Shared care template for the use of budesonide orodispersible tablets (Jorveza®) for maintaining remission of eosinophilic oesophagitis

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1. Background	Budesonide orodispersible tablet (ODT), marketed under the trade name Jorveza®, is licensed for induction and maintenance of remission in patients with eosinophilic oesophagitis (EoE).[1] This shared care document covers use of budesonide ODT for maintaining remission in EoE in adults only. For the use of budesonide ODT for inducing remission in EoE in adults, please refer to National Institute for Health and Care Excellence (NICE) technology appraisal 708 on EoE. As a technology appraisal is in place, this drug must be offered as an option to patients. **An integrated care pathway for the diagnosis and management of EoE is included at the end of this document.**
2. EoE background	EoE is a chronic allergy-/immune-mediated inflammatory condition of the oesophagus,[2-6] in which the body overproduces eosinophils, leading to inflammation in the oesophagus,.[7] EoE is characterised clinically by symptoms related to oesophageal dysfunction and histologically by eosinophil-predominant inflammation.[2,4,8] Initially, a swollen oedematous mucosa causes dysphagia and repeat episodes of food bolus obstruction, and patients adapt by modifying their eating habits.[2,4,9] However, fibrosis gradually develops, making the oesophagus non-compliant and narrow, which is associated with severe symptoms, including isolated strictures.[2] EoE rarely resolves spontaneously and follows a relapsing–remitting course requiring lifelong treatment.[4] 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.[2,4,10–12]
3. Budesonide ODT background	Budesonide ODT is the only drug licensed for induction and maintenance treatment of EoE in adults (older than 18 years of age).[1] Budesonide is a non-halogenated glucocorticosteroid that primarily acts through an anti-inflammatory action via binding to the glucocorticoid receptor.[13] Budesonide ODT was developed so that budesonide disperses in the mouth.[13]

	The tablet is placed on the tip of the tongue and gently pressed against the top of the mouth, where it disintegrates 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] Consequently, budesonide ODT has high topical anti-inflammatory activity and low systemic effects.[13] Budesonide ODT improves the symptoms of EoE, reduces the excess of eosinophils and is also effective in preventing recurrent episodes.[14] In clinical trials:[14–17] • 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 3 years. Side effects, which mainly affect the mouth and throat, are manageable.[13] No special monitoring is required.[1] Up to one third of patients who stopped treatment in a clinical trial with budesonide ODT experienced relapse within a median of 87 days.[17] Maintenance treatment is therefore important to keep patients in remission. The development process for NICE technology appraisal began in 2018 following the initial licencing of budesonide ODT for induction of remission in EoE.[7] 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]
3.1 Areas of responsibility for shared care	Patients should be at the centre of any shared care arrangements. Individual patient information and a record of their preferences should accompany shared care prescribing guidelines, where appropriate. Transfer of clinical responsibility to primary care should only be considered when the patient's clinical condition is stable or predictable. When transfer to primary care is appropriate, complete the shared care documentation and send to the patient's general practice, detailing the diagnosis, current and ongoing dose, any relevant test results, when the next monitoring is required, and contact information.

