**Hospital initiation to GP maintenance: Background information for including Jorveza onto the GP network formulary**

**What is eosinophilic oesophagitis?**

Eosinophilic oesophagitis (EoE) is a chronic, progressive inflammatory disorder in which eosinophils infiltrate the oesophageal epithelium.[1] Chronic eosinophilic inflammation leads to changes in oesophageal structure (oesophageal rigidity, fibrostenotic features such as rings, and ultimately strictures) and in oesophageal function (food feels like it is moving slowly or sticking in the chest after swallowing).[1,2]

Once regarded as a rare disease, the incidence and prevalence of EoE has risen consistently over the past 25 years reaching 118 per 100,000 persons in a recent Swedish study.[3,4] It is now the second most common disease of the oesophagus after gastro-oesophageal reflux disease (GORD), and the most likely cause of thoracic dysphagia and of food bolus obstruction (FBO) presenting to emergency departments.[3]

FBO is an increasingly common event in the everyday clinical practice of emergency physicians.[5] Emergent endoscopy, which is invasive and expensive, is the current preferred treatment.[6]
As EoE has become more common so too has FBO, adding to the workload burden on emergency and endoscopy staff.[6,7]

As well as being detrimental to the physical health of sufferers, EoE can also cause considerable psychological distress.[8] Without necessarily realising that they are doing so, people with EoE may adapt their diet to include softer foods and liquids because of their trouble swallowing solid food.[2] They are often the last to finish meals, chewing their food very thoroughly and drinking lots of fluid to wash it down.[9]

Spontaneous resolution of EoE is thought to be uncommon.[10] A delay/break in therapy can lead to progressive oesophageal narrowing, stricture, and FBO. Following induction treatment, maintenance therapy can help to prevent these complications developing.[10]

**How effective is traditional EoE treatment?**

Outcomes with traditional EoE therapies are relatively poor.[3] Proton pump inhibitors (which although widely used do not have a license for EoE) result in at least partial symptom improvement in ~70% of patients, but histological remission in fewer than 50%.[8,11] With an absence of clear usage instructions, off-label topical corticosteroids repurposed from asthma treatments (swallowed sprays from inhalers or home-made mixtures of budesonide in syrups) are similarly inconsistently effective in EoE.[3] Although elimination diets can be effective in maintaining disease control, downsides include the initial need for frequent endoscopies, the burden of a restrictive diet on quality of life and poor long-term adherence.[12] Active disease recurs when treatments are stopped.[13]

**What is Jorveza (orodispersible budesonide)?**

Topical steroids are only as effective as their ability to uniformly coat the oesophageal mucosa in EoE.[13] Jorveza is the only topical steroid specifically formulated to target the oesophagus.[14] The Jorveza tablet is placed on the tongue where it starts to effervesce, stimulating the production of saliva. As the saliva is swallowed, it coats the oesophagus delivering high concentrations of budesonide to the site of inflammation.[14]

In a phase III induction study, Jorveza achieved histological remission in over 90% of patients and symptom relief in 85% within 12 weeks of treatment.[15] It was equally effective for inducing histological remission in all parts of the oesophagus, suggesting it provides optimal targeting of the whole oesophagus.[13] Jorveza led to a

quick onset of symptom resolution, with a significant improvement vs placebo within 2 weeks. Both social function and disease-related worry were significantly improved with Jorveza vs placebo.[15]

Since cessation of EoE treatment leads to disease recurrence, the condition requires long-term management.[16] Jorveza proved to be an effective, well tolerated maintenance therapy in a phase III maintenance study with over 90% of patients remaining in remission at week 48; by contrast, over half of patients on placebo relapsed within 3 months.[17] No loss of efficacy was observed in an open-label extension study over a period of up to 3 years.[18]

In a recent meta-analysis, patients treated with Jorveza were four times as likely to achieve histological remission as those treated with off-label corticosteroids swallowed from an asthma inhaler or mixed with sweeteners to create a slurry.[19]

