Relvar ▼ Ellipta (fluticasone furoate and vilanterol as trifenate) for the treatment of patients with COPD

Medicines evidence pack to support formulary and guidelines decision making

Prescribing information and adverse event reporting information is provided at the back of this document
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# Relvar Ellipta overview in COPD

<table>
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<th>Brand Name</th>
<th>Relvar</th>
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<tr>
<td>Generic Name</td>
<td>fluticasone furoate (inhaled corticosteroid; ICS) and vilanterol as trifluoromethanesulfonate (long-acting β₂ agonist; LABA) combination</td>
</tr>
<tr>
<td>Device</td>
<td>Ellipta multi dose dry powder inhaler</td>
</tr>
<tr>
<td>COPD Licensed Indication</td>
<td>Relvar is indicated for symptomatic treatment of adult patients with COPD with a FEV₁ &lt;70% predicted normal (post-bronchodilator) with an exacerbation history despite regular bronchodilator therapy. [\text{FEV}_1 = \text{forced expiratory volume in 1 second}]</td>
</tr>
<tr>
<td>BNF Class</td>
<td>Respiratory systems: Corticosteroids: Compound preparations¹⁸</td>
</tr>
</tbody>
</table>
| Anticipated place in therapy | In accordance with NICE guidance, ICS/LABA combinations should be offered for patients with stable COPD:³  
- with a FEV₁ <50% who remain breathless or have exacerbations despite using a short acting bronchodilator (SABA)  
- ICS/LABA combinations may also be considered for patients with stable COPD:  
  - with a FEV₁ ≥50% who remain breathless or have exacerbations despite maintenance therapy with a long-acting β₂ agonist (LABA)  
  - who remain breathless or have exacerbations irrespective of their FEV₁, despite maintenance therapy with a long-acting muscarinic agonist (LAMA) |
| Dose | 92/22 mcg* fluticasone furoate/vilanterol, one inhalation once daily at the same time each day, in the morning or evening |
| Administration | Inhaled via an Ellipta multi dose dry powder inhaler |
| Cost | The 30-day cost of Relvar Ellipta 92/22 mcg is £22.00² |

* Delivered dose of medication referred to throughout
Background to COPD

Epidemiology

Someone dies in England and Wales from COPD every 20 mins\(^5\) and the rate of premature mortality for UK respiratory disease in 2008 was almost double that of Europe.\(^4\)

COPD is the second most common cause of emergency admission to hospital and around a third of those admitted to hospital as a result of their COPD are readmitted within a month of discharge.\(^5\)

The total annual direct healthcare cost of COPD to the NHS is estimated to be over £800 million.\(^4,5\)

Current management

In the UK, COPD treatment is managed through following NICE guidance: Management of chronic obstructive pulmonary disease in primary and secondary care.\(^3\)

- NICE guidance: Management of chronic obstructive pulmonary disease in primary and secondary care can be found at www.nice.org.uk

Internationally, the Global initiative for chronic Obstructive Lung Disease (GOLD) guidelines are utilised.\(^6\)

- The GOLD global strategy for diagnosis, management and prevention of COPD can be found at www.goldcopd.org
Efficacy: Head-to-head data

Head to head data of Relvar vs a currently available ICS/LABA combination

Study design

A randomised, multicentre, double blind, double dummy, parallel group comparative efficacy/safety study comparing once daily Relvar 92/22 mcg (fluticasone furoate/vilanterol) in the morning, versus twice daily Seretide Accuhaler 500/50 mcg (fluticasone propionate/salmeterol) in patients with moderate to very severe COPD.

Patients were randomised 1:1 to receive study medication for 12 weeks. Randomisation was preceded by a 2 week placebo run-in period.

This was a superiority study with the hypothesis that Relvar 92/22 mcg would demonstrate superior efficacy over fluticasone propionate/salmeterol 500/50 mcg.