	The secondary/tertiary provider must supply an adequate amount of the medication to cover the transition period. The patient should then be instructed to obtain further prescriptions from the general practitioner (GP). When clinical responsibility for prescribing is transferred to general practice, it is important that the GP, or other primary care prescriber, is confident to prescribe the necessary medicines. Shared care agreements play a key role in enabling primary care prescribers to prescribe medicines with which they may not initially be familiar. Clinical responsibility for prescribing is held by the person signing the prescription, who must also ensure adequate monitoring.
3.2 ***Maintenance of remission: specialist roles and responsibilities***	**Specialist roles and responsibilities** 1. To assess the patient and establish the diagnosis, determine a management strategy and ensure appropriate follow-up in conjunction with the GP. **2. To ensure the patient has given informed consent to their treatment.** 3. Where appropriate: • To initiate and stabilise the patient on treatment, providing sufficient to cover the induction treatment • To assess response after 6 and then 12 weeks (where applicable) of treatment • To write to the GP requesting shared care once the need for maintenance therapy has been identified. **4. To start maintenance treatment* with a 3-month supply of budesonide ODT (1 mg given twice daily or 0.5 mg given twice daily):** • To monitor the patient and their therapy at 3 months (initially) and then 12-monthly intervals. **5. To determine duration of maintenance therapy:** • Patients receiving oral corticosteroids for more than 3 weeks should be provided with a blue steroid card. • For budesonide ODT doses greater than 1.5 mg for more than 4 weeks, supply an emergency steroid card. • Consider potential long-term side effects of steroids, including diabetes and osteoporosis. 6. To explain the possible side effects of the medication to the patient. 7. To ensure that patients (or carers): • understand how to use the medication that is prescribed and the dosage regimen • know what to do and who to contact if they experience symptoms of acute pancreatitis (persistent, severe abdominal pain; back pain may also be present)

	• are aware of the importance of monitoring for any deterioration in symptoms to prompt reassessment and exclusion of oropharyngeal and oesophageal *Candida* infections (see the budesonide ODT summary of product characteristics [SPC]) • **Ensure a contact pathway is established (follow up via patient-initiated follow-up) if requested by the patient.** 8. To provide the GP with appropriate prescribing information and any additional information requested and to offer telephone support. 9. To concur with the GP's arrangements for any ongoing monitoring of the patient's condition in primary care to ensure the safe use of budesonide ODT. 10. To be available for advice if the patient's condition changes and to ensure that procedures are in place for rapid rereferral of the patient by the GP. 11. To liaise with the GP on any suggested changes in prescribed therapy. 12. To report any adverse events via https://yellowcard.mhra.gov.uk/. *The recommended daily dose is 1 mg budesonide as one 0.5 mg tablet in the morning and one 0.5 mg tablet in the evening or 2 mg budesonide 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 twice daily is recommended for patients with long-standing disease history and/or high extent of oesophageal inflammation in their acute disease state.[1]
4 Continuing treatment: general practitioner responsibilities	To ensure minimal disruption to the patient's treatment and minimal burden on the patient to seek and collect repeat prescriptions from secondary care, primary care will be asked to take on follow-on prescribing of budesonide ODT initiated by the responsible specialist. **General practitioner responsibilities** 1. Initially, to refer the patient for specialist advice. 2. Where appropriate, to continue to prescribe budesonide ODT at the agreed dose once stabilised by the specialist, as part of a shared care arrangement. 3. **To consider providing repeat prescriptions for budesonide ODT at 3-monthly intervals** 4. To carry out any agreed monitoring, with results to be reported to the specialist if appropriate. 5. **To manage general health issues of the patient.** 6. To monitor patient concordance with therapy, side effects and symptoms at their medication review dates or sooner if required. 7. To liaise with the consultant regarding any complications or adverse effects of treatment of EoE. 8. To consider any side effects reported by the patient and to discuss with the consultant if necessary.

	9. **To consider any drug interactions, cautions, contraindications, and special warnings and precautions when prescribing other medicines** • Budesonide | Drugs | British National Formulary (BNF) | NICE • Budesonide | Interactions | BNF | NICE 10. To ensure that therapy is discontinued where applicable, in liaison with the specialist. 11. To report any adverse events, via https://yellowcard.mhra.gov.uk/.
5 Patient's role	**Patient's responsibilities** **1. Report to the specialist or to primary care if they do not have a clear understanding of the treatment.** **2. Attend primary and secondary care appointments.** **3. Use written and other information on the medication prescribed.** **4. Seek help from a healthcare professional if suspected side effects develop or they are otherwise unwell.**
6 Supporting information	**Dose, route of administration and duration of treatment[1]** ***Maintenance of remission*** The recommended daily dose is 1 mg budesonide as one 0.5 mg tablet in the morning and one 0.5 mg tablet in the evening or 2 mg budesonide 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. A maintenance dose of 1 mg budesonide twice daily is recommended for patients with a long-standing disease history and/or high extent of oesophageal inflammation in their acute disease state. The duration of maintenance therapy is determined by the treating physician. ***Method of administration*** The ODT should be taken immediately once removed from the blister package. The ODT should be taken after a meal. It should be placed on the tip of the tongue and gently pressed against the top of the mouth, where it will dissolve. This will usually take at least two minutes but can take up to 20 minutes. The effervescence process of the tablet starts after budesonide ODT (Jorveza®) comes into contact with saliva and stimulates the production of further saliva. The dissolved material should be swallowed with saliva little by little while the ODT disintegrates. The ODT should not be taken with liquid or food. There should be at least 30 minutes before eating or drinking or performing oral hygiene. Any oral solutions, sprays or chewable tablets should be used at least 30 minutes before or after administration of budesonide ODT (Jorveza®).

