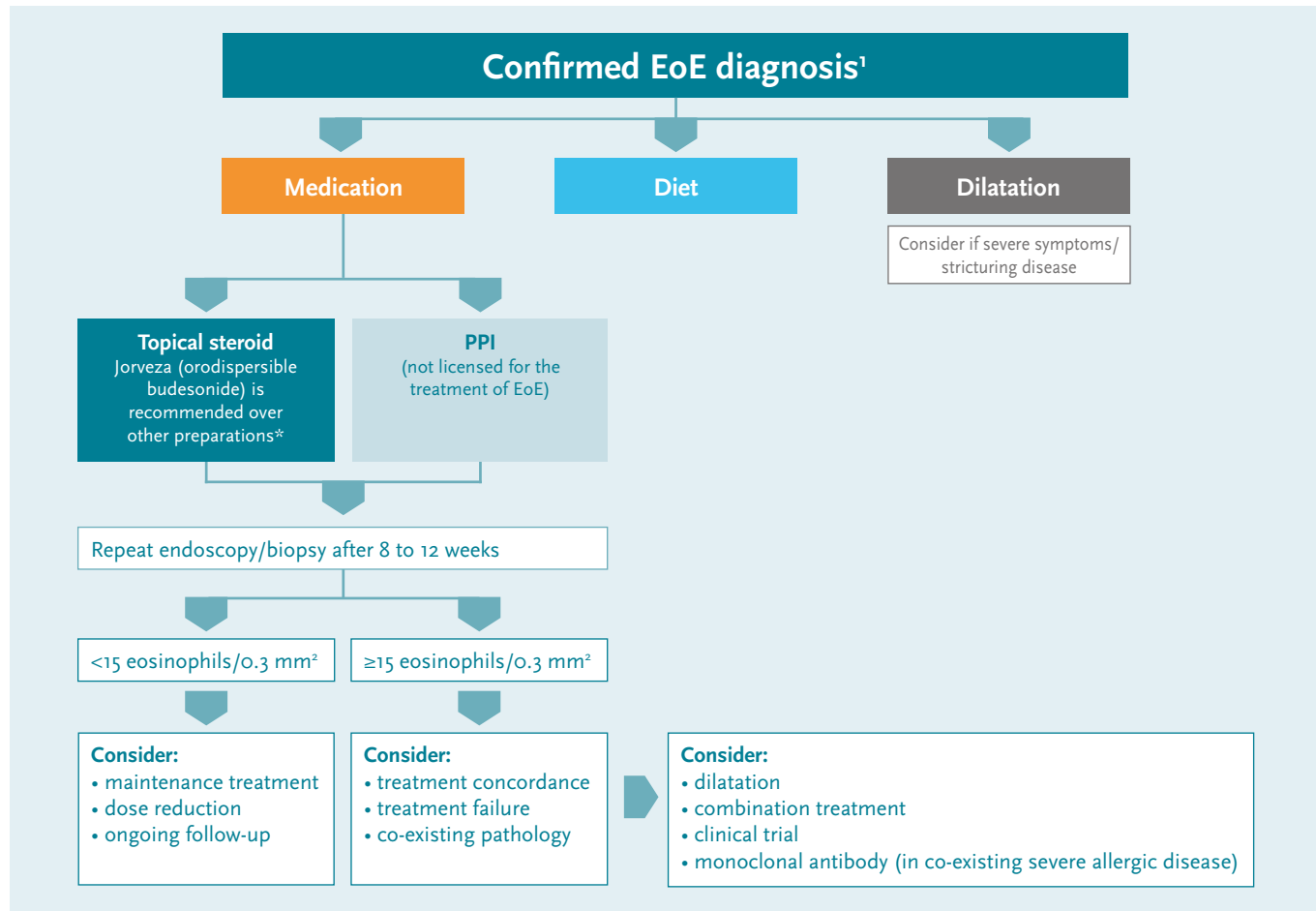


Eosinophilic oesophagitis treatment

Management: medication¹



*Data from a phase III induction study suggest prolongation of Jorveza therapy to 12 weeks is beneficial to bring more patients into clinico-histologic remission²

1. Dhar A *et al.* Gut 2022; 71(8): 1459-87.
2. Lucendo AJ *et al.* Gastroenterology 2019; 157: 74-86.

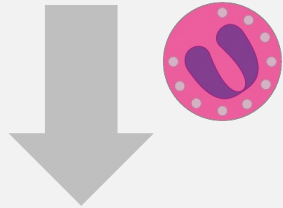
EoE: eosinophilic oesophagitis
PPI: proton pump inhibitor