Patient population:
- Clinical history of COPD in accordance with ERS definition
- Post salbutamol FEV₁/FVC ratio of ≤0.70 and FEV₁ ≤70% predicted normal
- ≥10 pack year smoking history
- Hospitalised or treated with oral corticosteroids or antibiotics for a COPD exacerbation within 3 years of screening

Primary efficacy endpoint assessment

- 24 hour effect on lung function after 12 weeks of treatment. This was assessed through the change from baseline in weighted mean FEV₁, measured serially over 24 hours on day 84

Secondary efficacy endpoint assessments

- Time to 100 ml increase from baseline from 0-4 hours on day 1
- Change from baseline in trough FEV₁ on day 85

Other efficacy endpoint assessments included:
- Quality of Life measured by the St George’s Respiratory Questionnaire (SGRQ-C)
  – This is a COPD specific questionnaire designed to measure impact of COPD and its treatment on the subject’s health related quality of life
Results (ITT population)

Demographics and baseline characteristics

The Intention to Treat (ITT) study population included 266 patients who received once daily fluticasone furoate/vilanterol (Relvar) 92/22 mcg and 262 patients who received twice daily fluticasone propionate/salmeterol 500/50 mcg via an Accuhaler.

Table 2: Demographics and baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Relvar 92/22 mcg (n=266)</th>
<th>fluticasone propionate/salmeterol 500/50 mcg (n=262)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean in years)</td>
<td>63.0</td>
<td>62.9</td>
</tr>
<tr>
<td>Male (%)</td>
<td>80</td>
<td>84</td>
</tr>
<tr>
<td>Caucasian (%)</td>
<td>82</td>
<td>79</td>
</tr>
<tr>
<td>Pre-bronchodilator FEV₁ (% predicted)</td>
<td>43.0</td>
<td>43.0</td>
</tr>
</tbody>
</table>

Primary efficacy endpoint

- A clinically meaningful improvement from baseline in 0–24 h weighted mean (wm) FEV₁ (day 84) was observed with both fluticasone furoate/vilanterol (Relvar) (mean ± SD = 130 ± 222 mL) and fluticasone propionate/salmeterol (mean ± SD = 108 ± 221 mL)
- The primary endpoint of superiority was not met because the difference in improvement between the two arms (22 mL) did not reach statistical significance (p=0.282)

Figure 1: Mean change in FEV₁ of Relvar 92/22 mcg versus fluticasone propionate/salmeterol Accuhaler 500/50 mcg at 12 weeks

Adapted from Agusti A et al., ERJ. 2014
Secondary efficacy endpoints

Because statistical significance was not achieved for the primary endpoint it cannot be inferred for comparisons of secondary efficacy endpoints. The details below should be considered as descriptive only:

- The median time to 100 mL improvement from baseline was 16 minutes in the fluticasone furoate/vilanterol (Relvar) arm and 28 minutes in the fluticasone propionate/salmeterol arm (p=ns)
- The mean change from baseline in trough FEV₁ on day 85 (an indicator of 24-h effect) was 111 mL in the fluticasone furoate/vilanterol (Relvar) arm and 88 mL in the fluticasone propionate/salmeterol arm; mean treatment difference was 23 mL (non-significant, 95% CI -20, 66)

Other endpoints: Quality of Life

- The SGRQ-C total score improved from baseline for both fluticasone furoate/vilanterol (Relvar) (-4.3) and fluticasone propionate/salmeterol (-3.0), although the difference in scores was not statistically significant (-1.3; 95% CI -3.5, 0.8)
- However only fluticasone furoate/vilanterol (Relvar) demonstrated an improvement of ≥4 units, which is considered to be the minimal clinically important difference for this measure

Safety

On treatment adverse events are reported in the safety section.
Efficacy: Exacerbation data

Relvar (fluticasone furoate/vilanterol) vs LABA alone (vilanterol) for prevention of exacerbations of COPD.\(^8\)

Exacerbations of COPD are important events that are associated with accelerated loss of lung function and poor health status.