	The ODT should not be chewed or swallowed undissolved. These measures ensure optimal exposure of the oesophageal mucosa to the active substance. **Adverse effects (incidence, identification, importance and management)[1]** ***Very common (≥ 1/10)*** • Oesophageal candidiasis ***Common (≥ 1/100 to < 1/10)*** • Oral and/or oropharyngeal candidiasis • Headache • Gastroesophageal reflux disease • Nausea • Oral paraesthesia • Dyspepsia • Fatigue • Blood cortisol decreased **Cautions[1]** ***Renal impairment*** • There are currently no data available for patients with renal impairment. Because budesonide is not excreted via the kidneys, patients with mild-to-moderate impairment may be treated with caution with the same doses as patients without renal impairment. Budesonide is not recommended for use in patients with severe renal impairment. ***Hepatic impairment*** • During treatment of patients with hepatic impairment with other budesonide-containing medicinal products, budesonide levels were increased. However, no systematic study investigating different levels of hepatic impairment is available. Patients with hepatic impairment should not be treated (see SPC). ***Paediatric population*** • The safety and efficacy of budesonide ODT (Jorveza®) in children and adolescents under the age of 18 years have not been established. No data are available. **Contraindications[1]** • Hypersensitivity to the active substance or to any of the excipients (see SPC)

	Special warnings and precautions for use[1] ***Infections*** • Suppression of the inflammatory response and immune function increases the susceptibility to infections and their severity. Symptoms of infections can be atypical or masked. In clinical studies conducted with budesonide ODT (Jorveza®) oral, oropharyngeal and oesophageal *Candida* infections have been observed with a high frequency. If indicated, symptomatic candidiasis of the mouth and throat can be treated with topical or systemic anti-fungal therapy whilst still continuing treatment with budesonide ODT (Jorveza®). Chickenpox, herpes zoster and measles can have a more serious course in patients treated with glucocorticosteroids. In patients who have not had these diseases, the vaccination status should be checked, and particular care should be taken to avoid exposure. ***Vaccines*** • The co-administration of live vaccines and glucocorticosteroids should be avoided as this is likely to reduce the immune response to vaccines. The antibody response to other vaccines may be diminished. ***Special populations*** • Patients with tuberculosis, hypertension, diabetes mellitus, osteoporosis, peptic ulcer, glaucoma, cataract, family history of diabetes or family history of glaucoma may be at higher risk of experiencing systemic glucocorticosteroid adverse reactions (see SPC) and should therefore be monitored for the occurrence of such effects. • Reduced liver function may affect the elimination of budesonide, causing higher systemic exposure. The risk of adverse reactions (systemic glucocorticosteroid effects) will be increased. However, no systematic data are available. Patients with hepatic impairment should therefore not be treated. • Systemic effects of glucocorticosteroids (e.g., Cushing's syndrome, adrenal suppression, growth retardation, cataract, glaucoma, decreased bone mineral density and a wide range of psychiatric effects) may occur (see SPC). These adverse reactions depend on the duration of treatment, concomitant and previous glucocorticosteroid treatment and the individual sensitivity. • Oral bisphosphonates can cause local irritation of the upper gastro-intestinal mucosa. Because there is a potential for worsening of the underlying disease, caution should be used when an oral bisphosphonate is given to patients with active