Drug treatment of EoE: corticosteroids

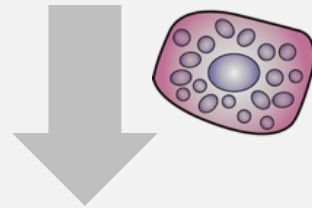
- As seen in a number of other allergic diseases, eosinophilia is relatively responsive to the administration of corticosteroids¹
- Topical corticosteroids, such as budesonide, have also been shown to reduce oesophageal remodelling²

Impact of budesonide in the oesophageal mucosa on factors associated with inflammation and lamina propria fibrosis³

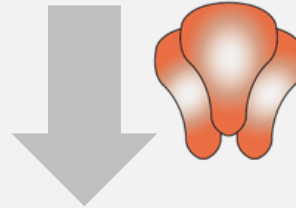
Eosinophils



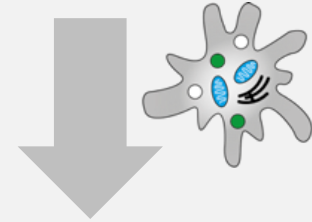
Mast cells



Tumour necrosis factor- α



Epithelial cell apoptosis

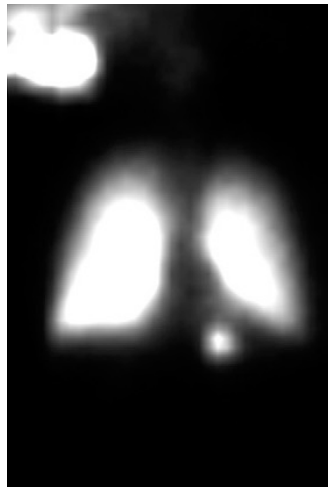


- While trials have used different agents, delivery systems, and dosages, at least a partial symptomatic response is seen in about 60-75% of adults; a similar proportion achieve a complete histologic response⁴
- Use of systemic steroids is not recommended because of adverse effects¹

1. Schroeder S *et al.* Expert Rev Clin Immunol 2010; 6(6): 929-37.
2. Straumann A, Katzka DA. Gastroenterology 2018; 154(2): 346-59.
3. Alexander JA, Katke DA. Gastroenterol Hepatol 2011; 7(1): 59-61.
4. Alexander JA. Gastroenterol Hepatol 2014; 10(5): 327-9.

Off-label corticosteroids are not optimised for oesophageal delivery¹

- Asthma steroid preparations have been swallowed rather than inhaled to coat the oesophagus, but are suboptimal for use in EoE¹
- Undesired lung deposition can result from medication administered into the mouth using metered-dose inhalers^{1,2}
- While there is greater oesophageal deposition with viscous solutions of topical steroids, non-standardised and variable drug concentrations are possible when patients mix aqueous forms into slurries^{1,2}



Nebulised
swallowed
budesonide²



Oral viscous
budesonide
solution or slurry²

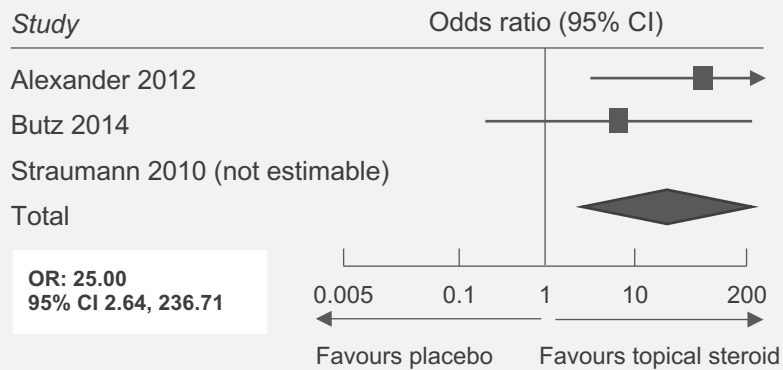
Reprinted from *Gastroenterology*, vol. 143, issue 2, Evan S. Dellon et al, Viscous Topical Is More Effective Than Nebulized Steroid Therapy for Patients With Eosinophilic Esophagitis, 321-324, © 2012 with permission from Elsevier.

1. Dellon ES *et al.* *Gastroenterology* 2017; 152(4): 776-86.
2. Dellon ES *et al.* *Gastroenterology* 2012; 143(2): 321-4.