Single agent vilanterol is not licensed for the treatment of COPD.

Study design

Two identically designed and analysed multicentre, randomised, double blind, parallel group studies were conducted comparing once daily Relvar 92/22 mcg (fluticasone furoate/vilanterol) with once daily vilanterol 22 mcg. Treatments were given in the morning using the Ellipta dry powder inhaler.

Both studies had a 4 week run-in period during which all subjects received open-label fluticasone propionate/salmeterol 250/50 mcg twice daily to standardise COPD pharmacotherapy and stabilise disease. (This is not a licensed dose for COPD in the UK)

Pooled data from the two studies is reported below. Although other doses of fluticasone furoate/vilanterol (Relvar) were tested in these studies, only data for the licensed dose for Relvar (92/22 mcg) are shown.

Patient population:

- Clinical history of COPD in accordance with ERS definition
- Post albuterol/salbutamol FEV\(_1\)/FVC ratio of ≤0.70 and FEV\(_1\) ≤70% predicted normal
- ≥10 pack year smoking history
- At least one COPD exacerbation in the 12 months prior to screening that required either systemic/oral corticosteroids, antibiotics and/or hospitalisation

Primary efficacy endpoint assessments

- The yearly rate of moderate and severe exacerbations
  - Moderate exacerbations were defined as worsening symptoms of COPD (≥2 consecutive days) necessitating treatment with oral corticosteroids or antibiotics, or both
  - Severe exacerbations were similar events that necessitated hospital admission

Secondary efficacy endpoint assessments

- Time to first on treatment moderate or severe exacerbation
- Yearly rate of exacerbations necessitating systemic or oral corticosteroids
- Change from randomisation in trough FEV\(_1\) at week 52
Results

Demographics and baseline characteristics

The ITT study population included 806 patients who received fluticasone furoate/vilanterol (Relvar) 92/22 mcg once daily and 818 patients who received vilanterol 22 mcg once daily. Patients were randomly assigned 1:1 to each of these arms.

Table 3: Demographics and baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Relvar 92/22 mcg (n=806)</th>
<th>Vilanterol 22 mcg (n=818)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean in years)</td>
<td>63.8</td>
<td>63.6</td>
</tr>
<tr>
<td>Caucasian (%)</td>
<td>85</td>
<td>84.6</td>
</tr>
<tr>
<td>Male (%)</td>
<td>56.2</td>
<td>57.9</td>
</tr>
<tr>
<td>Predicted post bronchodilator FEV₁ (%)</td>
<td>46.0</td>
<td>45.7</td>
</tr>
<tr>
<td>≥2 exacerbations in previous year (%)</td>
<td>37.2</td>
<td>40.9</td>
</tr>
</tbody>
</table>

Primary efficacy endpoint

- fluticasone furoate/vilanterol (Relvar) significantly reduced the mean yearly rate of moderate and severe exacerbations versus vilanterol alone (0.81 vs 1.11; 27% reduction; p<0.001)

Figure 3: Reduction in moderate/severe exacerbation rates over 52 weeks (pooled analysis of two studies)

In one of the studies no significant difference in exacerbation rate was seen for Relvar 92/22 mcg vs vilanterol

Secondary efficacy endpoints

- Compared to vilanterol, fluticasone furoate/vilanterol (Relvar) significantly reduced the risk in time to first on treatment moderate/severe exacerbation (Hazard ratio 0.8; p=0.0002)
- Compared to vilanterol, fluticasone furoate/vilanterol (Relvar) significantly reduced the annual rate of on treatment exacerbations requiring oral or systemic corticosteroids by 30% (0.61 vs 0.87, p<0.0001)
- Compared to vilanterol, fluticasone furoate/vilanterol (Relvar) demonstrated significantly higher trough FEV₁ at 52 weeks (changes from baseline 10 mL vs -30 mL, p<0.001)

These results are consistent with previous studies of twice daily ICS/LABA combinations that established the added value of ICS for these endpoints

Safety

On treatment adverse events are reported in the safety section.
Efficacy: 24-hour spirometric effect

24 hour spirometric effect of Relvar 92/22 mcg (fluticasone furoate/vilanterol)

Study design

This was a Phase III, multicentre, randomised, double blind, placebo controlled crossover study designed to evaluate the 24-hour spirometric effect of fluticasone furoate/vilanterol (Relvar) once daily in patients with COPD. Subjects completed a 2 week placebo run-in period prior to randomisation.

