Commissioned by Glenmark Pharmaceuticals Europe Ltd

Best practice guidance

Respiratory

Practical tips for maintaining asthma care prompted by a supply issue during the COVID-19 pandemic

Darush Attar-Zadeh, Respiratory Lead Pharmacist in Barnet CCG and RPS London North West

Early on during the novel coronavirus pandemic, it became apparent that coronavirus disease 2019 (COVID-19) has respiratory effects and that people with asthma or chronic obstructive pulmonary disease (COPD) are at risk of complications.[1] This led to a rush on inhalers as patients began ordering them for a variety of reasons.[2] People with asthma who may not have ordered preventer or reliever treatments for a while may have started to do so again. Others who did typically order inhalers may have ordered extra. Whatever the reasons, the result was that I and other pharmacists began receiving notification of supply issues—first with salbutamol and then later with beclometasone dipropionate 100 mcg pressurised metered-dose inhaler (pMDI) (Clenil® Modulite®) and a few other anti-inflammatory inhaler treatments. The Middlesex Group of Local Pharmaceutical Committees (LPC; www.middlesexlpcs.org.uk) kept the clinical commissioning groups (CCGs) up to speed with stock issues on the ground in community pharmacies.

None of the formularies in North Central London (NCL) and North West London (NWL) included a bioequivalent alternative to Clenil Modulite, so there was no obvious option to turn to in response to the supply issue; the other strengths of Clenil Modulite were also in short supply. In common with some other CCGs, choices of inhaled treatments in NCL and NWL had been narrowed down to keep options simple. Options in dry powder inhalers (DPIs) and pMDIs allowed tailoring to each patient's inspiratory ability.

There has been an influx of new inhalers on the market and it can be hard to decipher which is the most appropriate choice. It is vital that clinicians and patients understand the different device types, as inhaler technique varies between them.

Identifying an alternative to Clenil Modulite

Barnet CCG and colleagues from other neighbouring CCGs needed a rapid response to identify suitable alternatives and communicate these to pharmacies and prescribers as soon as possible. A multidisciplinary team (MDT) involving colleagues in the CCG and the LPC worked together to identify a suitable alternative. The MDT also communicated with wholesalers and the manufacturers of less-used alternatives, who could have struggled to meet increased demand once the usual product with the largest share of prescribing was in short supply.

Key points

- Without an alternative present on the CCG formulary, a suitable alternative had to be identifed rapidly when Clenil Modulite became unavailable during the COVID-19 pandemic
- Having more than one option for fast-moving lines (such as salbutamol, and beclometasone dipropionate, in a pressurised metered-dose inhaler and dry powder inhaler) is important to ensure continuity of treatment
- The alternative products should ideally be bioequivalent and with near-identical device technique
- Inhalers should be prescribed by brand to ensure the patient receives the same familiar device and medication each time
- Any changes to the device prescribed must be clearly communicated with the patient to ensure they understand any differences to their usual device.

Efficacy, safety and patient preference are the primary considerations when choosing an appropriate inhaler, but other important factors also need to be taken into account (Box 1).

Not all inhalers are licensed for children and adolescents. Good inhaler technique is a crucial aspect of successful treatment, and different types of inhaler require various inhalation techniques that may or may not be suited to an individual patient's inspiratory ability. Some devices have dose counters, while others do not. Some pMDI inhalers are compatible and licensed with certain spacers, others are not. This needs to be factored in if changes are made.

Overdosing and underdosing are a risk when changing brands due to differences in strengths, displayed strength (metered dose and delivered dose), and particle size. For example,

Box 1: Considerations when choosing an inhaler

- Efficacy
- Safety
- Patient preference
- Licensing
- Device and inhalation technique
- Dosing
- Particle size
- Spacers
- Carbon footprint
- Price.