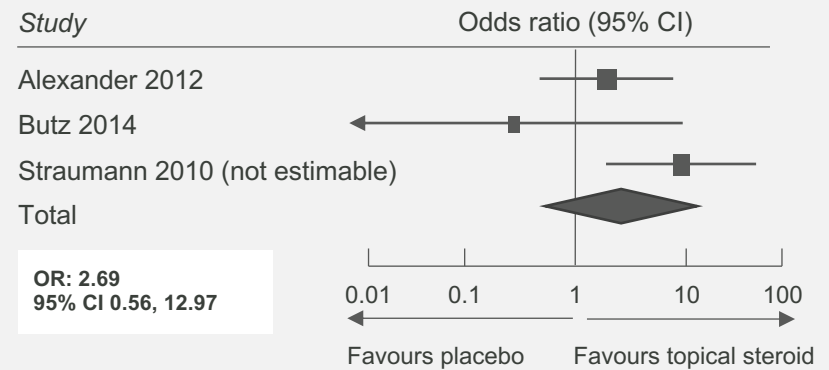
Off-label corticosteroids have not delivered consistent efficacy in EoE¹

Meta-analysis of placebo-controlled topical steroid RCTs in EoE: efficacy in adults¹

Histological remission



Clinical response



- Challenges in the use of unlicensed preparations include a lack of clear instructions regarding administration, appropriate dosing and treatment duration for EoE^{1,2}

1. Murali AR *et al.* J Gastroenterol Hepatol 2016; 31(6): 1111-9.

2. Shah NA *et al.* Clin Exp Gastroenterol 2016; 9: 281-90.

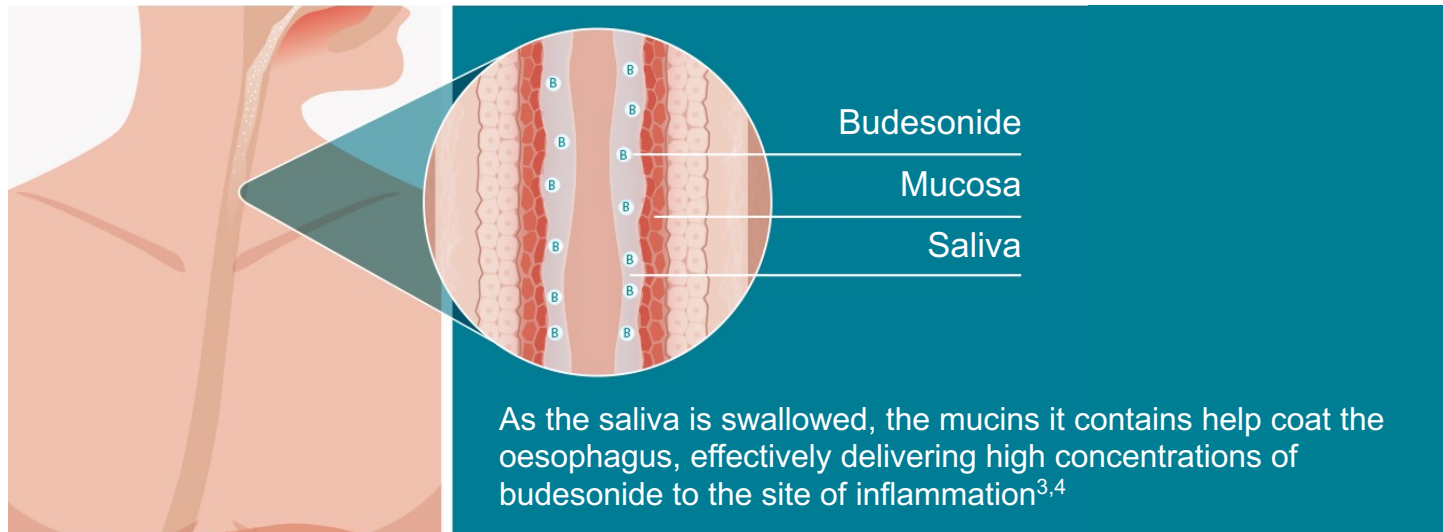
CI: confidence interval

EoE: eosinophilic oesophagitis

RCT: randomised control trial

Orodispersible budesonide (Jorveza) is the first licensed medical treatment for EoE¹

- Jorveza is an immediate release budesonide tablet specifically designed to treat EoE²
- The Jorveza tablet is placed on the tongue where it starts to effervesce, stimulating the production of saliva³

