Surrey Heartlands Integrated Care System Area Prescribing Committee (APC)

Evidence review for Area Prescribing Committee (APC)

Medicine details	
Name, brand name	Budesonide orodispersible tablet (Jorveza®)
Manufacturer	Dr. Falk Pharma UK Ltd
Proposed indication	Maintaining remission of eosinophilic oesophagitis
Requested by	Guan Lim Budesonide orodispersible tablet are approved for induction of remission for eosinophilic oesophagitis in Surrey in line with NICE TA 708. This application is for use to maintain remission in patients with a long standing disease and/or high extent of oesophageal inflammation in their acute disease state in line with product licence.

SUMMARY

Clinical Effectiveness

Induction of remission
NICE TA 708 and approved by Surrey Heartlands APC in September 2021

Maintenance of remission
The licence for use of budesonide orodispersible tablets to maintain remission was based on a randomised, placebo-controlled, double-blind phase III clinical study (1) which included 204 adult patients with EoE in clinico-pathological remission. Over a period of 48 weeks the rate of patients maintaining remission in three groups was observed, group 1 were given 1 mg twice daily, group 2 0.5 mg Twice daily and group 3 placebo. Maintaining remission was defined as **not** having any of the following: clinical relapse (dysphagia or pain during swallowing), histological relapse, food impaction requiring endoscopic intervention, need of an endoscopic dilation, or premature withdrawal for any reason.
Significantly more patients in the group 1 (73.5%) and group 2 (75.0%) group maintained remission at week 48 compared to placebo (4.4%).

Both dosages were superior to placebo and equally effective in maintaining remission of EoE.

1. Straumann et al; International EOS-2 Study Group.
Budesonide Orodispersible Tablets Maintain Remission in a Randomized, Placebo-Controlled Trial of Patients with Eosinophilic Esophagitis.
Gastroenterology. 2020 Nov;159(5):1672-1685.e5. doi: 10.1053/j.gastro.2020.07.039. Epub 2020 Jul 25. PMID: 32721437.

Safety

Overall, both doses of budesonide orodispersible tablets were well tolerated and no serious drug-related adverse events (AEs) were reported. No significant differences were observed among the study groups in commonly reported adverse events, most of them being unrelated to the investigational product.
The most reported drug-related AEs were mild to moderate symptoms of local candidiasis, which were easily treated with antimycotics, with no impact on daily life activities or need to stop study medication.

Patient factors

Alternatives to this therapy include off-label proton pump inhibitors (PPI) (such as omeprazole or lansoprazole) and corticosteroids (off-label fluticasone and unlicensed budesonide). People also try elimination diets such as the 6-food elimination diet (SFED), which involves eliminating the known allergens milk, eggs, nuts, wheat, soy and seafood.

Dosing and delivery of off-label corticosteroids is difficult and imprecise because it involves swallowing formulations originally designed for inhalation, which is counterintuitive and poorly understood by patients and clinicians.
Dietary interventions are hugely challenging, and professional support is often difficult to access. Specialist diets can be expensive, so they are not affordable for many people.
There is an unmet need for a licensed, effective maintenance treatment for eosinophilic oesophagitis.

Cost implications

Cost of product:
The list price is £323 per pack of 90 one-mg tablets (excluding VAT; BNF online, accessed April 2021). Costs may vary in different settings because of negotiated procurement discounts.

Annual cost per patient:
£2,620

Prescribed for 14 people in Epsom and St Helier Trust (serves a population of approximately 500,000) where it went on the formulary ahead of NICE.
Estimate 3 people with this condition might be treated with maintenance therapy per 100,000 £7,860 per 100,000 population

Relevant guidance / reviews

NICE do not currently recommend for maintenance therapy as it did not have the licence at the time of the NICE review for induction therapy. NICE do recommend budesonide orodispersible tablets for induction therapy - TA 708
The Canadian Journal of Health Technologies (CADTH) have published a review of Budesonide (Jorvesa®) for the induction AND maintenance of clinic-pathological remission in adults with eosinophilic oesophagitis (August 2021).
The Canadian review provides guidance on restricted use of budesonide orodispersible tablets for maintenance therapy for EoE which the APC may wish to adopt.