Each treatment was inhaled once a day in the morning for 28 days using the Ellipta dry powder device. Treatment periods were separated by 2-week, single-blind, placebo washout periods.

Although other doses of fluticasone furoate/vilanterol (Relvar) were tested in these studies, only data for the licensed dose for Relvar (92/22 mcg) are shown.

Patient population:
- Clinical history of COPD
- Post bronchodilator FEV₁ ≤70% predicted normal and FEV₁/FVC ratio of ≤0.70
- A current habit or history of ≥10 pack years of cigarette smoking
- A score of ≥2 (on a scale of 1–4) on the Modified Medical Research Council Dyspnoea Scale

Primary efficacy endpoint assessments

- Time-adjusted weighted mean (wm) 0 to 24-hour FEV₁ at the end of the 28-day treatment period
  - This was calculated from pre-dose FEV₁ and post-dose FEV₁ after 5, 15, 30 and 60 minutes and 2, 4, 6, 8, 12, 16, 20, 22, 23 and 24 hours
Results

Patient Population
33 patients were assigned to the fluticasone furoate/vilanterol (Relvar) 92/22 mcg arm and 51 patients to the placebo arm.
The mean patient age was 57.9 years and 46% were male and 89% white. 83% were current smokers and 53% had had COPD for ≥5 years. Mean post bronchodilator % predicted FEV₁ at baseline was 49.8%.

Primary efficacy endpoint
- Fluticasone furoate/vilanterol (Relvar) 92/22 mcg demonstrated significantly higher 0 to 24-hour wm FEV₁ vs placebo at the end of the 28 day treatment period (p<0.001)

Figure 4: 24-hour FEV₁ of Relvar 92/22 mcg (placebo-adjusted curve), days 28-29

Safety
On treatment adverse events are reported in the safety section.
Safety

Data from large asthma and COPD Phase III clinical trials were used to determine the frequency of adverse reactions associated with Relvar. In the Relvar COPD and asthma clinical development programme, the safety population comprised of a total of 7,034 patients with asthma and 6,237 patients with COPD. Very common, common and important adverse reactions from the SmPC are reported in Table 4.1

Table 4: Relvar adverse events in asthma and COPD

<table>
<thead>
<tr>
<th>Frequency of adverse event</th>
<th>Headache, nasopharyngitis</th>
</tr>
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<tbody>
<tr>
<td>Very common adverse reactions (≥1/10)</td>
<td></td>
</tr>
<tr>
<td>Common adverse reactions (≥1/100 to &lt;1/10)</td>
<td>Pneumonia, upper respiratory tract infection, bronchitis, influenza, candidiasis of mouth and throat, oropharyngeal pain, sinusitis, pharyngitis, rhinitis, cough, dysphonia, abdominal pain, arthralgia, back pain, fractures, muscle spasms, pyrexia</td>
</tr>
<tr>
<td>Other important adverse reactions include</td>
<td>Vision blurred</td>
</tr>
<tr>
<td>Frequency: Uncommon (≥1/1,000 to &lt;1/100)</td>
<td>Paradoxical bronchospasm, hypersensitivity reactions including anaphylaxis, angioedema, rash, urticaria</td>
</tr>
<tr>
<td>Frequency: Rare (≥1/10,000 to &lt;1/1,000)</td>
<td></td>
</tr>
</tbody>
</table>

Considerations

Please consult the full Summary of Product Characteristics for further information and guidance on discontinuation of treatment and/or appropriate patient referral in the event of disease deterioration, paradoxical bronchospasm, cardiovascular effects, hyperglycaemia, systemic steroid effects, visual disturbance, psychological effects, pneumonia and use in hepatic impairment.