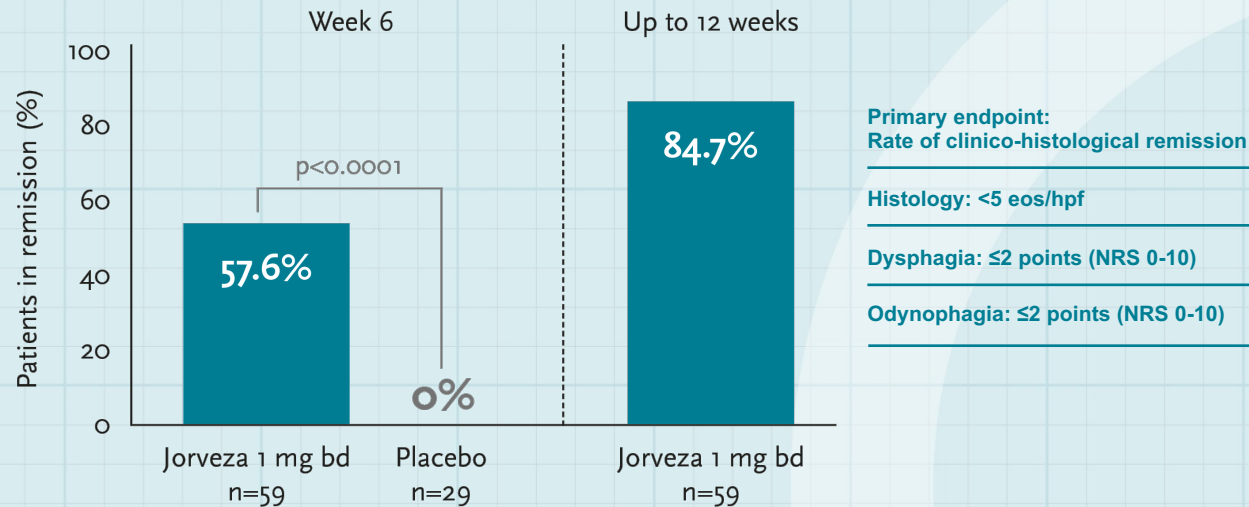


The BSG recommend Jorveza - the only medicine with European regulatory approval for EoE - over other steroid formulations for both the induction and maintenance of remission in adults⁵

1. Jorveza Summary of Product Characteristics.
2. Lucendo AJ *et al.* *Gastroenterology* 2019; 157(1): 74-86.
3. Data on file, Dr Falk.
4. Dodds MWJ *et al.* *J Dentistry* 2005; 33(3): 223-33.
5. Dhar A *et al.* *Gut* 2022; 71(8): 1459-87.

Jorveza 1 mg bd rapidly improves EoE symptoms and reduces disease activity¹

Clinical-histological remission with orodispersible Jorveza 1 mg bd induction therapy¹



Adapted from Lucendo¹



Prolongation of Jorveza therapy to 12 weeks is beneficial to bring more patients into clinico-histologic remission¹

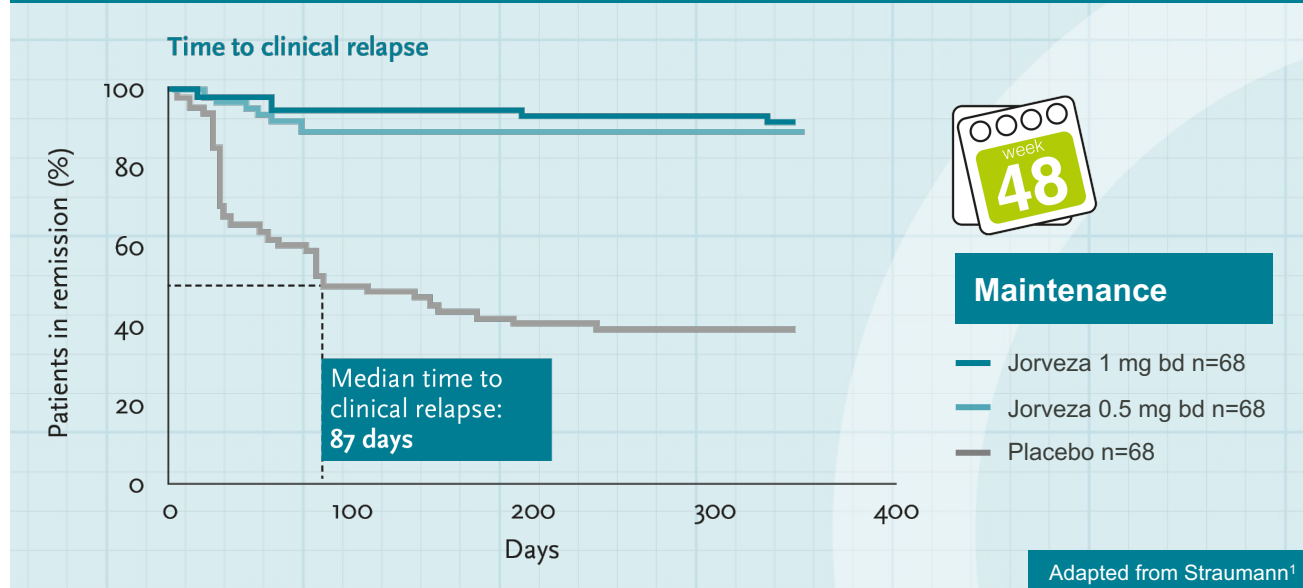
1. Lucendo AJ *et al.* Gastroenterology 2019; 157: 74-86.