Likely place in therapy relative to current treatments

Adult patients with confirmed clinical and histological (endoscopy confirmed) diagnosis of eosinophilic oesophagitis.

- With long standing disease and/or high extent of oesophageal inflammation in their acute disease state
- With symptoms refractory to an adequate trail (>4 weeks) of standard dose PPI
- Who have experienced resolution of symptoms after receiving induction therapy with budesonide orodispersible.

Response to therapy should be assessed by a gastroenterologist at 3 months and every 12 months thereafter.
Budesonide orodispersible should be discontinued if patients experience clinical relapse, histological relapse or require treatment for food impaction.

Suitable for primary care use

Recommendation to APC

BLUE – initiation by gastroenterologist with potential for transfer of prescribing if effectiveness confirmed at 3 month assessment and with annual gastroenterologist review

Potential patient group (if appropriate to include)

Brief description of disease	Sometimes described as Oesophageal Asthma, EoE is a chronic disease that affects the oesophagus, which is the tube that connects the mouth and stomach. Having too many eosinophils, a type of white blood cell, in the oesophagus causes inflammation that

	makes swallowing difficult.
Potential patient numbers per 100,000	Eosinophilic Oesophagitis (EoE) is a rare condition affecting around 13,000 people in England. Prescribed for 14 people in Epsom and St Helier Trust (serves a population of approximately 500,000) where it went on the formulary ahead of NICE. Royal Surrey County have 5-6 patients prescribed maintenance Jorveza, started as they had no response to high dose PPI and/or no response or unable to maintain an elimination diet, after dietetic review. It is expected this patient group will increase over time and will be transferred to primary care prescribing. Estimate 8 people with this condition might be treated with maintenance therapy per 100,000 (a third of the patients with the condition)
Outcomes required	Maintaining remission, not having pain when swallowing and not having food impaction requiring endoscopic intervention

Summary of current treatment pathway

The budesonide orodispersible tablets are available for use by secondary care for the induction of remission only (in line with NICE TA 708)
Alternatives to this therapy for maintenance include off-label proton pump inhibitors (such as omeprazole or lansoprazole) and corticosteroids (off-label fluticasone and unlicensed budesonide). People also try elimination diets such as the 6-food elimination diet (SFED), which involves eliminating the known allergens milk, eggs, nuts, wheat, soy and seafood.

Evidence review

NICE have not yet published a review for maintenance therapy as it did not have the licence at the time the NICE review was done.
The Canadian Journal of Health Technologies (CADTH) Published a review of Budesonide (Jorvesa®) for the induction AND maintenance of clinic-pathological remission in adults with eosinophilic oesophagitis in August 2021.
Although not UK based it is a trusted good quality source of reviews used to help Canadian Health Care decision makers make well informed decisions to improve the quality of health care services. (Similar to our NICE) Link below and paper attached.
https://www.cadth.ca/sites/default/files/DRR/2021/SR0666%20Jorveza%20-%20CADTH%20Final%20Rec.pdf

The paper contains a structured evaluation of the evidence and makes restrictive recommendations for the use of Jorvesa® in Canada.
Recommendations for use table copied from the CADTH paper