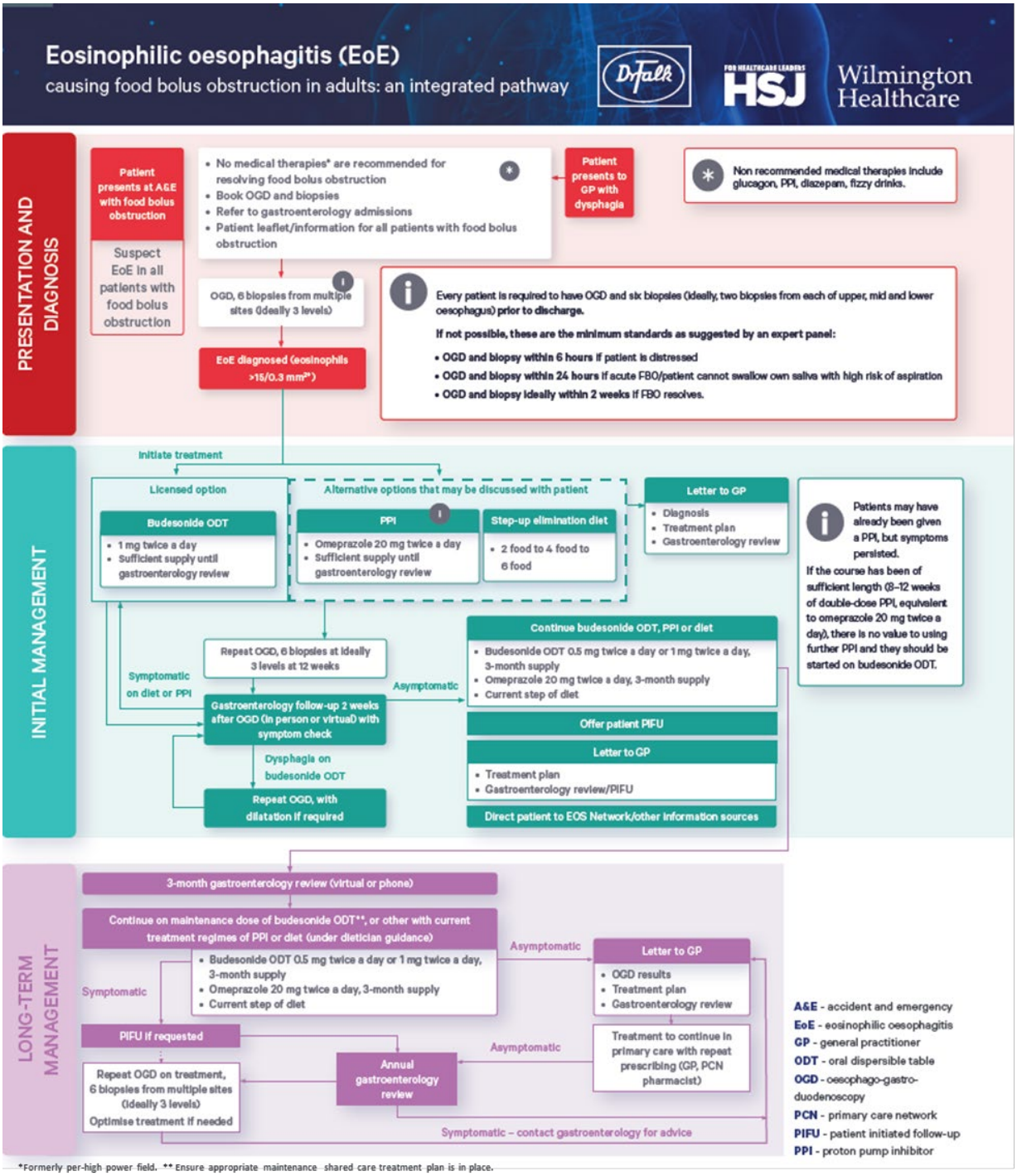
	upper gastro-intestinal problems, including EoE. Seek specialist advice on the benefits and potential risks for an individual patient. • Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR), which have been reported after use of systemic and topical corticosteroids. • 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. • Interference with serological testing: Because adrenal function may be suppressed by treatment with budesonide, an adrenocorticotropic hormone (ACTH) stimulation test for diagnosing pituitary insufficiency might show false results (low values). • Sodium content: Jorveza® 0.5 mg and 1 mg ODT contain 52 mg of sodium per daily dose, equivalent to 2.6% of the World Health Organization (WHO)-recommended maximum daily intake of 2 g sodium for an adult. **Interaction with other medicinal products and other forms of interaction** ***CYP3A4 inhibitors*** • Co-treatment with potent CYP3A inhibitors such as etoconazole, ritonavir, itraconazole, clarithromycin, cobicistat and grapefruit juice may cause a marked increase of the plasma concentration of budesonide and is expected to increase the risk of systemic adverse reactions. Therefore, concomitant use should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid adverse reactions, in which case patients should be monitored for systemic corticosteroid adverse reactions. • Ketoconazole 200 mg once daily orally increased the plasma concentration of budesonide (3 mg single dose) approximately 6-fold during concomitant administration. When ketoconazole was administered approximately 12 hours after budesonide,

