Protocol for Management of Methylphenidate Shortages.

This document aims to support switching between different formulations of Methylphenidate Long-Acting Preparations.

Actions for Primary Care Before Seeking Specialist Referral

- Follow Primary Care flow charts below:
  1-adults-primary-care-management-during-adhd-medication-shortage.pdf
  2-children-primary-care-management-during-adhd-medication-shortages.pdf
- If a medication holiday is not appropriate or the proposed steps within the relevant flow chart have failed / are unsuitable, seek advice from the patient's specialist who may consider a switch in formulations as per guidance below.

Actions for Specialist

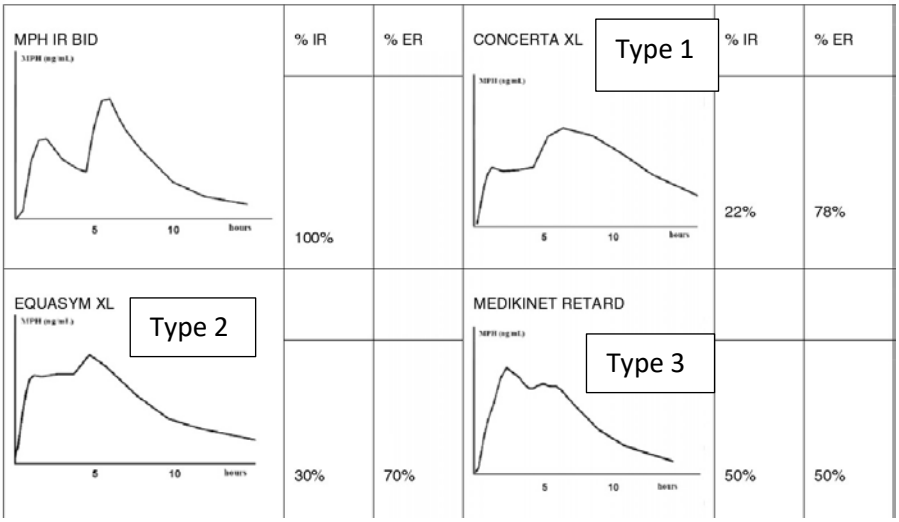
Step 1. Prior to considering a switch in modified release preparation:

i. Undertake an urgent review / risk assessment of the patient, weighing the pros and cons of undertaking a switch.
ii. Consider whether a treatment holiday is the best option for the patient.
iii. Discuss with patient the possible difference in symptom management.
iv. Consider the timing of target symptoms and use this to guide which capsule formulation may be best.
v. Discuss the possible side effects and escalation processes.
vi. Ensure family / carers are aware that any changes to symptoms of co-morbidities should be reported to the prescriber.

Step 2. Formulation Comparison:

- 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.
- Switching between long – acting preparations should be guided by the different pharmacokinetic profiles in addition to the other considerations outlined in by the Specialist Pharmacy Services (1).

Pharmacokinetic Profiles



Step 3. Switching between preparations:

- Note that switching between formulations can result in changes in symptom management at different time periods during the day. An example of this is that **TYPE 3** medications such as Medikinet XL will target symptoms in the morning more potently whereas **TYPE 1** medications such as Concerta XL have greatest clinical effect on symptoms later in the day, typically in the early afternoon. Patients should be reviewed after the switch and doses adjusted if required.
- Switching between bioequivalent tablets (**TYPE 1**) is the preferred choice for switching. During the shortage, as indicated on the APC website and formulary, prescriptions for TYPE 1 should be prescribed generically to allow community pharmacies to obtain whichever equivalent brand is currently available. Where no supplies are available, consider switching to a suitable long-acting capsule (**TYPE 2 or TYPE 3**).
- Modified Release capsules **MUST** be prescribed by brand, as the release profiles are different among the different capsule preparations.
- Data from head-to head studies comparing long-acting MPH formulations (2, 3) 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.
- Using the reference tables as a guide, see worked example below: -

Reference Tables

Type 1: (IR:MR = 22:78)		
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 – 12 hours
18mg/day	4 mg	14 mg
27mg/day	6 mg	21 mg
36mg/day	8 mg	28 mg
45mg/day	10 mg	35 mg
54mg/day	12 mg	42 mg
63mg/day	14 mg	49 mg
72mg/day	16 mg	56 mg

*Note though IR:MR ratio is 25:75, manufacturers' state are bioequivalents

Type 2: (IR:MR = 30:70)		
Equasym XL®		
Total daily dose	Immediate - Release component	Slow - Release component
	0 - 4 hours	4 – 8 hours
10mg/day	3 mg	7 mg
20mg/day	6 mg	14 mg
30mg/day	9 mg	21 mg
40mg/day	12 mg	28 mg
50mg/day	15 mg	35 mg
60mg/day	18 mg	42 mg

Type 3: (IR:MR = 50:50)		
***Medikinet XL®, Meflynate XL®, Metyrol XL®**		
Total daily dose	Immediate - Release component	Slow - Release component
	0 - 4 hours	4 – 8 hours
*5mg/day	2.5 mg	2.5 mg
10mg/day	5 mg	5 mg
20mg/day	10 mg	10 mg
30mg/day	15 mg	15 mg
40mg/day	20 mg	20 mg
50mg/day	25 mg	25 mg
60mg/day	30 mg	30 mg

Worked Example 1

Switching between Type 2 & Type 3 (Equasym XL 20mg to Meflynate XL)

Use the reference table below to identify the IR component of Equasym XL 20mg.