Table 1: Reimbursement Conditions and Reasons

Reimbursement condition	Reason
Initiation	
1. Adult patients (≥ 18 years of age) with a confirmed clinico-pathological diagnosis of EoE according to established diagnostic criteria: 1.1. History of symptoms of esophageal dysfunction (at least 1 of the following: transient or self-cleared food impaction, dysphagia, chest pain, epigastric discomfort, vomiting/regurgitation) 1.2. History of peak eos ≥ 15 in at least 1 HPF; (magnification: 400x) found pathologically on endoscopy.	Patients enrolled in Study BUL-2/EER were adults (18 to 75 years of age) and had to have a confirmed clinico-pathological diagnosis of EoE.
2. Patients must have experienced resolution of symptoms (dysphagia and pain during swallowing) after receiving induction treatment with budesonide	Patients enrolled in Study BUL-2/EER had clinico-pathological remission after receiving induction treatment with budesonide.
3. Failed an adequate trial of PPI treatment before initiation of induction treatment with budesonide 3.1. PPI failure is defined as refractory symptoms after at least 4 weeks of PPI treatment at a standard dose (omeprazole 20 mg/day, pantoprazole 40 mg/day, esomeprazole 40 mg/day, lansoprazole 30 mg/day, or rabeprazole 20 mg/day).	All patients enrolled in Study BUL-2/EER were required to have a documented trial with PPIs before initiation of induction treatment with budesonide to exclude PPI-REE.
Renewal	
4. Response to treatment should be assessed 3 months after initiating maintenance treatment with budesonide, then every 12 months thereafter.	The clinical experts noted to CDEC that in clinical practice, the response to treatment is assessed 3 months after initiating maintenance therapy, then every 6 months to 1 year thereafter.
Discontinuation	
5. Patients who experience clinical relapse, histological relapse, food impaction that needed endoscopic intervention, or need for an endoscopic dilation while receiving budesonide as maintenance therapy, should discontinue budesonide.	There is insufficient evidence to demonstrate whether patients who relapse while receiving budesonide for the maintenance of remission would respond to a subsequent reinduction course of treatment with budesonide or in the same manner as they responded to the initial treatment course.
Prescribing	
6. The patient must be under the care of a specialist with experience in the diagnosis and management of EoE.	Accurate diagnosis and follow-up of patients with EoE are important to ensure that budesonide is prescribed to the most appropriate patients.
7. Budesonide should not be reimbursed when used in combination with other corticosteroids used to maintain remission in patient with EoE	There is no evidence to demonstrate that patients with EoE would derive additional benefit from treatment with budesonide when used in combination with other corticosteroids for the treatment of patient with EoE.

Budesonise (Jorvesa®) are available in 2 strengths in Canada: 0.5mg and 1mg. CADTH concluded that the 1mg twice daily dosage may be used for induction of remission but only the 0.5mg twice daily dose was approved for reimbursement in Canada for the maintenance of remission.

In the UK only the 1mg tablet is licensed, so the licenced maintenance dose is 1mg twice daily until the 0.5 mg tablet become available here.
Local clinicians advocate using 1mg at night as recommended by Eosinophilic Oesophagitis research expert Prof Attwood.

Equity / Stakeholder views (if relevant)	
Decisions of local Trusts DTCs and neighbouring APCs	Include decisions from neighbouring APCs or DTCs if known St Georges Hospital – On formulary RED drug Kingston Hospital -– On formulary RED drug Epsom and St Helier -– On formulary Gastroenterologists only Royal Surrey County Hospital –RED drug Gastroenterologists only Ashford and St Peter's–RED drug Gastroenterologists only Surrey and Sussex–RED drug Gastroenterologists only
Recommendations from national / regional decision making groups	Include conclusions or recommendations from NICE, SMC, AWMSG, MTRAC etc
Stakeholder views	Use the enclosed proforma to obtain views from clinicians Summarise who has been consulted e.g. secondary care consultants, what their views are and any declared conflict of interest Have views of patient groups been sought?
CCG priorities	Does this treatment fit with existing national, regional or local priorities, policies or activity?

References

Include references written in Vancouver style

1. Straumann et al; International EOS-2 Study Group. Budesonide Orodispersible Tablets Maintain Remission in a Randomized, Placebo-Controlled Trial of Patients with Eosinophilic Esophagitis. Gastroenterology. 2020 Nov;159(5):1672-1685.e5. doi: 10.1053/j.gastro.2020.07.039. Epub 2020 Jul 25. PMID: 32721437.
2. Budesonide orodispersible tablet for inducing remission of eosinophilic oesophagitis; Technology appraisal guidance [TA708]Published: 23 June 2021
3. CADTH Reimbursement Recommendation Budesonide (Jorveza) Canadian Journal of Health Technologies August 2021, Volume 1, Issue 8

Prepared by:

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NHS Surrey Heartlands Clinical Commissioning Group

Declaration of Interest:

None

Date: 16/09/2021

Reviewed by:

Dr Guan Lim and Gastroenterology Network