This supplement has been commissioned and funded by Glenmark Pharmaceuticals Europe Ltd and developed in partnership with *Guidelines in Practice*. Glenmark Pharmaceuticals Europe Ltd suggested the topic and author, and carried out full medical approval on all materials to ensure compliance with regulations. The sponsorship fee included an honorarium for the author. The views and opinions of the author are not necessarily those of Glenmark Pharmaceuticals Europe Ltd, or or *Guidelines in Practice*, its publisher, advisers, or advertisers. No part of this publication may be reproduced in any form without the permission of the publisher.

Prescribing information can be found on the final page.

PP-UK-SOP-0113

Date of preparation: November 2020

beclometasone dipropionate (the ingredient in Clenil Modulite and Soprobec®) is also available in a fine particle form in a pMDI (Qvar® and Kelhale®).[3–6] Because of the difference in particle size, Qvar and Kelhale are twice the potency of Clenil Modulite and Soprobec and so not interchangeable in normal circumstances.[7] The British Thoracic Society's table showing equivalence of potencies is helpful in this regard.[8]

These differences all highlight the importance of prescribing inhalers by brand.[7]

In this case of short supply of Clenil Modulite, Soprobec was determined by the MDT to be the logical alternative, as it is equivalent to Clenil Modulite.[9] The final decision took into account all the factors discussed above, and was aided by the RightBreathe resource, which enabled easy comparison of available inhalers.[10]

Implementing the new formulary option

Communicating the decision to healthcare professionals

Once the decision to recommend Soprobec was made, communication with primary care prescribers and community pharmacists was quickly needed to ensure all stakeholders were aware of the issue and the alternative recommendation. All respiratory contacts for the MDT, including national and local respiratory WhatsApp groups, were notified of the decision to use Soprobec as a recommended pMDI alternative if stocks were available. If a person was better suited to a DPI after a clinical review, then alternative beclometasone treatments were offered that were on formulary.

Communicating the change to patients

Prescribers were advised to have virtual consultations with patients about the enforced substitution, which was intended to be temporary, as patients needed to agree to the change. Inhaled corticosteroid potency charts from the British Thoracic Society (BTS) and RightBreathe were used to support these informed discussions.[8,10]

Any differences between the usual product and the alternative needed to be flagged up to the patient. In this case, for example, there is a colour difference between the Soprobec inhaler and the Clenil Modulite device. Patients' personal asthma action plans (PAAPs) needed to be updated with the new product. Prescribers were advised to change the duration of each prescription on EMIS/SystmOne to ensure that only 1 month of replacement treatment was prescribed rather than 2 months, so asthma control could be checked after a month to ensure the switch had not had any negative effect.

After the stock issue was resolved

Once Clenil Modulite was back in stock, prescribers discussed with each patient whether they were happy to continue with Soprobec or wanted to revert back to Clenil Modulite. Once the patient and clinician had decided as part of a shared decision-making process, the chosen treatment was prescribed by brand to ensure the patient received the right treatment every month.

Key points in asthma medicines optimisation

This stock shortage situation offered an opportunity to review patients' asthma control and management, as discussions with patients were needed to explain the reason for the change and to reassure them. Box 2 provides a reminder of the key points in asthma control and medicines optimisation, including some additional considerations for the COVID-19 pandemic.

Virtual consultations to discuss the patient's current level of asthma control should be held during the COVID-19 pandemic. Telemedicine apps, such as AccuRx, should be utilised so that the prescriber can see the patient and assess their inhaler technique. If this is not possible, the patient could upload a video of them using their inhaler. Many patients may actually be happier to have remote consultations and this may be a good way to run asthma reviews in the future.

Reviewing the patient's repeat prescription history can help to determine whether they are not ordering enough preventer inhalers or are over-reliant on rescue inhalers. Community pharmacy patient medication records are also useful to identify if a patient is at risk of poorly controlled asthma. Discuss with patients who have not ordered repeat prescriptions for months until the COVID-19 pandemic whether they are usually symptom free and have good control (to establish if they genuinely need the inhaler).

Inhaler choice should be based on the drug but more importantly the patient's ability to optimise technique to ensure that the prescribed drug reaches the patient's lungs. It is essential not only to check whether patients can correctly use their current device but also whether the current treatment is still appropriate, including the level of treatment and the use of spacers, and to step down or up as required.

