Department of Health & Social Care

NHS

Supply Disruption Alert

SDA/2019/009 Issued: 28 November 2019 Valid until:28 February 2020

Slo-phyllin® (Theophylline) 60mg/125mg/250mg capsules

Summary

- Merck, the suppliers of Slo-phyllin® (theophylline), have reported that due to manufacturing issues from their supplier, the manufacture of this product has ceased immediately, and will be discontinued. Merck anticipate estimated 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 table below).

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 table below).

Deadlines for actions

Actions initiated: on receipt of this alert
Actions completed: 28 February 2020

Product details

Slo-phyllin® 60mg, 125mg and 250mg capsules

Background

Merck has ceased manufacture of Slo-phyllin® capsules, at short notice due to the discontinuation of manufacture of product from their supplier. This decision has not been taken due to safety concerns. As a result, all patients currently prescribed Slo-phyllin® will need to be reviewed and if theophylline is still required, will need to be switched to an alternative.

Supporting Clinical Information

Slo-phyllin® (theophylline) capsules are indicated as a bronchodilator in the symptomatic and prophylactic treatment of asthma and for reversible bronchoconstriction associated with chronic bronchitis and bronchial asthma.

Uniphyllin Continus® (theophylline) tablets are indicated for the treatment and prophylaxis of bronchospasm associated with asthma, COPD and chronic bronchitis.

Use in children is relatively low, however the BTS/ SIGN guidelines 2019 recognise the potential value of theophylline for childhood asthma, particularly in those over 5 years of age. Theophylline is also recommended for some children with exercise-induced asthma.

Theophylline is infrequently prescribed for adult asthma outside of patients with relatively severe disease and is an add-on in addition to inhaled corticosteroid/long acting beta agonist+/- long-acting muscarinic antagonists +/- montelukast. It is also sometimes used in COPD or asthma-COPD overlap.

Although the rate of absorption from modified-release preparations can vary between brands and ideally patients should be maintained on the same brand, this is not an option in these circumstances.

Advice on switching and monitoring

For patients in whom ongoing treatment is still required, the following advice and information in the table 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 (see table below)
- 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.

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 5mg/kg 3-4 times a day)	As directed by prescriber	N/A

Monitoring:

Drug level monitoring after switching is not usually required unless clinically indicated, i.e. suspected adverse effect/ worsening disease control. Side effects that could indicate toxicity include nausea, vomiting, epigastric pain, haematemesis, restlessness, hypertonia, exaggerated limb reflexes, convulsions, hypotension, and sinus tachycardia. Where theophylline drug level monitoring is clinically indicated, consider the following advice.

- Plasma-theophylline concentration should be measured 5 days after starting oral treatment and at least 3 days after any dose adjustment.
- A blood sample should usually be taken 4–6 hours after an oral dose of a modified-release preparation (sampling times may vary—consult local guidelines), for immediate release products samples should be taken 1-2 hours after administration. In most individuals, a plasma-theophylline concentration of 10–20 mg/litre (55–110 micromole/litre) is required for satisfactory bronchodilation, although a lower plasma-theophylline concentration of 5–15 mg/litre may be effective.
- Adverse effects can occur within the range 10–20 mg/litre and both the frequency and severity increase at concentrations above 20 mg/litre.

Distribution

If you are responsible for cascading these alerts in your organisation, these are our suggested distribution lists.

Trusts (NHS boards in Scotland)

CAS and SABS (NI) liaison officers for onward distribution to all relevant staff including:

- A&E consultants
- A&E departments
- A&E nurses
- Cardiologists
- Cardiology departments
- Cardiology nurses
- Cardiology, directors of
- Cardiothoracic departments
- Cardiothoracic surgeons
- Cardiothoracic surgery directors
- Chief pharmacists
- Clinical governance leads
- Clinical Procurement Specialists [NEW]
- Community children's nurses
- Community hospitals
- Community nurses
- Day surgery units
- District nurses
- Haematologists
- Hospital pharmacies
- Hospital pharmacists
- Intensive care medical staff/paediatrics
- Intensive care nursing staff (adult)
- Intensive care nursing staff (paediatric)
- Intensive care units
- Intensive care, directors of
- Medical directors
- Neonatal nurse specialists
- Neonatology departments
- Neonatology directors
- NHS walk-in centres
- Outpatient clinics
- Paediatric intensive care units
- Paediatric medicine, directors of
- Paediatric nurse specialists
- Paediatric oncologists
- Paediatric surgeons
- Paediatric surgery, directors of
- Paediatric wards
- Paediatricians
- Paediatrics departments
- Palliative care teams
- Paramedics
- Pharmaceutical advisors
- Pharmacists
- Purchasing managers
- Risk managers
- School nurses
- Special care baby units
- Supplies managers
- Walk-in centres

Department of Health & Social Care

NHS

NHS England Regional Offices

For onward distribution to all relevant staff including:

- Community pharmacists

General Practice

For onward distribution to all relevant staff including:

- General practitioners
- Nutritional nurse specialists
- General practice managers
- General practice nurses

Independent distribution

Establishments registered with the Care Quality Commission (CQC) (England only)

- Adult placement
- Care homes providing nursing care (adults)
- Care homes providing personal care (adults)
- Clinics
- Hospices
- Hospitals in the independent sector
- Independent treatment centres
- Nursing agencies
- Private medical practitioners

Enquiries

England
Send enquiries about this notice to the DHSC Supply Resilience Team, quoting reference number SDA**/2019/009**

Email: supplyresiliencemd@dhsc.gov.uk