The British Society of Gastroenterology recommend Jorveza - the only oral medicine with European regulatory approval for EoE - over other steroid formulations for both the induction and maintenance of remission in adults:[8]

- Induction: *"In adults, the GDG support the use of orodispersible budesonide over other swallowed steroid formulations in the induction treatment of EoE given its regulatory approval in both the UK and the Europe"*

- Maintenance: *"Based on this initial data of maintenance of remission with orodispersible budesonide treatment over a 12-month period, the GDG recommends the use of this formulation over others for the maintenance of remission of EoE in adult"*

Recognising the need for a licensed, effective treatment for EoE, NICE considered the use of Jorveza cost-effective for the treatment of active EoE:[20]

- Guidance: *"Budesonide as an orodispersible tablet is recommended as an option for inducing remission of eosinophilic oesophagitis in adults"*

While its use in maintaining remission has yet to be reviewed by NICE, the MHRA have licensed Jorveza for the maintenance of remission.[20,21]

**What is the licensed indication/dosage for Jorveza?**
Jorveza is indicated for the treatment of EoE in adults (older than 18 years of age).[21] It is prescribed at 1 mg twice a day for induction and 0.5 mg or 1 mg twice a day for maintenance treatment.[21]

**What are the starting criteria for using Jorveza?**
Patients require a diagnosis of EoE to receive Jorveza treatment.[21]

While symptoms point to EoE, it takes histology to confirm the diagnosis.[8] At least six biopsies are taken from different anatomical sites within the oesophagus.[8] A dense infiltration of eosinophils within the oesophageal epithelium with a peak count of ≥15 eosinophils /0.3 $mm^2$ in any biopsy specimen is the distinguishing feature of EoE.[8]

Non-malignant FBO is strongly associated with an underlying diagnosis of EoE.[22] Consequently, FBO presents a unique opportunity to diagnose, treat and establish care for patients with EoE.[23]

At a UK university hospital, 38% of patients newly diagnosed with EoE had received an OGD for prior episodes of food obstruction before their diagnosis.[24] By focusing on appropriate patient diagnostic work-up after the first episode of impaction a proportion of FBO cases could be prevented, relieving pressure on A&E.[5]

Distinguishing between GORD and EoE can be a challenge - especially when EoE patients use terms like 'reflux' and 'heartburn', not realising their discomfort is not the same as that felt by people with GORD.[2,9] While patients may regurgitate fluid if they suffer a food bolus obstruction, the taste is not acidic and so quite distinct from reflux in GORD.[5] Symptoms also occur at different times – during eating with EoE but after meals or at night for GORD.[9]

EoE is several times more prevalent in patients with allergic disease than in the general population.[25] It has been recommended that physicians who care for patients with allergic conditions ask about solid food dysphagia and food impactions as part of routine treatment.[25]

Jorveza is initiated by the specialist gastroenterology team prescribing for the 12-week induction period, but maintenance prescribing can continue in primary care.

**Who needs maintenance therapy?**

It has become increasingly clear that most, if not all, patients with EoE will need maintenance therapy to control the inflammation.[26] Not only is spontaneous resolution thought to be uncommon, disease activity recurs when treatments are stopped and untreated disease can also lead to fibrostenotic complications.[10]

Long-term maintenance therapy targeted at the histologic resolution of eosinophilic inflammation and symptoms reduces the risk of oesophageal impactions and the need for oesophageal dilation and is associated with improved quality of life.[27]

The BSG / BSPGHAN 2022 guidelines recognise that clinical and histological relapse is high after withdrawal of topical steroid treatment and suggest that following clinical review, maintenance treatment should be recommended.[8]

Historically, swallowed topical corticosteroids have been used in the long-term treatment of EoE. However, remission rates have generally been lower than those observed after induction therapy.[28]

Over a period of up to three years, Jorveza was highly effective in preventing clinical, endoscopic and histological relapse in adult EoE patients.[29] 83% of patients were in clinical remission, 79% achieved deep histological remission (no eosinophils in any biopsies) and 67% had deep endoscopic remission (no signs of oedema, rings, exudate, furrows or strictures).[18] No loss of efficacy was observed over the three-year period.[29]