Equasym XL 20mg IR Component = 6mg

Use the reference table for Type 3 to identify the closest match in IR component.

Meflynate closest IR component = 5mg, contained in Meflynate XL 10mg capsules

Therefore, suitable switch would be **Meflynate XL 10mg Capsules** along with monitoring for symptom control.

Worked Example 2

Switching between Type 1 & Type 2 (Concerta XL 54mg to Equasym XL)

Use the reference table below to identify the IR component of Concerta XL 54mg.

Concerta XL 54mg IR Component = 12 mg

Use the reference table for Type 2 to identify the closest match in IR component.

Equasym XL closest IR component = 12mg, contained in Equasym XL 40mg capsules

Therefore, suitable switch would be **Equasym XL 40mg Capsules** along with monitoring for symptom control.

Step 4. Monitoring and Contingency Planning

- Ensure adequate safety netting is in place post switch. As a minimum, ensure an appropriate escalation plan is in place to address any concerns post switch.
- Where possible, schedule a follow-up review in 3 – 4 weeks to assess the effectiveness of the switch and to identify any adverse effects. Offer advice to patients to contact their specialist if any issues occur post switch, as a minimum.
- Assess symptom control and inquire about side effects such as insomnia, appetite changes, gastrointestinal discomfort, or mood changes.
- Adjust the dose as needed to optimize therapeutic outcomes and minimize side effects.

- If the patient does not tolerate the new formulation well, consider reverting to the original MR tablet or adjusting to a different dosage or release profile.
- If neither formulation is well-tolerated, explore other medication options or non-pharmacological interventions.

Further Information

- Specialist Pharmacy Services Supply Tool *registration required. (Available here)
- Choice and Medication Handy Fact Sheet for Methylphenidate Shortage (Available here)
- NICE [NG87] Attention Deficit Hyperactivity Disorder: Diagnosis and Management (Available here)
- Electronic Medicines Compendium for Manufacturer's Summary of Product Characteristics (Available here)

References

1. Specialist Pharmacy Services (Online). Comparison of pharmacokinetic profiles. Retrieved from Considerations when prescribing modified-release methylphenidate – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice. [Accessed August 09, 2024]
2. Coghill D, et al. Long-acting methylphenidate formulations in the treatment of attention-deficit/hyperactivity disorder: a systematic review of head-to-head studies. *BMC Psychiatry* 2013,13:237
3. Sonuga –Barke EJ, et al. Efficacy of two once-daily methylphenidate formulations compared across dose levels at different times of the day: preliminary indications from a secondary analysis of the COMACS study data. *BMC Psychiatry* 2004, 4:28.

VERSION CONTROL

Prepared By:	**Woodrow Blake - Lead Pharmacist – ID and NDD, NottsHC**
Reviewed By:	**Jacqueline Dziewanowska – ASD Nurse Consultant, NeSS – NottsHC**
	Allison Woodhead - Clinical Lead Neurodevelopmental Disorder – NottsHC (OH)
	NottsHC Pharmacy Medicines Optimisation Group - NottsHC
	Amy Taylor - Consultant Community Paediatrics, NUH
	Esther Corker – Consultant Community Paediatrician, SFH
	Joseph Kilgariff – ACP, Developmental Neuropsychiatry - NottsHC
Ratified By:	**NottsHC Trust Medicines Optimisation Group**
Ratification Date:	**14/10/2024**

Appendix

Quick Reference Guide

TYPE 1: Affenid XL®, Concerta XL®, *Delmosart XL®, Matoride XL®, *Xaggitin XL®, Xenidate XL®

TYPE 2: Equasym XL®

TYPE 3: Medikinet XL®, Meflynate XL®, Metyrol XL®

- Switch between different brands within the same type where possible.
- If not possible, use the below table to switch between types, each row shows approximately equivalent immediate release component.

TYPE 1	TYPE 2	TYPE 3
18mg/day	10mg/day	5mg/day
27mg/day	20mg/day	10mg/day
36mg/day	30mg/day	20mg/day
45mg/day	30mg/day	20mg/day
54mg/day	40mg/day	30mg/day
63mg/day	50mg/day	30mg/day
72mg/day	50mg/day	30mg/day

Table showing proposed switches based on the Immediate Release Component of the different Methylphenidate Modified Release Preparations.

Note Carefully: A switch to TYPE 3 may result in the greatest change in symptom control due to the release characteristics. In all cases, monitoring for symptom control is necessary and consideration for top up with immediate release preparations may be required.