Together we *know more.*
Together we *do more.*

Eosinophilic oesophagitis maintenance therapy

Why maintenance therapy is needed

Rationale for continuing treatment in EoE[1-4]

- Spontaneous resolution is thought to be uncommon
- Active disease recurs when treatments are stopped
- Untreated disease can lead to fibrostenotic complications

Clinical and histological relapse is high after withdrawal of topical steroid treatment and, following clinical review, maintenance treatment should be recommended[5]

BSG / BSPGHAN Guidelines May 2022

Who should be offered maintenance therapy?

Those with a long diagnostic delay before treatment

As delay to diagnosis increases, so too does the risk of finding fibrostenotic features such as oesophageal rings and strictures at OGD[6]

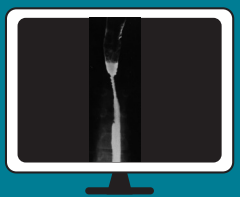
Fibrosis takes a long time to develop and, in some, a long time to resolve[7]

Those with a previous food bolus obstruction (FBO) requiring emergency extraction

Maintenance therapy with topical steroid reduces the risk of recurrent FBO[5]

Registry data suggest the longer patients use topical steroids, the less likely they are to have another FBO requiring endoscopic removal[8]

Those with a previous dilation



Patients on maintenance therapy are significantly less likely to require repeat dilation compared with patients not on treatment[9]

One study found that within a year of stopping topical steroid therapy, previously dilated oesophageal strictures had renarrowed almost back to their predilation diameter[10]

Prescribing information may be found on the back cover

Who should be offered maintenance therapy?

Those with moderate to severe disease activity prior to induction

Within 3 months of stopping topical steroid therapy, as many as half of patients whose disease activity was moderate to severe will clinically relapse[11]

As few as one in 20 will remain in clinical and histological remmission at one year[11]

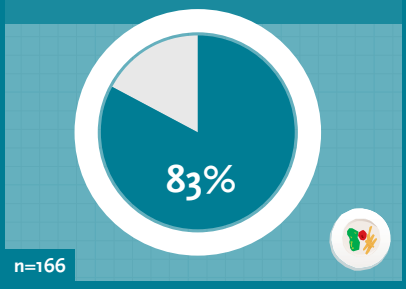
Those who have responded to Jorveza (orodispersible budesonide) induction treatment

The BSG 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[5]

96-week, open-label extension in patients completing a double-blind, 48-week study[12]

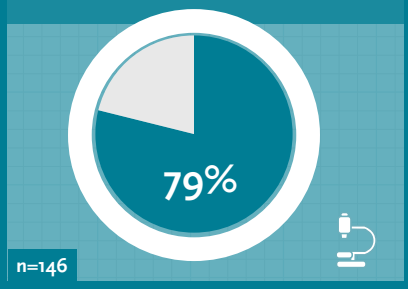
Clinical remission

(EEsAI-PRO ≤20)



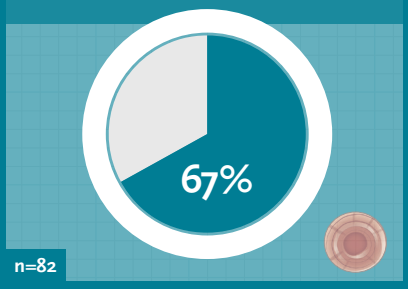
Deep histologic remission

(Peak eos in all biopsies: 0/hpf)



Total EREFS of 0

(Grade 0 for oedema, rings, exudate, furrows & stricture)



Over a period of up to three years, Jorveza was well tolerated:[11-13]

Jorveza (orodispersible budesonide) recommended dosage

Induction of remission[14]

1 mg bd

6 to 12 weeks*

*Prolongation of therapy to 12 weeks is beneficial to bring more patients into remission[15]

Maintenance of remission[14]

0.5 mg or 1 mg bd*

Duration determined by the treating physician

*1 mg bd is recommended for patients withlong-standing disease history and/or high extent of oesophageal inflammation in the acute disease state

Those who have responded to PPI induction treatment

There are limited published data, no published studies of >12 months duration, and no prospective randomised trials to define appropriate long-term maintenance strategies in PPI-responsive patients[5]