Given the myriad of available inhaler devices, the RightBreathe resource[10] and the *Guidelines* device choice algorithm[11] can be helpful guides for prescribers. Switching between device types—for example, from metered-dose inhalers to dry powder inhalers, or vice versa—should be avoided, even (or perhaps especially) for a temporary switch, as the different types require different techniques that may not suit the patient. As inhalers for respiratory diseases are not interchangeable, prescribing by brand is always essential to minimise errors and optimise efficacy and safety.

Switching devices may be tempting since advice was issued by NICE and the GP contract was updated to encourage use of low-carbon footprint inhalers to gain QOF points,[12–14] but all inhalers, not just pressurised aerosols, have a level of environmental impact through their manufacture and transportation. The temptation to enact a blanket switch should be resisted, as it is most important for each patient to have the right device for their inspiratory ability.

Differences between devices should be highlighted so patients know what to expect, including differences in inhaler colour, whether or not there is a dose counter (and how to tell if the inhaler is running out if there is not), different mouthpieces, different spacers, and different presentations of the same doses. The PAAP should be updated every time a treatment is changed, even if it is only a temporary switch, and should be updated again if the patient returns to the original product.

Box 2: Key points

Assessment

- Use remote video consultations to assess inhaler technique during the COVID-19 pandemic, wherever possible
- Review repeat prescription history for preventer and reliever inhalers to assess symptom control
- Use tools like the Asthma Control Test to check recent asthma control; this can be sent (e.g. via AccuRx) for patients to complete prior to a consultation
- Use the Asthma Right Care slide rule (Box 3) to stimulate a discussion about over-reliance on short-acting beta$_2$-agonists
- Explore patients' knowledge and beliefs about disease management.

Inhaler choice

- Choose an inhaler based on the drug but, more importantly, the patient's inspiratory ability and inhaler technique
- Avoid switching between device types (pMDI and DPI) unless the new device is better suited to the patient
- Try to ensure consistency in device type, e.g. both preventer and reliever in a pMDI (or both in a DPI)
- Consider differences in dose strength, dose presentation, and particle size (refer to the BTS table on potencies[8])
- Consider a low carbon DPI inhaler if the patient is able and happy to use it and the treatment is licensed for that patient[12]
- Prescribe by brand[7]
- Agree changes in treatment with patients after an informed discussion.

Patient education

- Coach patients on their new device, even it is only a temporary change
- Highlight differences in devices so patients know what to expect
- Explore patients' ideas, concerns, and expectations
- Identify and help manage triggers, encouraging smokers to stop and make their home smoke-free if possible—Very Brief Advice (Box 3) can take as little as 30 seconds to help you become a 'Quit Catalyst'
- Flu and pneumococcal vaccinations should be encouraged for relevant patients
- Update the patient's personal asthma action plan (PAAP)
- Provide links to patient information on inhaler technique (e.g. RightBreathe[10]) and Asthma UK (Box 3)
- Encourage patients to contact their prescriber or Asthma UK if they have further questions
- Discourage patients from stockpiling medicines
- Encourage patients to use all the doses in each of their medicines before recycling them in a pharmacy participating in a recycling scheme.

Lessons learned

Supply issues are not isolated to the setting of the COVID-19 pandemic and are also reported for other inhalers, but this example highlights the potential problem of having no alternative on the local formulary for fast-moving medicines like salbutamol and beclometasone dipropionate, in both a DPI and pMDI option. In case of supply and other issues in the future, it therefore is important to have alternative drugs on formulary. A script-switch message for the formulary alternative can be added to guide the prescriber when there are stock issues.

When a switch is needed when problems arise, even when temporary, prescribers should take the opportunity to review the patient, check their inhaler technique and asthma control, and update their PAAP with any updated information that the patient understands and has co-created with the clinician.