EoE: eosinophilic oesophagitis
eos: eosinophils
hpf: high-power field
NRS: numerical rating scale

Jorveza is highly effective at maintaining remission in patients with EoE¹

Clinical remission

While half of placebo patients had relapsed within 3 months, over 90% of Jorveza patients were still in remission at week 48¹



Histological remission
90% of placebo patients had experienced a histological relapse versus only 12% of Jorveza patients at week 48¹

20
BSG GUIDELINES
22

“ This study reported greater efficacy than all previous studies on maintenance therapy using swallowed inhaled topical steroids² ”

1. Straumann A *et al.* *Gastroenterology* 2020; 159(5): 1672-85.
2. Dhar A *et al.* *Gut* 2022; 71(8): 1459-87.

Drug treatment of EoE: PPIs

Please note, while PPIs are a very commonly prescribed class of drugs in the UK, when it comes to EoE, they are not licensed for use^{1,2}

- The proposed mechanism(s) through which PPIs function to reduce eosinophilia in EoE have been the subject of much debate and include:³

PPI induced gastric acid-suppression leading to a restoration of oesophageal barrier function³

Since oesophageal exposure to acid causes more pain in patients with EoE than in healthy individuals, acid blockade may also reduce the symptoms of EoE⁴

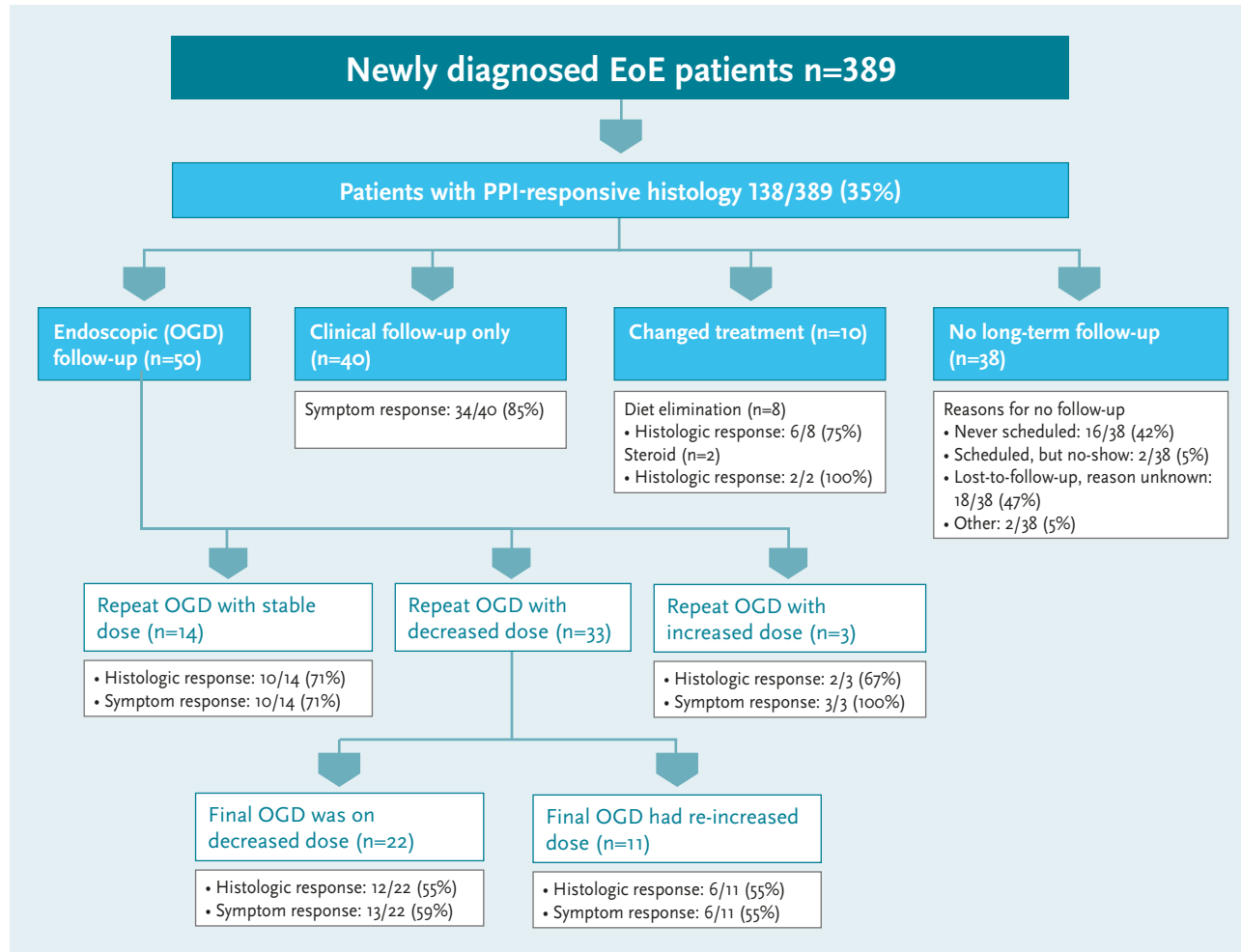
PPI mediated anti-inflammatory effects unrelated to gastric acid suppression³

