Formulary application template for budesonide orodispersible tablet (ODT) maintenance treatment

Intervention under application

Budesonide orodispersible tablet (ODT), marketed under the trade name Jorveza,[1] is currently on formulary for induction of remission in patients with eosinophilic oesophagitis (EoE) in line with the recommendation in National Institute for Health and Care Excellence (NICE) technology appraisal 708.[2] As the scope for NICE TA708 was set out in 2018,[3] it did not consider maintenance use of budesonide ODT, which was approved by the Medicines and Healthcare products Regulatory Agency (MHRA) in March 2021.[1]

Until NICE undertakes an appraisal of the use of budesonide ODT for maintenance and offers its opinion, budesonide should be provided as the only licensed product for the maintenance of remission of EoE.[1] This application is therefore for an extension to the formulary for use of budesonide ODT in **maintenance of remission** and for **follow-on prescribing in primary care** to ensure patients have continued access to this licensed product as determined by their responsible specialist.

EoE

EoE is a chronic allergy-/immune-mediated inflammatory condition of the oesophagus,[4-8] in which the body overproduces eosinophils, leading to inflammation in the oesophagus.[2] It is characterised clinically by symptoms related to oesophageal dysfunction and histologically by eosinophil-predominant inflammation.[4,6,9] Initially, a swollen oedematous mucosa causes dysphagia and repeat episodes of food bolus obstruction and patients adapt by modifying their eating habits.[4,6,10] However, fibrosis gradually develops, making the oesophagus non-compliant and narrow, which is associated with severe symptoms, including isolated strictures.[4] EoE rarely resolves spontaneously and follows a relapsing–remitting course requiring lifelong treatment.[6] Undiagnosed and ineffectively treated, patients with EoE experience a cycle of persistent episodes of food bolus obstruction, often leading to repeat attendances at accident and emergency (A&E) departments and deterioration in patients' quality of life.[4,6,11–13]

Budesonide ODT

Budesonide ODT is licensed for the treatment of EoE in adults (older than 18 years of age).[1]

Budesonide ODT 1 mg tablets were first licensed for **induction of remission in EoE** on 8 January 2018.[1] In March 2021, the indication was extended to include **maintenance of remission** in adults using 1 mg tablets and a further 0.5 mg tablet.[14]

Budesonide ODT is the only drug licensed for treatment of EoE.[1] It improves the symptoms, reduces the excess of eosinophils and is also effective in preventing recurrent episodes.[14] In clinical trials:[15–18]

- 57.6% of patients had achieved clinical-histological remission and more than 93% had achieved histological remission by 6 weeks
- 85% of patients had achieved clinical-histological remission by 12 weeks
- symptom control was maintained by 80% of patients for at least 2 years.

Side effects, which mainly affect the mouth and throat, are manageable.[14] Budesonide ODT was authorised on the basis that its benefits are greater than its risks.[14]

Budesonide ODT is taken orally and disintegrates in the mouth.[1]

The tablet is placed on the tip of the tongue and gently pressed against the top of the mouth, where it will disintegrate over 2–20 minutes.[1] Effervescence starts after budesonide ODT comes into contact with saliva and stimulates production of further saliva.[1] Budesonide-loaded saliva is swallowed little by little while the ODT disintegrates.[1]

Treatment with budesonide ODT is initiated by a gastroenterologist or a physician experienced in the diagnosis and treatment of EoE.[1]

For **induction of remission**, the recommended daily dose is 2 mg budesonide ODT as one 1 mg tablet in the morning and one 1 mg tablet in the evening.[1] Real-world experience in clinical practice has shown that the optimal duration of induction treatment to obtain remission is 12 weeks.

Up to one third of patients who stop treatment experience relapse, with median time to clinical relapse of 87 days.[18]

For **maintenance of remission**, the recommended daily dose is 1 mg budesonide ODT as one 0.5 mg tablet in the morning and one 0.5 mg tablet in the evening or 2 mg budesonide ODT as one 1 mg tablet in the morning and one 1 mg tablet in the evening, depending on the individual clinical requirement of the patient.[1] A maintenance dose of 1 mg budesonide ODT twice daily is recommended for patients with long-standing disease history and/or high extent of oesophageal inflammation in their acute disease state.[1] The duration of maintenance therapy is determined by the treating physician.[1]

No special monitoring is required.

Costs

The cost for a 3-month induction course of budesonide ODT is £322.20. The cost for a 12-month course of budesonide ODT for maintenance is £1,288.80.

NICE appraisal

On 23 June 2021, NICE published technology appraisal guidance 708 (TA708), which recommends budesonide ODT as an option for inducing remission of EoE in adults.[2]

The guidance noted that the recommendation was not intended to affect treatment with budesonide ODT that was started in the NHS before the guidance was published.[2] People having treatment outside this recommendation could continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician considered it appropriate to stop.[2]

The development process for NICE technology appraisal began in 2018[3] following the initial licencing of budesonide ODT for induction of remission in EoE.[1] Although TA708 was published after the extension to include maintenance of remission was granted in March 2021, it does not include a recommendation for maintenance of remission as that was not part of the original scope.