	the plasma concentration of budesonide increased approximately 3-fold. ***Oestrogens, oral contraceptives*** • Elevated plasma concentrations and enhanced effects of glucocorticosteroids have been reported in women also receiving oestrogens or oral contraceptives. No such effect has been observed with budesonide and concomitant intake of low-dose combination oral contraceptives. ***Cardiac glycosides*** • The action of glycoside can be potentiated by potassium deficiency which is a potential and known adverse reaction of glucocorticoids. ***Saluretics*** • Concomitant use of glucocorticoids may result in enhanced potassium excretion and aggravated hypokalaemia. **Fertility, pregnancy and lactation** ***Pregnancy*** • Administration during pregnancy should be avoided unless there are compelling reasons for therapy with budesonide ODT (Jorveza®). There are few data of pregnancy outcomes after oral administration of budesonide in humans. Although data on the use of inhaled budesonide in a large number of exposed pregnancies indicate no adverse effect, the maximal concentration of budesonide in plasma has to be expected to be higher in the treatment with budesonide ODT (Jorveza®) compared to inhaled budesonide. In pregnant animals, budesonide, like other glucocorticosteroids, has been shown to cause abnormalities of foetal development (see SPC). The relevance of this to man has not been established. ***Breast-feeding*** • Budesonide is excreted in human milk (data on excretion after inhalative use is available). However, only minor effects on the breast-fed child are anticipated after oral use of budesonide ODT (Jorveza®) within the therapeutic range. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from budesonide therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

	Fertility • There are no data on the effect of budesonide on human fertility. Fertility was unaffected following budesonide treatment in animal studies (see SPC). **Clinically important drug interactions and their management** This is a steroid drug, take this into consideration with concomitant use of other steroids, due to the additive effect, and consider the need for a blue steroid card and an emergency steroid card. *This document is not exhaustive. The manufacturer's SPC and the most current edition of the BNF should be consulted for full information on contra-indications, warnings, side effects and drug interactions.* **Drug costs** ***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 September 2023 BNF and Drug Tariff online. **Useful documents** • NICE TA708: Budesonide ODT for inducing remission of eosinophilic oesophagitis (accessed February 2024). • Summary of product characteristics: Jorveza 1 mg orodispersible tablets (accessed February 2024). • Refer to page 10 of NHS England's guidance on *Responsibility for prescribing between Primary & Secondary/Tertiary Care* for more information/guidance about taking on prescribing of specialist medicines (accessed February 2024).

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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