Relvar Ellipta 184/22 micrograms is not indicated for patients with COPD. There is no additional benefit compared with 92/22 mcg and there is a potential increased risk of adverse reactions.
Pneumonia

In common with other ICS containing medicines, there is an increased risk of pneumonia in COPD patients treated with Relvar 92/22 mcg. There is no conclusive clinical evidence for intra-class differences in the magnitude of the pneumonia risk among inhaled corticosteroid products.

In the two replicate, 1 year, exacerbation studies in COPD patients, pneumonia occurred in 6% of patients receiving fluticasone furoate/vilanterol (Relvar) 92/22 mcg compared with 3% of patients receiving vilanterol 22 mcg alone. The number of pneumonia events per 1000 patient years was 85.7 with fluticasone furoate/vilanterol (Relvar) 92/22 mcg and 42.3 with vilanterol 22 mcg alone.

Risk factors for pneumonia in patients with COPD receiving Relvar include current smokers, patients with a history of prior pneumonia, patients with a body mass index <25 kg/m² and patients with a (forced expiratory volume) FEV₁ <50% predicted.

Fractures

In the two replicate, 1 year, exacerbation studies in COPD patients, the incidence of fractures was higher in the fluticasone furoate/vilanterol (Relvar) 92/22 mcg arms (2%) versus the vilanterol 22 mcg alone group (<1%). Fractures typically associated with corticosteroid use (e.g., spinal compression/thoracolumbar vertebral fractures, hip and acetabular fractures) occurred in <1% of the patients on fluticasone furoate/vilanterol (Relvar) 92/22 mcg.

Additional points to note:

Relvar should not be used to treat an acute exacerbation in COPD, for which a short-acting bronchodilator is required.

No dose adjustment is required in patients with renal impairment. The effects of haemodialysis have not been studied.

Caution should be exercised when dosing patients with hepatic impairment who may be more at risk of systemic adverse reactions associated with corticosteroids. Systemic effects may occur with any inhaled corticosteroid, particularly at high doses prescribed for long periods. These effects are much less likely to occur than with oral corticosteroids.

With Relvar, clinically significant drug interactions are considered unlikely due to the low plasma concentrations achieved after inhaled dosing. Interactions with other medicinal products are reported in section 4.5 of the Summary of Product Characteristics.

For more details on adverse events, please refer to the Summary of Product Characteristics.
National Health Technology Assessments

The National Institute for Health and Care Excellence (NICE) did not consider Relvar for a NICE technology appraisal but developed an evidence summary for Relvar in COPD, ESNM21, which was published on 18th June 2013.

Both the Scottish Medicines Consortium (SMC) and the All Wales Medicines Strategy Group (AWMSG) published advice for Relvar in COPD.\textsuperscript{16,17}

The SMC advice for Relvar in COPD is as follows (www.scottishmedicines.org.uk/home):\textsuperscript{16}

- Fluticasone furoate/vilanterol (Relvar Ellipta) is accepted for restricted use within NHS Scotland
- Indication under review: symptomatic treatment of adults with chronic obstructive pulmonary disease (COPD) with a forced expiratory volume in 1 second (FEV\textsubscript{1}) <70% predicted normal (post-bronchodilator) with an exacerbation history despite regular bronchodilator therapy
- SMC restriction: in patients with severe COPD (FEV\textsubscript{1} <50% predicted normal)
- In a comparative, 12-week study there was no statistically significant difference between fluticasone furoate/vilanterol 92/22 micrograms and another inhaled corticosteroid/long-acting beta agonist combination inhaler for change from baseline trough in 24-hour weighted-mean FEV\textsubscript{1}
- SMC advice on medicines use can be found at www.scottishmedicines.org.uk/Home

