Prif Swyddog Fferyllol
Chief Pharmaceutical Officer

GIG CYMRU NHS WALES

Llywodraeth Cymru
Welsh Government

MEDICINES SHORTAGE ADVISORY GROUP WALES

MEDICINE SHORTAGE

Distribution:	As Appendix 2
From:	Chief Pharmaceutical Officer, Welsh Government
Date:	28/11/19
Reference:	CPhO/MedsLet/2019/21
Category:	Level 3 – High impact

Title: Disruption to supply of Slo-Phyllin® (Theophylline)

For Action by:

- All General Practitioners – please ensure this message is seen by all working in your dispensary and retain a copy in your 'locum information pack'. (Action and information as below)
- Dispensing General Practitioners – please ensure this message is seen by all working in your dispensary and retain a copy in your 'locum information pack'. (Action and information as below)
- Community Pharmacists. (Action and information as below)
- Chief Pharmacists. (Action and information as below)

Timeframe: Action within 24 hrs

For Information: See Appendix 2 – Distribution List

What is this about:

Medicine shortage affecting supply of Slo-Phyllin® 60mg,125mg and 250mg capsules. These products will be discontinued.

Issue

- Merck, the suppliers of Slo-Phyllin® (theophylline) have reported that due to manufacturing issues, the manufacture of this product has ceased immediately, and will be discontinued. This decision has not been taken due to safety concerns.
- Merck anticipate out of stock dates from the end of November.
- Limited stock is available to order directly from Merck's customer services, if unavailable from wholesalers.
- Prescribers will need to review and switch all affected patients who still require theophylline, from Slo-Phyllin® to alternative preparations.

Action

Adult patients:
All healthcare professionals in primary, secondary or specialist healthcare services who prescribe theophylline preparations should:

- Review patients to determine if theophylline is still required as it may be of minimal benefit for that patient and has a significant side effect profile
- Review patients on Slo-Phyllin® preparations and transfer patients to the closest equivalent dose of Uniphyllin Continus® to be taken twice a day, or
- If the above is deemed unsuitable consider switching to aminophylline tablets (Phyllocontin Continus®/ Forte Continus®). When switching patients to aminophylline the dose will need to be converted from theophylline to aminophylline (see Appendix 1).

Paediatric patients:
All healthcare professionals in primary, secondary or specialist healthcare services who prescribe theophylline preparations should:

- Review patients to determine if theophylline is still required
- Consider use of Uniphyllin Continus® if theophylline is deemed necessary. Specialists should be consulted for advice to determine the new dose of theophylline in accordance with the available strengths of Uniphyllin Continus (200mg, 300mg or 400mg); or
- Consider the use of unlicensed specials of theophylline oral syrup (immediate release) to deliver lower doses.
- Consider the use of aminophylline (Phyllocontin Continus®/ Forte Continus® tablets which are licensed for use in the paediatric population aged 6 years and above (see Appendix 1).

Advice on switching and monitoring

For patients in whom ongoing treatment is still required, the following advice and information in Appendix 1 should be used to support local decision

making.

- Patients switching to Uniphyllin Continus® (theophylline) tablets should be prescribed the closest equivalent dose which is also taken twice a day.
- Patients switching to Phyllocontin Continus®/ Forte Continus® (aminophylline hydrate) tablets should have their dose converted from theophylline to aminophylline.
- For patients on lower doses of Slo-Phyllin® (theophylline) capsules and who are not considered suitable for switching to a higher dose of alternative theophylline product or for patients who cannot swallow tablets, an unlicensed oral syrup of theophylline 50mg/5ml is available.

Drug level monitoring after switching is not usually required unless clinically indicated i.e. suspected adverse effect/ worsening disease control. Plasma-theophylline concentration should be measured 5 days after starting oral treatment and at least 3 days after any dose adjustment. Consult local guidelines for when samples should be taken relative to dosing times as these may vary.

Queries

For all queries:

Medicinesshortages@gov.wales

Information about current medicines shortages can be found on the NHS intranet at:
http://howis.wales.nhs.uk/sites3/page.cfm?orgid=428&pid=77202

Yours faithfully,

Anne Hinchliffe
All Wales Specialist Pharmacist-Contingency Planning/
Fferyllydd Arbenigol Cymru Gyfan-Cynllunio Wrth Gefn
Welsh Government/Llywodraeth Cymru

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Appendix 1: Theophylline and aminophylline oral preparations

Product	Formulation	Adult dose	Paediatric dose	Administration	Dose conversion
Slo-Phyllin®	Prolonged release capsule (60, 125 and 250mg)	250 - 500 mg twice daily	6-12 years (20 - 35kg) - 120 -250mg twice daily over 12 years 250-500mg twice daily	Capsules contain individual slow-release granules and young children /adults with swallowing difficulty may find the loose granules (which can be sprinkled on a spoonful of soft food e.g. yoghurt) easier to swallow. However, the loose granules must not be chewed.	N/A
Uniphyllin®	Prolonged release tablet (200, 300 and 400mg)	200 mg twice daily, titrated to either 300 mg or 400 mg dependent on therapeutic response.	9 mg/kg twice daily. Some children with chronic asthma require and tolerate much higher doses (10-16 mg/kg twice daily).	These tablets must be swallowed whole and not broken, crushed or chewed as doing so may lead to a rapid release of theophylline with the potential for toxicity.	Patients should be switched closest equivalent dose of Uniphyllin Continus ® .
Aminophylline	Prolonged release tablet (225 and 350mg)	225 mg twice daily (may be titrated to higher dosage as required)	10 mg/kg twice daily. Some children with chronic asthma require and tolerate much higher doses (11-18 mg/kg twice daily).	Tablets should be swallowed and not chewed.	Aminophylline is a mixture of theophylline and ethylenediamine and readily releases theophylline in the body. Oral tablets (extended release) have 90-100% bioavailability Salt factor for aminophylline ~0.8 ***225mg aminophylline ~180mg theophylline***
Theophylline	Oral syrup (unlicensed Special) 50mg/5ml	Current total daily dose of theophylline, to be split into four times a day dosage.	Current total daily dose of theophylline, to be split into four times a day dosage. (In new patients, usual dose 5 mg/kg 3-4 times a day)	As directed by prescriber	N/A

Appendix 2

DISTRIBUTION LIST

Send to:

Chief Executives of Health Boards

Medical Directors of Health Boards

Nurse Directors Health Boards

Directors of Public Health

Health Board Chief Pharmacists

Hospital Chief Pharmacists

Health Board Prescribing Advisers

PHW Consultants in Pharmaceutical Public Health

Chief Executives of NHS Trusts

Principal Pharmacist Welsh Quality Control

Principal Pharmacist Continuing Care Services

Principal Pharmacist Welsh Medicines Information Centre

CSSIW

NHS Direct

NHS Wales Shared Services Partnership to forward to:

General Practitioners

Dispensing General Practitioners

Community Pharmacists

Independent / Private clinics and Hospitals and Hospices throughout Wales

Community Optometrists

Dental Practitioners

Welsh Government:

Chief Medical Officer

Chief Nursing Officer

Chief Dental Officer

Chief Optometric Officer

Chief Scientific Officer

Chief Therapies Officer

Director General Health and Social Services Group

Emergency Planning Adviser

Deputy Director Primary Care

Director Primary Care & Innovation

HSSG Comms

NHS Procurement Specialists