For example, PPIs decrease IL-4-stimulated eotaxin-3 expression and so may have an anti-eosinophil effect⁵

1. Audi S *et al.* Br J Clin Pharmacol 2018; 84(11): 2562-71.
2. Dhar A *et al.* Gut 2022; 71(8): 1459-87.
3. Franciosi JP *et al.* J Asthma Allergy 2022; 15: 281-302.
4. Straumann A, Katzka DA. Gastroenterology 2018; 154(2): 346-59.
5. Zhang X *et al.* PLoS One 2012; 7(11): e50037.

EoE: eosinophilic oesophagitis
PPI: proton pump inhibitor

Efficacy of PPIs in the treatment of EoE¹



Retrospective cohort study of patients at a US university hospital¹

1. Thakkar KP *et al.* Dig Liver Dis 2022; 54(9): 1179-85.

OGD: oesophago-gastro-duodenoscopy
EoE: eosinophilic oesophagitis
PPI: proton pump inhibitor

Long-term safety of PPI treatment

- While the short-term use of PPIs is considered generally safe, their long-term safety profile is controversial^{1,2}
- Side effects associated with PPI use are also known to be dose dependent²
- The daily dose used for induction therapy – for example, omeprazole 20 mg bd - is generally double the standard PPI dose^{3,4}
- Use of quadruple doses has also been reported⁴