While the short-term use of PPIs is considered generally safe, their long-term safety profile is controversial - moreover, side effects associated with PPI use are known to be dose dependent[16,17]

Continued observation versus long-term maintenance therapy

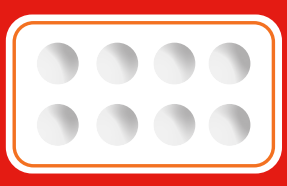
> "The problem with continued observation is that it is unclear how to follow these patients . . . some objective measure is needed"[18]

Patients who opt for as needed or intermittent therapy should be advised of potential risks of discontinuing treatment[19]

Histologic recurrence occurs in the vast majority of patients regardless of whether or not they have symptom recurrence[20]

Moreover, patients who adopt symptom-masking behaviours may not recognise they have active disease[21]

Patients who have rapidly recurring symptoms after treatment is stopped should be strongly advised to undergo maintenance therapy[1]



Which patients with EoE should maintenance therapy be offered to?

Responded to induction?

Long diagnostic delay before treatment?

Moderate to severe disease activity prior to induction?

Rapid symptom recurrence?

Already has fibrostenotic complications?

Previous FBO requiring emergency extraction?

Previous dilatation?

Anxious about symptoms returning?

Jorveza is the only oral medical treatment licensed for the maintenance of remission in adults with EoE

SMC Advice[25]

Jorveza is accepted for use within NHS Scotland in adult patients unsuccessfully treated with proton pump inhibitors

NICE Guidance[26]

Jorveza is recommended as an option for inducing remission of eosinophilic oesophagitis in adults