Acknowledgements

The author would like to thank Gerald Alexander and LPC colleagues for supporting the CCG with information on stock shortages and relaying information to the community pharmacists, and Suzanne Lever for setting up the script switch messages and supporting suggestions for temporary formulary alternatives.

Conflicts of interest

Darush Attar-Zadeh works closely with most pharmaceutical companies that produce inhaled and smoking cessation treatments to benefit patients and clinicians, and received an honorarium from Glenmark Pharmaceuticals for this supplement.

Box 3: Useful resources

- Asthma UK: www.asthma.org.uk
- British Thoracic Society: www.brit-thoracic.org.uk
- Primary Care Respiratory Society: www.pcrs-uk.org
- RightBreathe: www.rightbreathe.com
- Asthma UK inhaler videos: www.asthma.org.uk/advice/inhaler-videos
- Asthma Right Care slide rule: www.pcrs-uk.org/asthma-right-care
- Smoking cessation: www.pcrs-uk.org/resource/tobacco-dependency-pragmatic-guide
- *Choosing an appropriate inhaler device for the treatment of adults with asthma or COPD*: www.guidelines.co.uk/inhalerchoice

References

1. NHS. *Advice for people at higher risk*. Available at: www.nhs.uk/conditions/coronavirus-covid-19/people-at-higher-risk (Accessed 5 July 2020).
2. MIMS. *Inhaler prescribing guidance issued as spike in demand causes shortages*. www.mims.co.uk/article/1679208 (Accessed 5 July 2020)
3. Chiesi Limited. *Clenil Modulite 100 micrograms inhaler (with Dose Indicator)—summary of product characteristics*. December 2018. www.medicines.org.uk/emc/product/6975 (Accessed 5 July 2020)
4. Glenmark Pharmaceuticals Europe Ltd. *Soprobec 100 micrograms per actuation pressurised inhalation solution—summary of product characteristics*. December 2018. www.medicines.org.uk/emc/product/9816 (Accessed 5 July 2020)
5. Teva UK Limited. *Qvar MDI 50 micrograms—summary of product characteristics*. November 2019. www.medicines.org.uk/emc/product/604 (Accessed 5 July 2020)
6. Cipla EU Ltd. *Kelhale 50 micrograms per actuation pressurised inhalation solution—summary of product characteristics*. March 2020. www.medicines.org.uk/emc/product/10117 (Accessed 5 July 2020)
7. British National Formulary. *Beclometasone dipropionate*. https://bnf.nice.org.uk/drug/beclometasone-dipropionate.html (Accessed 5 July 2020)
8. British Thoracic Society. *BTS information: respiratory inhalers*. Available at: www.brit-thoracic.org.uk/document-library/quality-improvement/covid-19/bts-information-respiratory-inhalers (Accessed 28 June 2020).
9. MHRA. *April 2019 Public Assessment Report: Soprobec 50, 100, 200, 250 mcg, UK/H/6818/001-004/DC* https://mhraproductsprod.blob.core.windows.net/docs-20200302/3bc836d25349185931b189bf3ba25c395c23447b
10. RightBreathe online tool. Available at: www.rightbreathe.com (Accessed 5 July 2020).
11. MGP Ltd. *Choosing an appropriate inhaler device for the treatment of adults with asthma or COPD*. MGP, 2020. Available at: www.guidelines.co.uk/inhalerchoice
12. NICE. *NICE encourages use of greener asthma inhalers*. www.nice.org.uk/news/article/nice-encourages-use-of-greener-asthma-inhalers (Accessed 5 July 2020).
13. NICE. *Patient decision aid: inhalers for asthma*. London: NICE, 2019. Available at: www.nice.org.uk/guidance/ng80/resources/inhalers-for-asthma-patient-decision-aid-pdf-6727144573 (accessed 21 June 2020).
14. General Pharmaceutical Council. Update to the GP contract agreement 2020/21 – 2023/24. London: GPC, 2020.