Until NICE undertakes an appraisal of the use of budesonide ODT for maintenance and offers its opinion, budesonide ODT should be provided as the only licensed product for the maintenance of remission of EoE.[1]

The unmet need

Budesonide ODT is the only licensed treatment for EoE.[1]

Prior to approval of budesonide ODT, patients had few treatment options. They were often prescribed off-licence proton pump inhibitors (PPIs) or fluticasone propionate inhalers (to be swallowed rather than inhaled) or exclusion diets. Of the PPIs, only omeprazole has been trialled in patients with EoE.[19] Most patients have no or partial symptom response[11] and it is ineffective in maintaining remission in the patients who do achieve it.[20] Patients often found swallowing the inhaled dose of fluticasone propionate difficult, and primary care prescribers either did not understand the need for swallowing the dose and prescribed as per its inhaled indication or switched patients back to PPIs. Dietary changes, which must be lifelong, are variably effective and places severe restrictions on patient's lives, leading to poor compliance.

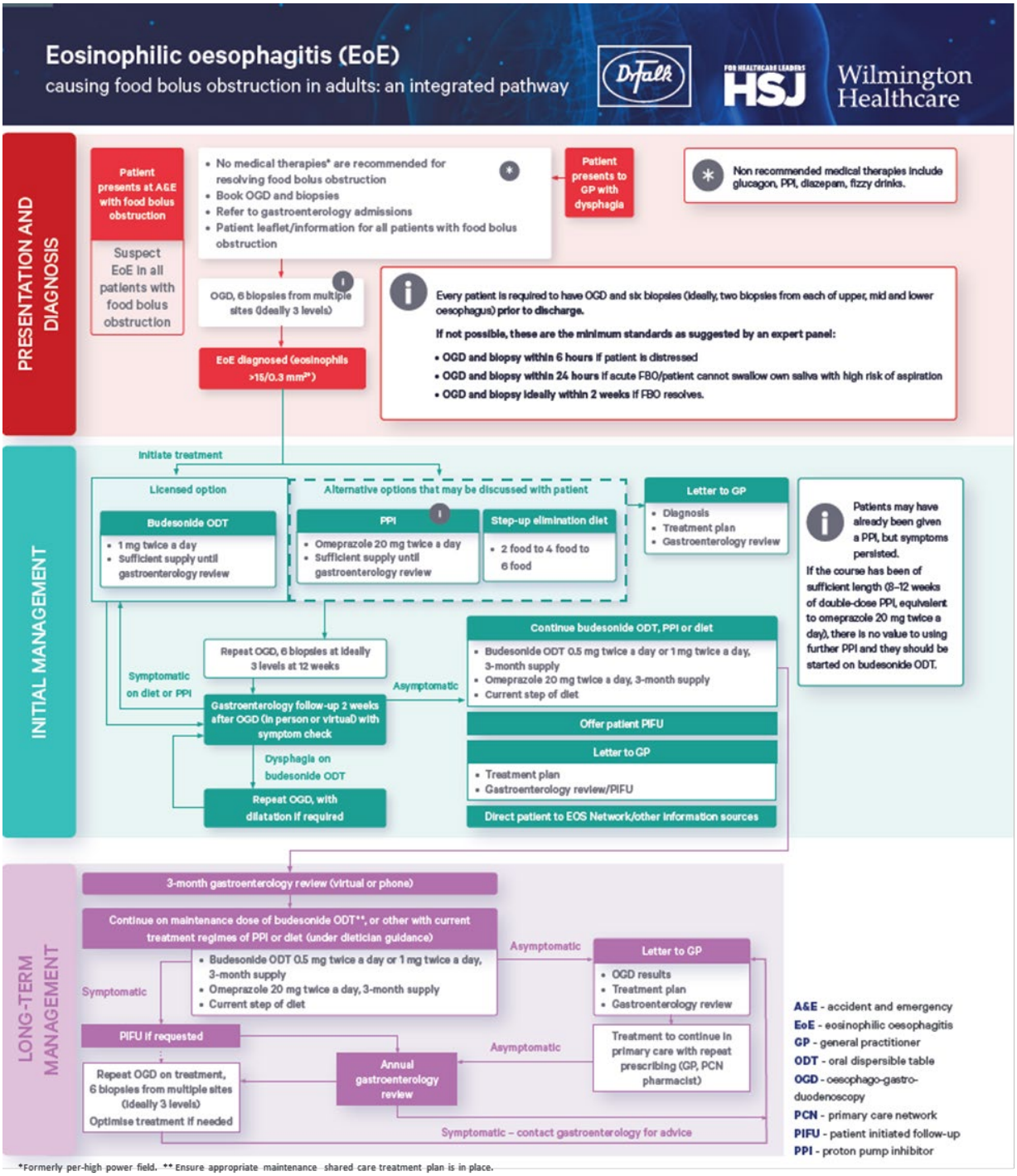
Gastroenterologists are increasingly prescribing budesonide ODT for induction of remission in patients with EoE as the only licensed treatment and in accordance with NICE TA708.[1,2] After the initial induction course, patients are often prescribed budesonide ODT as maintenance due to the high likelihood of relapse once this treatment is stopped. If budesonide ODT is not included in the local formulary for maintenance, primary care physicians are often reluctant to take on follow-on. Patients therefore have to obtain repeat prescriptions through the hospital, requiring them to remember to contact the consultant's secretary to arrange a repeat prescription before their supply runs out and then collect the medicine from their hospital pharmacy – unless it can be delivered to their home or community pharmacy.

By adding budesonide ODT to the local formulary for maintenance, patients will have increased and easier access to the only licensed treatment for their condition. This will result in fewer interactions with their gastroenterology team and likely reduce the number of relapses and repeat admissions to A&E with food bolus obstructions.

A proposed shared care pathway to support follow-on prescribing of budesonide ODT in primary care accompanies this application.

Figure 1 shows an integrated care pathway for the diagnosis and management of EoE.

Figure 1. Integrated care pathway for the diagnosis and management of EoE



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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 low-dose 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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