for management advice.
- Blood pressure and pulse should be checked after any dose increases. Those titrating onto methylphenidate from another medicine should inform their GP of their blood pressure and pulse before any dose increases can be made.
- Any switches to or from non-stimulant medicines will be managed by secondary care who can advise on appropriate monitoring.









8. Switching Back Advice

8.1 Switching Back to Previous Methylphenidate Product

- If the patient was switched to a different brand of the same type of methylphenidate during the shortage (e.g. Type 1 to Type 1), have a conversation with the patient to ascertain whether to switch back, taking into account adequate symptom control and product acquisition cost.
- The BNSSG formulary first line choice and lowest acquisition cost methylphenidate product is Xaggitin XL[®]. If switching back to their original product then do so as soon as their next prescription is due. Please ensure you check the SPS stock checker to ensure the intended strength is back in stock before switching.
- Differences between preparations are very slight but the effect on each patient will vary, therefore any decision about switching brands needs to be a shared decision between the patient and their prescriber. Pay consideration to the local BNSSG formulary choices, bearing in mind that in BNSSG the first line methylphenidate product is Xaggitin XL[®].
- If switching back to a different type of methylphenidate products (e.g. Type 2 to Type 1), ensure relative dose equivalences are consulted when switching back, as per the tables above, to ensure they are switched back to the appropriate dose. Advise patients to report any changes in their symptom control or side effects after switching, and review the patient post switch.
- If the patient remains on the switched brand of methylphenidate, there is no need to update the shared care paperwork or let the ADHD specialists know.
- All ongoing methylphenidate prescribing should be by brand. When switching products, the prescriber should ensure there are no undispensed prescriptions pending before issuing a script for a different product, to reduce the risk of diversion, misuse or overdose. Prescribers should always request that the pharmacy mark any items no longer required as 'not dispensed' before issuing a new prescription for an alternative product. See <u>BNSSG guidance on cancelling Electronic Prescriptions</u>.

8.2 Switching back to Lisdexamfetamine

- For those patients switched to dexamfetamine, restart Elvanse[®] / Elvanse Adult[®] back on the previous dose once supply resumes.
- For those patients switched to methylphenidate, restart at half (or close to half) the previous Elvanse[®] / Elvanse Adult[®] dose for a week, and then increase and prescribe their previous dose.









- If for any reason the patient does not wish to switch back to lisdexamfetamine, e.g. patient switched from lisdexamfetamine to methylphenidate, who wishes to remain on methylphenidate, then this would require communication to the ADHD specialist and a new shared care agreement would be needed.
- If the patient was switched from lisdexamfetamine to dexamfetamine and wishes to remain on dexamfetamine, this should be discussed with the ADHD specialist as this would need careful consideration long term. This would also require a new shared care agreement.

8.3 Switching back to Dexamfetamine

• For those patients switched to Elvanse® / Elvanse Adult®, restart dexamfetamine back on the previous dose once supply resumes.

8.4 Switching back to Guanfacine or Atomoxetine

• Switching back to these medicines should be overseen or advised by the ADHD specialist. Restarting within primary care will be possible in some cases but please contact the specialist for advice on how to titrate the dose.

References

1) Lisdexamfetamine to dexamfetamine switching advice from Oxford Health NHS Foundation Trust, March 2022

2) Zamboulis C, et al. Withdrawal of guanfacine after long-term treatment in essential hypertension. Observations on blood pressure and urinary noradrenaline. *Eur J Clin Pharmacol.* 1981, 19(1)

3) Reid et al. Guanfacine: effects of long-term treatment and withdrawal. Br J Clin Pharmacol 1980, 10 (suppl1)

4) Newcorn JH et al. Extended release guanfacine hydrochloride in 16-17 year olds with ADHD: a randomised-withdrawal maintenance efficacy study. *J Child Psychol & Psych.* 2016, 57:6

5) Psychotropic drug Directory 2020/21



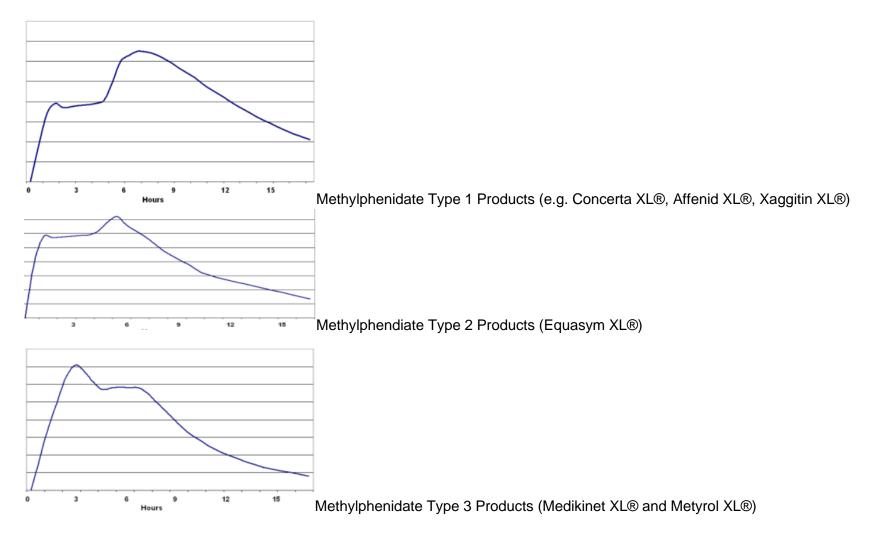




Appendix - Release Profiles of Methylphenidate and Lisdexamfetamine

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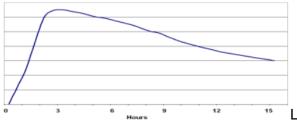








Avon and Wiltshire Mental Health Partnership NHS Trust



Lisdexamfetamine (Elvanse® and Elvanse Adult®)