Soprobec (beclometasone dipropionate) 50, 100, 200 or 250 micrograms per actuation pressurised inhalation solution. Please refer to the Summary of Product Characteristics (SmPC) before prescribing. **Indications:** Soprobec is indicated for the maintenance treatment of asthma when the use of pressurised metered dose inhaler is appropriate. **Dosage and administration:** Soprobec is for inhalation use. Adjust starting dose of inhaled beclometasone dipropionate to severity of disease, then adjust until control is achieved and then titrate to the lowest dose at which effective control of asthma is maintained. Adults (including the elderly): usual starting dose is 200 micrograms twice daily. Severe cases may be increased to 600 to 800 micrograms daily. (Soprobec 250 only: usually 1000 micrograms daily, which may be increased to 2000 micrograms daily). Dose may be reduced when the patient's asthma has stabilised. The total daily dosage should be administered as 2 to 4 divided doses. The Volumatic™ spacer device must always be used when Soprobec is administered to adults and adolescents 16 years of age and older taking total daily doses > 1000 micrograms. Children: usual starting dose is 100 micrograms twice daily. Depending on the severity of asthma, the daily dose may be increased up to 400 micrograms administered in 2 to 4 divided doses. Soprobec 200 and 250 is not recommended for children. Soprobec must always be used with the Volumatic™ spacer device when administered to children and adolescents 15 years of age and under, whatever dose has been prescribed. Patients with hepatic or renal impairment: No dosage adjustment needed Soprobec is for inhalation use. To ensure proper administration of the medicinal product, the patient should be shown how to use the inhaler correctly by a physician or other health professional. Correct use of the pressurised metered dose inhaler is essential in order that treatment is successful. The patient should be advised to read the Package Leaflet carefully and follow the instructions for use as given in the Leaflet. **Please refer to the SmPC for details of testing the inhaler and instructions for use**. Patients who find it difficult to co-ordinate actuation with inspiration of breath should be told to use a Volumatic™ spacer device to ensure proper administration of the product. Young children may find it difficult to use the inhaler properly and will require help. Using the inhaler with the Volumatic™ spacer device with a face mask may help in children under 5 years. Advise the patient to thoroughly rinse the mouth or gargle with water or brush the teeth immediately after using the inhaler. The patient should be told of the importance of cleaning the inhaler at least weekly to prevent any blockage and to carefully follow the instructions on cleaning the inhaler printed on the PIL. The inhaler must not be washed or put in water. The patient should be told also to refer to the PIL accompanying the Volumatic™ spacer device for the correct instructions on its use and cleaning. **Contraindications:** Hypersensitivity to norflurane (HFA-134a), ethanol anhydrous, glycerol or beclometasone dipropionate . **Warnings and precautions:** Patients should be properly instructed on the use of the inhaler to ensure that the drug reaches the target areas within the lungs. Patients should also be informed that Soprobec should be used on a regular basis, even when they are asymptomatic. Soprobec should not be used as the first treatment for asthma for treatment of acute asthma attacks patients. For such cases patients should be advised to have their rapid-acting bronchodilator available at all times.. Treatment with Soprobec should not be stopped abruptly. If patients find the treatment ineffective medical attention must be sought. Increasing use of rescue bronchodilators indicates a worsening of the underlying condition and warrants a reassessment of the asthma therapy. Sudden and progressive deterioration in control of asthma is potentially life- threatening and the patient should undergo urgent medical assessment. Systemic effects of inhaled corticosteroids may occur, particularly when prescribed at high doses for prolonged periods. Possible systemic effects include Cushing's syndrome, cushingoid features, adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract and glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). It is important that the dose of inhaled corticosteroid is titrated to the lowest dose at which effective control of asthma is maintained. It is recommended that the height of children receiving prolonged treatment with inhaled corticosteroids is regularly monitored. If growth is slowed, therapy should be reviewed with the aim of reducing the dose of inhaled corticosteroids, if