Department of Health & Social Care

Supply Disruption Alert

SDA/2021/003 Issued: 09 February 2021

Phyllocontin® (Aminophylline) 225mg and 350mg modified release tablets

Summary

- Phyllocontin® (aminophylline) Continus 225mg and Phyllocontin® Forte Continus 350mg modified-release tablets are being discontinued in the UK.
- Remaining supplies of the 225mg strength are expected to be exhausted by 2nd March 2021 and the 350mg strength are expected to be exhausted by 5th April 2021.
- Phyllocontin® (aminophylline) is used in adults for the treatment and prophylaxis of bronchospasm associated with asthma, chronic obstructive pulmonary disease and chronic bronchitis. For children, it is used for the management of asthma.
- Prescribers will need to review all affected patients and optimise inhaled therapies. Patients who still require a methylxanthine, will need to be switched to theophylline tablets (Uniphyllin Continus®).

Action

All healthcare professionals in primary, secondary and specialist healthcare services who prescribe aminophylline preparations should **not initiate** new patients on aminophylline tablets (Phyllocontin® Continus 225mg and Forte Continus 350mg modified-release tablets);

Primary and secondary care services that prescribe aminophylline should identify all patients prescribed Phyllocontin® (aminophylline) Continus 225mg and Forte Continus 350mg modified-release tablets and:

For adult patients:

- make early contact with the patient or patient's carer to allow time to plan for any treatment reviews or switch strategies;
- seek support from specialists for patients with unstable asthma or if deemed essential for specific patients;
- review patients to determine if a methylxanthine is still required as it may be of minimal benefit and has a significant side effect profile;
- refer to local or national treatment guidelines to optimise inhaled therapies in place of aminophylline;
- ensure an up to date asthma plan is in place, advise the patient or patient's carer not to interrupt inhaled corticosteroid medications and ask if a repeat prescription of steroid inhaler is required; and
- if treatment with a methylxanthine is deemed necessary, then consider switching patients to theophylline tablets (Uniphyllin Continus®). When switching patients to theophylline the dose will need to be converted from aminophylline to theophylline (see below) with appropriate monitoring carried out by prescribers (see advice below in monitoring section).

For paediatric patients:

- make early contact with the patient or patient's carer to allow time to plan for any treatment reviews or switch strategies;
- refer to a secondary/tertiary care centre to decide on further management.

Product details

Phyllocontin® (aminophylline) Continus 225mg and Phyllocontin® (aminophylline) Forte Continus 350mg modified-release tablets.

Background

Napp Pharmaceuticals Ltd, are sole suppliers of oral aminophylline. They have discontinued Phyllocontin® Continus 225mg and Phyllocontin® Forte Continus 350mg modified-release tablets due to a commercial decision.

Supporting Clinical Information

Aminophylline is a mixture of theophylline and ethylenediamine and readily releases theophylline in the body. Theophylline is the only available oral methylxanthine agent for patients that require treatment with this class.

Phyllocontin® Continus (aminophylline) is licensed in adults and children aged 6 years and above for the treatment and prophylaxis of bronchospasm associated with asthma, chronic obstructive pulmonary disease and chronic bronchitis. It can however be used off-label for children less than 6 years old. Aminophylline should not be used as the first line drug of choice in the treatment of asthma in children.

Uniphyllin Continus® (theophylline) is licensed for the same indications as above.

Oral aminophylline is not widely used in children, 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 therapy 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.

Advice on switching and monitoring

For patients in whom ongoing treatment with a methylxanthine 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 have their dose converted from aminophylline to theophylline (see below).

Switching:

The below conversions from aminophylline to theophylline can be followed if patients are tolerating treatment and levels are within therapeutic range.

- Patients taking 225mg aminophylline should be converted to theophylline 200mg
- Patients taking 350mg aminophylline should be converted to theophylline 300mg
- Patients taking 450mg aminophylline should be converted to theophylline 400mg

Product	Adult dose	Paediatric dose	Administration
Aminophylline (Phyllocontin Continus®) Prolonged release tablets (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.
Theophylline (Uniphyllin Continus®) Prolonged release tablets (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.
Oral aminophylline tablets (extended release) have 90-100% bioavailability. Salt factor for aminophylline ~ 0.8 ***225mg aminophylline ~180mg theophylline***			

Monitoring:

Therapeutic drug level monitoring of theophylline should be undertaken when patients are switched from aminophylline to theophylline and when clinically indicated with oversight from specialists if needed, 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.

Prescribers should 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). 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.

Alternative products

Unlicensed imports
Prescribers should follow the advice given above as per action section to manage patients who are currently prescribed oral aminophylline as supplies of unlicensed imports are very limited and would not meet current demands. The following specialist importer company is able to source very limited quantities of aminophylline 225mg modified release tablets (please note there may be other companies that can also source supplies):

- UL Global

Any decision to prescribe an unlicensed medicine must consider the relevant guidance and NHS Trust or local governance procedures. Please see the links below for further information:

- The supply of unlicensed medicinal products, Medicines and Healthcare products Regulatory Agency (MHRA)
- Professional Guidance for the Procurement and Supply of Specials, Royal Pharmaceutical Society (RPS)
- Prescribing unlicensed medicines, General Medical Council (GMC)

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
- All departments
- Cardiologists
- Cardiology departments
- Cardiology nurses
- Cardiothoracic surgeons
- Cardiothoracic surgery directors
- Cardiothoracic departments
- Chief pharmacists
- Clinical governance leads
- Clinical Procurement Specialists
- Community hospitals
- Community nurses
- Community children's nurses
- Day surgery units
- District nurses
- EBME departments
- Emergency Preparedness and Response officer
- Equipment stores
- Equipment libraries and stores
- 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
- Occupational health departments
- 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
- Respiratory specialists
- Risk managers
- School nurses
- Special care baby units
- Supplies managers
- Walk-in centres

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
- Domiciliary care providers
- Further education colleges registered as care homes
- Hospices
- Hospitals in the independent sector
- Independent treatment centres
- Nursing agencies
- Private medical practitioners

Enquiries

England
Send enquiries about this notice to the DHSC Medicines Supply Team, quoting reference number **SDA/2021/003**

Email: DHSCmedicinesupplyteam@dhsc.gov.uk

Addressees may take copies for distribution within their own organisations