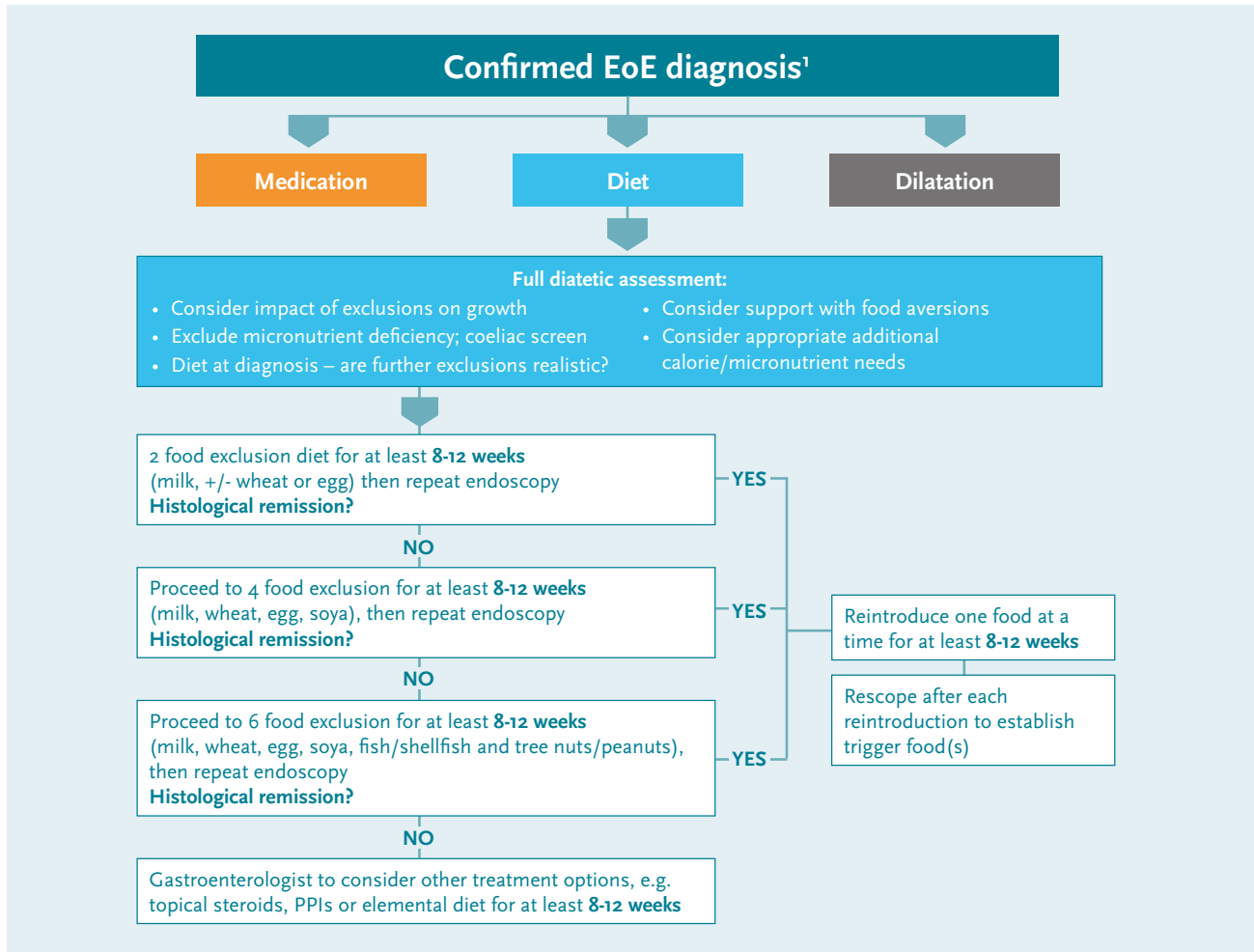


“ As PPI therapy in EoE may potentially be long-term and high dose, consideration of adverse events is important for prescribers and patients² ”

1. He Q *et al.* Am J Gastroenterol 2021; 116(11): 2286-91.
2. Franciosi JP *et al.* J Asthma Allergy 2022; 15: 281–302.
3. Dhar A *et al.* Gut 2022; 71(8): 1459-87.
4. Laserna-Mendieta EJ *et al.* Aliment Pharmacol Ther 2020; 52(5):798-807.

EoE: eosinophilic oesophagitis
PPI: proton pump inhibitor

Management: diet¹



*Data from a phase III induction study suggest prolongation of Jorveza therapy to 12 weeks is beneficial to bring more patients into clinico-histologic remission²

1. Dhar A *et al.* Gut 2022; 71(8): 1459-87.

EoE: eosinophilic oesophagitis
PPI: proton pump inhibitor

Dietary approaches for the treatment of EoE

- Given the link between EoE and food allergens, dietary avoidance is a logical treatment option¹
- The three approaches:¹⁻⁵

1. Elemental diet

- amino acid-based allergen-free formula, followed by slow reintroduction of foods
- the most effective but also the most strict diet
- the need to forgo all food has significant social limitations
- patients often have difficulties with adherence

2. Testing-directed elimination diet

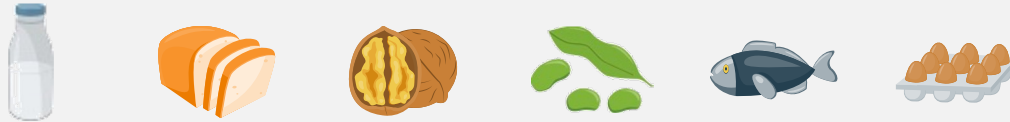
- elimination of food groups based on allergy testing
- avoiding only 1-2 foods based on tests is appealing to patients
- can be time-consuming, expensive, and limited by false-positive rates
- overall poor efficacy and the least favoured of the 3 dietary regimens

3. Empiric elimination diet (2-4-6 food elimination diet)

- avoidance of the food types that are most commonly associated with allergy
- milk and wheat are most frequently implicated; followed by eggs and soy, then nuts and seafood
- entails stepwise reintroduction of foods with multiple follow-up endoscopies
- probably the preferred diet despite the cumbersome process

1. Goyal A, Cheng E. *World J Gastrointest Pharmacol Ther* 2016; 7(1): 21-32.
2. Lipowska AM I *et al.* *EMJ Allergy Immunol* 2016; 1(1): 74-81.
3. Yaxley JP, Chakravarty B. *Aust Fam Physician* 2015; 44(10): 723-7.
4. Eluri S, Dellon ES. *Clin Gastroenterol Hepatol* 2017; 15(11): 1668-70.
5. Dhar A *et al.* *Gut* 2022; 71(8): 1459-87.