The duration of maintenance therapy is determined by the treating physician.[21]

**Is Jorveza well tolerated?**

In clinical studies, the frequency of adverse events was similar in the Jorveza and placebo groups.[17]

Local fungal infections with *Candida* occurred at a higher frequency with Jorveza.[17] The rate of confirmed and symptomatic oesophageal candidiasis was 5.9% and 1.5% for Jorveza 0.5 mg and 1 mg twice daily respectively.[17] Long-term treatment with Jorveza did not increase the rate of local candidiasis; cases were generally mild in intensity and did not impact upon the treatment effect.[29]

No clinically relevant changes in serum morning cortisol levels were observed in the phase III studies or open-label extension.[15,17,29]

**What impact will GP maintenance prescribing have on patients/hospitals/GPs?**

Obviating the need for time consuming and inconvenient visits to the hospital for each repeat prescription is an important benefit for patients. Being able to pick up their prescription more locally may also reduce car travel and its associated environmental cost.

Effective maintenance treatment most likely reduces progression of EoE to a fibrostenotic phenotype and so too complications such as food bolus impaction, strictures, and the need for endoscopic interventions.[16]

While reducing pressure on hospital pharmacies and clinics, the impact of maintenance prescribing on GP workload should be minimal with no routine monitoring required in primary care.

If indicated, symptomatic candidiasis of the mouth and throat can be treated with topical or systemic anti-fungal therapy whilst continuing treatment with Jorveza.[21]

Regular clinic follow-up is recommended to assess disease activity and open a window to monitoring side effects, adjusting therapy, and encouraging adherence to treatment.[16] Regular clinic visits every [TO BE COMPLETED ON A LOCAL LEVEL] months will therefore be organised. Worsening symptoms despite therapy adherence and/or the occurrence of an FBO should prompt an early return to the clinic.

**Who pays – the ICS or NHS England?**

Jorveza is not a specialised product, so the cost will be borne locally by the ICS

**What are the likely costs to the ICS by moving the costs from hospital to primary care?**

[TO BE COMPLETED ON A LOCAL LEVEL]

**What is the cost of Jorveza?**

| Drug | Pack size | Cost |
|---|---|---|
| Budesonide ODT (Jorveza®) 0.5 mg ODT | 60 | £214.80 |
| Budesonide ODT (Jorveza®) 1 mg ODT sugar free | 90 | £323.00 |

*Prices correct as per February 2024 BNF and Drug Tariff online.*

**Useful materials**

**Integrated care pathway for the diagnosis and management of EoE:**

https://drfalk.co.uk/wp-content/uploads/2024/02/EoE-An-integrated-pathway_Interactive-Document.pdf

**Summary of Product Characteristics: Jorveza 1 mg orodispersible tablets**:

https://www.medicines.org.uk/emc/product/9446/smpc#gref

**NICE Guidance: NICETA708: Budesonide ODT for inducing the remission of eosinophilic oesophagitis**:

https://www.nice.org.uk/guidance/ta708/resources/budesonide-orodispersible-tablet-for-inducing-remission-of-eosinophilic-oesophagitis-pdf-82611079825093#:~:text=Budesonide%20ODT%20is%20recommended%20for%20routine%20use&text=The%20committee%20concluded%20that%20the,in%20adults%20with%20eosinophilic%20oesophagitis.

**Abbreviations**

BSG: British Society of Gastroenterology
BSPGHAN: British Society of Paediatric Gastroenterology, Hepatology and Nutrition
EoE: eosinophilic oesophagitis
FBO: food bolus obstruction
GDG: guideline development group
GORD: gastro-oesophageal reflux disease
ICS: integrated care systems
MHRA: Medicines and Healthcare products Regulatory Agency
NICE: National Institute for Health and Care Excellence
ODT: orodispersible tablet
OGD: oesophagogastroduodenoscopy

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