AWMSG recommendation for Relvar in COPD is as follows (www.awmsg.org):\textsuperscript{17}

- Fluticasone furoate/vilanterol (as trifenate) (Relvar Ellipta) is recommended as an option for use within NHS Wales for the symptomatic treatment of adults with chronic obstructive pulmonary disease with a FEV\textsubscript{1} <70% predicted normal (post-bronchodilator) with an exacerbation history despite regular bronchodilator therapy

Additional note:

- Fluticasone furoate/vilanterol (as trifenate) (Relvar Ellipta) should be used in line with NICE Clinical Guideline on chronic obstructive pulmonary disease for the symptomatic treatment of adults
- Fluticasone furoate/vilanterol (Relvar Ellipta) is recommended as an option for use within NHS Wales for the regular treatment of asthma in adults and adolescents aged 12 years and older where use of a combination medicinal product (long-acting beta\textsubscript{2}-agonist and inhaled corticosteroid) is appropriate:
  - patients not adequately controlled with inhaled corticosteroids and ‘as needed’ inhaled short acting beta\textsubscript{2}-agonists.
- AWMSG guidance on medicines use can be found at www.awmsg.org
Relvar Ellipta device for COPD

Administration for COPD

One inhalation of Relvar Ellipta 92/22 mcg once daily for adults aged 18 years and over. Relvar should be administered at the same time of the day, each day (morning or evening). If a dose is missed the next dose should be taken at the usual time the next day.

Figure 5: Relvar Ellipta device

The Ellipta inhaler consists of two aluminium foil laminate strips of regularly distributed blisters, each containing the active drug.

Every time the inhaler cover is opened one dose of medicine is prepared. The Ellipta inhaler has a dose counter which shows how many doses of medicine are left in the inhaler.

- Before the inhaler has been used, it shows exactly 30 doses
- It counts down by 1 each time the cover is opened
- When fewer than 10 doses are left, half of the dose counter shows red
- After the last dose has been inhaled, the counter shows 0

Relvar Ellipta has a 2 year shelf life. It has an in-use shelf life of 6 weeks after opening the tray and must not be stored above 25°C.
Patient experience

Ease of use of the Ellipta device in COPD patients has been tested during the development programme of another medicinal product. Following initial instruction on how to use the inhaler in two such studies, 98% of COPD patients (n=632) used Ellipta correctly at Day 1. Correct inhaler use was re-assessed after 6 weeks of treatment using the demonstration inhaler, without further verbal instruction or demonstration to the patient; 98-99% of subjects (n=587) still used their Ellipta correctly. After 6 weeks of treatment, patients were asked to rate the ease of use of the inhaler; 98-99% of patients (n=587) rated it as either very easy or easy to use.\textsuperscript{10}

COPD patients of all severities were able to generate a peak inspiratory flow rate (PIFR) of greater than 43 L/min through the Ellipta device.\textsuperscript{11} The inhalation profiles generated by this range of patients were replicated using the Electronic Lung (GSK) breathing simulator. In vitro drug delivery to the lung was consistent across the full range of PIFR values.\textsuperscript{12}

Qualitative data from COPD patients (n=42) using the Ellipta device in a trial for an investigational medicinal product has shown that nearly 9 out of 10 patients preferred Ellipta to their current respiratory inhaler device: \textsuperscript{13}

- 95% of those using Handihaler (n=20) preferred Ellipta
- 86% of those using Accuhaler (n=21) preferred Ellipta
- 85% of those using MDI/HFA (n=20) preferred Ellipta

Adherence

Once daily treatment has the potential to improve adherence and simplify treatment in chronic diseases such as COPD, however there is no current data to directly support increased adherence with Relvar Ellipta compared to other ICS/LABA combinations in COPD.