Dietary therapy for EoE

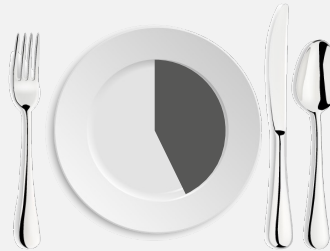


Multiple endoscopies (>7) are required to identify the causative foods¹

Patients need intensive dietetic support to prevent vitamin and nutrient deficiencies²

Significant modification of lifestyle is to the detriment of quality of life^{3,4}

The initial success rate of 2-4-6 diet was only 43%⁵



Few adults have the perseverance required⁶

Specialised diets causes psychosocial difficulties in children and adolescents⁷

1. Dhar A *et al.* Gut 2022; 71(8): 1459-87.
2. Goyal A, Cheng E. World J Gastrointest Pharmacol Ther 2016; 7(1): 21-32.
3. Lucendo AJ *et al.* Aliment Pharmacol Ther 2017; 46(4): 401-9.
4. Lucendo AJ *et al.* United European Gastroenterol J 2015; 6(1): 38-45.
5. Molina-Infante J *et al.* J Allergy Clin Immunol 2018; 141(4): 1365-72.
6. Gonsalves N *et al.* Gastroenterology 2012; 142: 1451-5.
7. Case C *et al.* J Pediatr Gastroenterol Nutr 2017; 65(3): 281-4.

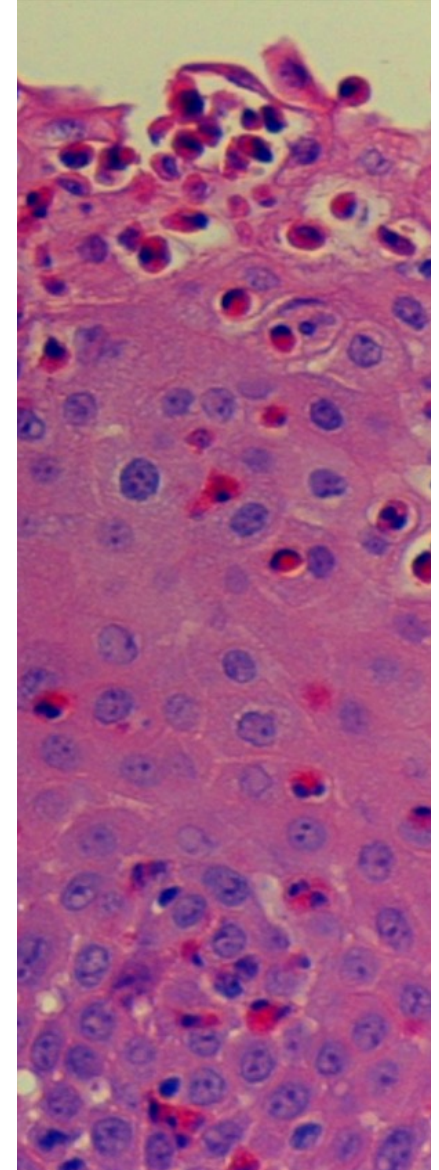
EoE treatment endpoints: histology or symptoms?

Histologic measures provide “hard” outcomes^{1,2}

- May not correlate with symptoms from one patient to another
- Obtaining biopsies requires repeat endoscopic procedures with associated risks and costs

Symptom control is of great importance for patients¹

- Can be assessed without an invasive procedure
- May result in an underestimate of the efficacy of an intervention because patients with longstanding dysphagia may have established patterns of dietary modification to limit their swallowing difficulties



1. Dougherty T Jr *et al.* *Gastroenterol Hepatol* 2014; 10(2): 106-16.
2. Nguyen N *et al.* *Gastroenterol Hepatol* 2015; 11(10): 670-4.

Prescribing information

Please click on the following link for the prescribing information:

<https://www.dr Falk.co.uk/jorveza-1mg-oro-dipsersible-tablet/>

Jorveza[®] (budesonide) is indicated for the treatment of eosinophilic oesophagitis (EoE) in adults (older than 18 years of age)

Adverse events should be reported. Reporting forms and information can be found at www.yellowcard.mhra.gov.uk (UK residents) or www.hpra.ie (Irish residents). Adverse events should also be reported to Dr Falk Pharma UK Ltd at pv@drfalkpharma.co.uk.

www.dr Falk.co.uk

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