possible, to the lowest dose at which effective control of asthma is maintained. In addition, consideration should also be given to referring the patient to a paediatric respiratory specialist. Prolonged treatment with high doses of inhaled corticosteroids may result in adrenal suppression and acute adrenal crisis. Situations which could potentially trigger acute adrenal crisis, include trauma, surgery, infection or any rapid reduction in dosage. Presenting symptoms are typically vague and may include anorexia, abdominal pain, weight loss, tiredness, headache, nausea, vomiting, hypotension, decreased level of consciousness, hypoglycaemia, and seizures. Additional systemic corticosteroid cover should be considered during periods of stress or elective surgery. Care should be taken when transferring patients to Soprobec therapy, particularly if there is any reason to suppose that adrenal function is impaired from previous systemic steroid therapy. Patients transferring from oral to inhaled corticosteroids may remain at risk of impaired adrenal reserve for a considerable time. Patients who have required high dose emergency corticosteroid therapy in the past or have received prolonged treatment with high doses of inhaled corticosteroids may also be at risk. This possibility of residual impairment should always be borne in mind in emergency and elective situations likely to produce stress, and appropriate corticosteroid treatment must be considered. The extent of the adrenal impairment may require specialist advice before elective procedures. Patients weaned off oral steroids whose adrenocortical function is impaired should carry a steroid warning card indicating that they may need supplementary systemic steroids during periods of stress, e.g. worsening asthma attacks, chest infections, major intercurrent illness, surgery, trauma, etc. Replacement of systemic steroid treatment with inhaled therapy sometimes unmasks allergies such as allergic rhinitis or eczema previously controlled by the systemic drug. As with all inhaled corticosteroids, special care is necessary in patients with active or quiescent pulmonary tuberculosis. As with other inhalation therapy, paradoxical bronchospasm may occur with an immediate increase in wheezing, shortness of breath and cough after dosing. This should be treated immediately with a fast-acting inhaled bronchodilator. Soprobec should be discontinued immediately, the patient assessed and, if necessary, alternative therapy institute. To reduce the risk of Candida infection, patients should be recommended to rinse their mouth properly after each drug administration. Special care is necessary in patients with viral, bacterial and fungal infections of the eye, mouth or respiratory tract. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for ophthalmologist evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids. Soprobec contains 7.47 mg of alcohol (ethanol) in each actuation which is equivalent to 13% w/w. **Interactions:** Theoretical potential for interaction of ethanol (excipient) in particularly sensitive patients taking disulfiram or metronidazole. Suppressive effect on adrenal function occurs with concomitant systemic or intranasal steroids. Caution and appropriate monitoring in CYP3A inhibitors (e.g. ritonavir, cobicistat). **Pregnancy and lactation:** There is no experience of the use of this product in pregnancy and lactation in humans. **Adverse reactions:** Very common and common: Oral candidiasis (of the mouth and throat), hoarseness, throat irritation. Uncommon: hypersensitivity reaction with the following manifestations: Rash, urticaria, pruritus, erythema. Very rare: oedema of the eyes, face, lips and throat, anaphylactic / anaphylactoid reactions, Cushing's syndrome, cushingoid features, adrenal suppression, growth retardation (in children and adolescents), bone density decreased, cataract, glaucoma, paradoxial bronchospasm, wheezing, dyspnoea, cough. Unknown frequency: Psychomotor hyperactivity, sleep disorders, anxiety, depression, aggression, behavioural disorders (predominantly in children), headache, vision blurred. Please consult the summary of product characteristics for a full list of adverse reactions. **Marketing authorization number:** PL 25258/0279. **Marketing Authorization Holder:** Glenmark Pharmaceuticals Europe Limited, Laxmi House, 2B Draycott Avenue, Kenton, Middlesex, HA3 0BU, United Kingdom **Distributor:** As above. **Legal classification:** POM. **Price:** 50mcg £2.78, 100mcg £5.57, 200mcg £12.13, 250mcg £12.22. **Job code:** PP-UK-SOP-0116 **Date PI was drawn up:** Nov 2020

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk. Adverse events should also be reported to medical_information@glenmarkpharma.com or call 0800 458 0383