There is some evidence in the LAMA class that a once daily COPD inhaler therapy may improve compliance. In a retrospective analysis of 50,076 patients in the US, looking specifically at adherence, COPD patients who were initiated on treatment with once-daily dosing (tiotropium; n=3,678) had significantly higher adherence (measured using proportion of days covered) over 12 months than patients initiated on treatments which were dosed twice a day (n=25,011) e.g. Seretide and Symbicort; (43.3% vs 37.0%, p<0.0001).\textsuperscript{14}

Further, there is qualitative evidence that more COPD patients would prefer to have a therapy that is dosed once daily than not. In a retrospective observational study using data from a primary care database of 2138 patients who were posed the question: “I would prefer to take my inhaler/regular COPD treatment once a day”, 44.7% preferred a once daily schedule (agreed or strongly agreed), 24.9% were not sure, and 30.4% did not prefer once daily therapy (disagreed or strongly disagreed).\textsuperscript{15}

Finally, with an increasing number of COPD patients taking ‘triple therapy’ (concomitant ICS/ LABA and LAMA preparations), a once daily ICS/LABA would complement the once daily dosing schedule of the most widely prescribed LAMAs.
Cost

The 30-day cost of Relvar Ellipta 92/22 mcg is £22.00\(^2\)

- Each Relvar Ellipta device contains 30 doses
- Relvar Ellipta is taken as one inhalation once a day

Data to calculate the budget impact of use of Relvar, specific to a locality, can be provided by your local GSK account manager and health outcomes specialists if required.

Information sources

Should you require further medical information on Relvar please contact the GSK medical information team via our customer contact centre:

- By phone on 0800 221 441. Lines are open from Monday-Friday 8.30am to 5.30pm. Outside these hours and on bank holidays, an answer phone service is available
- By email at customercontactuk@gsk.com

Your local GSK account team of therapy, medical and health outcomes specialists will also be able to support you if required.
References

1. Relvar Ellipta Summary of Product Characteristics. GlaxoSmithKline
2. eMims. ICS/LABA combination prices. Accessed April 2017
11. Prime D et al. Comparison of inhalation profiles through A novel dry powder inhaler (nDPI) and lung function measurements for healthy subjects, asthma and Chronic Obstructive Pulmonary Disease (COPD) patients. Am J Respir Crit Care Med. 2012; 185: A2941
14. Toy EL et al. Treatment of COPD: Relationships between daily dosing frequency, adherence, resource use, and costs. Respiratory medicine (2011); 105: 435-441
treatment of adults with COPD with a FEV1<70% predicted normal (LABA) and ICS combination is appropriate.