Adapted from references 1-2,9-10,14,19,22-24

Prescribing Information (refer to full SmPC before prescribing).
Presentations: Jorveza 1mg and 0.5mg orodispersible tablets containing 1mg or 0.5mg of budesonide. **Indications:** treatment of eosinophilic esophagitis (EoE) in adults (older than 18 years of age). **Dosage:** Induction of remission: one 1mg tablet taken twice daily (morning and evening) after a meal and immediately after removal of the tablet from the blister pack. Usual duration of induction treatment is 6 weeks. Extend up to 12 weeks for non-responding patients. Maintenance of remission: 0.5mg twice daily or 1mg twice daily depending on clinical need. A maintenance dose of 1mg twice daily is recommended for patients with long-standing disease history and/or high extent of esophageal inflammation in the acute disease state. Duration of maintenance treatment - to be determined by the treating physician. Administration: tablet is placed on tip of tongue and pressed to top of mouth then swallowed slowly without liquid or food and without chewing or swallowing undisintegrated. May take 2 to 20 minutes to disintegrate and swallow completely. Wait at least 30 minutes before eating, drinking or performing oral hygiene. **Contra-indications**: hypersensitivity to budesonide or any ingredient of the tablets. **Warnings/precautions:** infections - Suppression of inflammatory response and immune function increases susceptibility to infections and their severity which can be atypical or masked. Oral, oropharyngeal and esophageal candida infections occur at high frequency. Treat symptoms with topical or systemic anti-fungals. Jorveza treatment can continue. Chickenpox, herpes zoster and measles - can be more serious in patients treated with glucorticosteroids. Check vaccination status. Avoid exposure. Vaccines - avoid co-administration of live vaccines and glucocorticosteroids. The antibody response to other vaccines may be diminished. Special populations - monitor patients with tuberculosis, hypertension, diabetes mellitus, osteoporosis, peptic ulcer, glaucoma, cataract, family history of diabetes, family history of glaucoma. Systemic effects of glucocorticosteroids may occur, depending on duration of treatment, concomitant and previous glucocorticosteroid treatment and individual sensitivity. Patients with reduced liver function - an increased systemic availability of budesonide may be expected, with increased risk of adverse reactions. Patients with hepatic impairment should not be treated. Not recommended for use in patients with severe renal impairment. Angioedema - treatment should be stopped if signs of angioedema are observed. Visual disturbance - patients with blurred vision or other visual disturbances should be considered for referral to an ophthalmologist. Causes may include cataract, glaucoma or central serous chorioretinopathy resulting from corticosteroid use. Others - glucocorticosteroids may cause suppression of the hypothalamic–pituitary–adrenal (HPA) axis and reduce the stress response. When patients are subject to surgery or other stresses, supplementary systemic glucocorticosteroid treatment is therefore recommended. Concomitant treatment with ketoconazole or other CYP3A4 inhibitors should be avoided. Serological testing - adrenal function may be suppressed by budesonide so an ACTH stimulation test for diagnosing pituitary insufficiency might show false (low) results. Sodium - contains 52 mg of sodium per daily dose. **Interactions:** CYP3A4 inhibitors - concomitant treatment with ketoconazole or other potent CYP3A inhibitors including grapefruit juice should be avoided to reduce the risk of systemic side effects unless the benefit outweighs the risk. Such treatment should be monitored. Oestrogens, oral contraceptives - may elevate plasma concentrations and enhance effects of glucocorticosteroids. Concomitant intake of lowdose combination oral contraceptives has not shown this effect. Cardiac glycosides - action of glycoside can be potentiated by potassium deficiency - a potential and known adverse reaction of glucocorticoids. Saluretics - potassium excretion can be enhanced and hypolalaemia aggravated. Use in pregnancy should be avoided unless there are compelling reasons for therapy. Breast-feeding - budesonide is excreted in human milk. The benefit of breast feeding for the child and the benefit of therapy for the woman should be assessed. Fertility - there are no data on the effect of budesonide on human fertility. **Undesirable effects:** fungal infections in the mouth, pharynx and the oesophagus were the most frequently observed adverse reactions in clinical studies. Long term treatment did not increase the rate. Adverse reactions and frequencies: Very common: esophageal candidiasis, oral and/or oropharyngeal candidiasis, Common: sleep disorder, headache, dysgeusia, dry eyes, gastroesophageal reflux disease, nausea, oral paraesthesia, dyspepsia, upper abdominal pain, dry mouth, glossodynia, tongue disorder, oral herpes, fatigue, blood cortisol decreased. Uncommon: nasopharyngitis, pharyngitis, angioedema, , anxiety, agitation, dizziness, , hypertension, cough, dry throat, oropharyngeal pain, abdominal pain, abdominal distension, , dysphagia, erosive gastritis, gastric ulcer, lip edema, gingival pain, rash, urticaria, sensation of foreign body, osteocalcin decreased, weight increased. . Other (class) effects with unknown frequency that may occur: increased risk of infection, Cushing's syndrome, adrenal suppression, growth retardation in children, hypokalaemia, hyperglycaemia, depression, irritability, euphoria, psychomotor hyperactivity, aggression, pseudotumor cerebri including papilloedema in adolescents, glaucoma, cataract (including subcapsular cataract), blurred vision, central serous chorioretinopathy (CSCR), increased risk of thrombosis, vasculitis (withdrawal syndrome after long-term therapy), duodenal ulcers, pancreatitis, constipation, allergic exanthema, petechiae, delayed wound healing, contact dermatitis, ecchymosis, muscle and joint pain, muscle weakness and twitching, osteoporosis, osteonecrosis, malaise. **Legal category**: POM. **Cost**: 1mg - pack of 90 - £323; 0.5mg - pack of 60 - £214.80. Not currently available in Ireland. **Product licence holder**: Dr. Falk Pharma GmbH. **Product licence number:** IE/NI: 1mg: EU/1/17/1254/004, 0.5mg: EU/1/17/1254/008. GB: 1mg: PLGB08637/0030; 0.5mg: PLGB08637/0032. **Date of preparation:** February 2023.

Further information is available on request.

Adverse events should be reported. In the UK visit www.mhra.gov.uk/yellowcard. In Ireland: https://www.hpra.ie/homepage/about-us/report-an-issue/human-adverse-reaction-form.Adverse events should also be reported to Dr Falk Pharma UK Ltd on pv@drfalkpharma.co.uk or 0044 (0)1628 536600.

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BSG: British Society of Gastroenterology
BSPGHAN: British Society of Paediatric Gastroenterology, Hepatology and Nutrition
EEsAI-PRO: EoE Activity Index - Patient Reported Outcome
EoE: eosinophilic oesophagitis
eos/hpf: eosinophils/high power field
EREFS: endoscopic reference score
FBO: food bolus obstruction
OGD: oesophago-gastro-duodenoscopy
PPI: proton pump inhibitor

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For more information about EoE and to access resources, please visit know-eoe.co.uk

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