short-acting inhaled ß2-agonists, where a long-acting ß2-agonist controlled on inhaled corticosteroids (ICS) and “as needed” Regular treatment of asthma in patients ≥12 years not adequately dose of 184 mcg of FF and 22 mcg of VI. Each single inhalation of FF 200 mcg and VI 25 mcg provides a delivered dose of 92 mcg FF and 22 mcg VI. Each single inhalation of fluticasone furoate (FF) 100 micrograms (mcg) and vilanterol (VI) 100 micrograms (mcg) and vilanterol (VI) 25 mcg provides a delivered dose of 92 mcg FF and 22 mcg VI. Each single inhalation of FF 200 mcg and VI 25 mcg provides a delivered dose of 184 mcg of FF and 22 mcg of VI. Indications: Asthma: Regular treatment of asthma in patients ≥12 years not adequately controlled on inhaled corticosteroids (ICS) and “as needed” short-acting inhaled ß2-agonists, where a long-acting ß2-agonist (LABA) and ICS combination is appropriate. COPD: Symptomatic treatment of adults with COPD with a FEV1<70% predicted normal (post-bronchodilator) and an exacerbation history despite regular bronchodilator therapy. Dosage and administration: Inhalation only. Asthma: Adults and adolescents ≥12 years: one inhalation once daily of Relvar 92/22 mcg for patients who require a low to mid dose of ICS in combination with a LABA. If patients are inadequately controlled then the dose can be increased to one inhalation once daily Relvar 184/22 mcg. Relvar 184/22 mcg can also be considered for patients who require a higher dose of ICS in combination with a LABA. Regularly review patients and reduce dose to lowest that maintains effective symptom control. COPD: one inhalation once daily of Relvar 92/22 mcg. Relvar 184/22 mcg is not indicated for patients with COPD. Contraindications: Hypersensitivity to the active substances or to any of the excipients (lactose monohydrate & magnesium stearate). Precautions: Pulmonary tuberculosis, severe cardiovascular disorders or heart rhythm abnormalities, thyrotoxicosis, uncorrected hypokalaemia, patients predisposed to low levels of serum potassium, chronic or untreated infections, diabetes mellitus, paradoxical bronchospasm. In patients with moderate to severe hepatic impairment 92/22 mcg dose should be used. Acute symptoms: Not for acute symptoms, use short-acting inhaled bronchodilator. Warn patients to seek medical advice if short-acting inhaled bronchodilator use increases. Therapy should not be abruptly stopped without physician supervision due to risk of symptom recurrence. Asthma-related adverse events and exacerbations may occur during treatment. Patients should continue treatment but seek medical advice if asthma symptoms remain uncontrolled or worsen after initiation of Relvar. Systemic effects: Systemic effects of ICSs may occur, particularly at high doses for long periods, but much less likely than with oral corticosteroids. Possible Systemic effects include: Cushing’s syndrome, Cushingoid features, adrenal suppression, decrease in bone mineral density, growth retardation in children and adolescents. Eye symptoms such as blurred vision may be due to underlying serious conditions such as cataract, glaucoma or central serous choroideropathy (CSCR); consider referral to ophthalmologist. More rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). Increased incidence of pneumonia has been observed in patients with COPD receiving inhaled corticosteroids. Risk factors for pneumonia include: current smokers, old age, patients with a history of prior pneumonia, patients with a body mass index <25 kg/m² and patients with a FEV1 <50% predicted. If pneumonia occurs with Relvar treatment should be re-evaluated. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take Relvar. Interactions with other medicinal products: Interaction studies have only been performed in adults. Avoid ß-blockers. Caution is advised when co-administering with strong CYP3A4 inhibitors (e.g. ketoconazole, ritonavir, cobicistat-containing products). Concomitant administration of other sympathomimetic medicinal products may potentiate the adverse reactions of FF/VI. Relvar should not be used in conjunction with other long-acting ß2-adrenergic agonists or medicinal products containing long-acting ß2-adrenergic agonists. Pregnancy and breast-feeding: Experience limited. Balance risks against benefits. Side effects: Very Common (≥1/10): headache, nasopharyngitis. Common (≥1/100 to <1/10): candidiasis of the mouth and throat, dysphonia, pneumonia, bronchitis, upper respiratory tract infection, influenza, oropharyngeal pain, sinusitis, pharyngitis, rhinitis, cough, abdominal pain, arthralgia, back pain, fractures, pyrexia, muscle spasms. Other important side effects include: Uncommon (≥1/100 to <1/10): blurred vision. Rare (≥1/10,000 to <1/100): paradoxical bronchospasm and hypersensitivity reactions including anaphylaxis, angioedema, rash, urticaria. See SmPC for other adverse reactions. Legal category: POM. Presentation and Basic NHS cost: Relvar Ellipta 1 inhaler x 30 doses. Relvar Ellipta 92/22 - £22.00. Relvar Ellipta 184/22 - £29.50. Marketing authorisation (MA) nos. 92/22 mcg 1x30 doses [EU/1/13/886/002]; 184/22 mcg 1x30 doses [EU/1/13/886/005]. MA holder: Glaxo Group Ltd, 980 Great West Road, Brentford, Middlesex TW8 9GS, UK. Last date of revision: September 2017. UK/F/T/0227/15(3). Trademarks are owned by or licensed to the GSK group of companies. © 2017 Glaxo group of companies or its licensor. Relvar Ellipta was developed in collaboration with Innoviva Inc.