BNSSG Shared Care Guidance
Please complete all sections

Section 1: Heading

Drug	Budesonide
Amber ***three months***	
Indication	Eosinophilic Esophagitis (EoE)
Speciality / Department	Paediatric Gastroenterology
Trust(s)	University Hospitals Bristol NHS Foundation Trust
	Click here to enter details
	Click here to enter details

Section 2: Treatment Schedule

Usual dose and frequency of administration	<10 years 1 mg once daily orally >10 years 1mg twice daily orally (may also be prescribed as 2mg once daily) Dose may be increased by the hospital team to 4mg daily for patients that do not respond to standard dosage.
Route and formulation	**<u>Jorveza (budesonide) 1mg orodispersible tablets (preferred preparation)</u>** The orodispersible tablet 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 about two minutes. The dissolved material should be swallowed with saliva little by little while the orodispersible tablet disintegrates. The orodispersible tablet 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 Jorveza. The orodispersible tablet should not be chewed or swallowed undissolved. These measures ensure optimal exposure of the esophageal mucosa to the active substance.

<table>
<tr><td></td><td>

<u>Budesonide 500micrograms (0.5mg) in 2mL nebules (</u>Alternative preparation for those unable to comply with administration instructions for Jorveza):

This strength of budesonide needs to be supplied to ensure that there is enough volume. Since there is no commercial topical viscous budesonide medicine for EoE, it needs to be compounded. Each nebule needs to be mixed with 2.5g (5 teaspoons) of granulated Splenda® (sucralose) to make a slurry (see table below). Granulated Splenda® is our recommended sweetener, as different sweeteners affect the viscosity of the slurry. The granulated Splenda® should be gradually dissolved into the budesonide to form a slurry (see Section 7). The slurry should be taken immediately. Granulated Splenda® can be obtained from a supermarket.

<table>
<tr><th>Dose</th><th>Number of Budesonide 500 microgram (0.5mg) nebule</th><th>Number of teaspoons of granulated Splenda®</th></tr>
<tr><td>1mg</td><td>2</td><td>10 (=5 grams)</td></tr>
<tr><td>2mg</td><td>4</td><td>20 (=10 grams)</td></tr>
</table>

One teaspoon of granulated Splenda® equals 0.5 grams

The slurry is swallowed and mouth rinsed (not swallowed) with water to minimise the risk of oropharyngeal candida infection. The patient must not eat, drink, take medication or brush their teeth for 30 minutes after the dose to prevent the steroid from being washed off the oesophagus. Ideally the dose should be given at bedtime after brushing their teeth. The slurry is sugar-free so teeth can be brushed beforehand.

Licensing
- Jorveza is licensed for treatment of eosinophilic esophagitis (EoE) in adults. Not currently licensed in paediatrics.
- Budesonide nebules are not licensed for this indication

</td></tr>
<tr><td>Duration of treatment</td><td>Ongoing. Treatment will be reviewed by the hospital at 3 months.</td></tr>
</table>

Section 3: Monitoring

Please give details of any tests that are required before or during treatment, including frequency, responsibilities (please state whether they will be undertaken in primary or secondary care), cause for adjustment and when it is required to refer back to the specialist.

Baseline tests - where appropriate
Nil applicable
Subsequent tests - where appropriate
1. Primary care: nil applicable 2. Secondary care: Disease remission will be assessed by symptom resolution and where possible endoscopic assessment. If course is prolonged height and weight will monitored annually.

Section 4: Side Effects

Please list the most common side effects and management. Please provide guidance on when the GP should refer back to the specialist.

Side effects and management	Nil particular Systemic corticosteroid effects are less likely to occur with topical treatment than oral. Long-term data is not available; however there have been no documented systemic side effects with budesonide slurry in the current literature. The most important adverse effect of topical steroid preparations is oropharyngeal candida which can be managed with antifungal treatment (e.g. topical nystatin) without discontinuing treatment. If severe, refer back to the hospital team.
Referral back to specialist	If there are any concerns with growth, adrenal suppression and bone density refer back to the hospital team.

Section 5: Drug Interactions

Please list clinically significant drug interactions (eMC link please click here)

Significant Drug Interactions

There have been no reported drug interactions in the clinical trials undertaken. Budesonide has a poor systemic availability when taken orally and therefore, theoretically there will be a lower systemic absorption when used topically. However, drug interactions have occurred with high dose inhaled budesonide therefore there is a need to be vigilant for possible interactions.

Drug	Significance/Action
Antidiabetic medicines	Corticosteroids can affect glucose intolerance. Increased glucose monitoring may be necessary.
Azoles (itraconazole, voriconazole, ketoconazole)	Azoles may increase the exposure of budesonide by inhibiting the CYP3A4 which metabolises budesonide. Avoid combination if an alternative treatment is possible. Time interval between drugs should be increased to as long as possible. Patients/carers should monitor for increased corticosteroid effects (moon face, weight gain and hyperglycaemia).
CYP3A4 macrolides (erythromycin and clarithromycin)	Erythromycin and clarithromycin are known to inhibit CYP3A4. Lack of data. No need to avoid combination. Patients/carers should monitor for increased corticosteroid effects (moon face, weight gain and hyperglycaemia).
Diltiazem/Verapamil	Diltiazem and verapamil are moderate inhibitors of CYP3A4; therefore increased budesonide exposure is possible. Lack of data. Patients/carers should monitor for increased corticosteroid effects (moon face, weight gain and hyperglycaemia).
Grapefruit juice	Grapefruit juice inhibits CYP3A4. Avoid if possible, otherwise, increase time interval between juice and dose. Patients/carers should monitor for increased corticosteroid effects (moon face, weight gain and hyperglycaemia).
NSAIDS	Risk of gastrointestinal bleeding increased with concomitant NSAID. Avoid regular use of NSAIDs with budesonide if possible; otherwise consider GI protection (e.g. ranitidine or a proton pump inhibitor).
QT prolonging drugs	Corticosteroids can cause hypokalaemia which can increase the risk of torsade de pointes when taken in combination with QT prolonging drugs. Topical budesonide does not commonly cause hypokalaemia. The risk of torsades de pointes depends on

	<table><tr><td></td><td>patient factors and current medication. Assess the patient's risk factors. For more information refer to the UKMI Q&A on QT prolongation. Accessed online at: https://www.sps.nhs.uk/wp-content/uploads/2017/09/QA237_2_DruginducedQTprolongation-2017-update.pdf</td></tr><tr><td>Ritonavir and all HIV protease inhibitors</td><td>Inhibits CYP3A4 and increase exposure to budesonide. Avoid combination if an alternative treatment is possible. Time interval between drugs should be increased to as long as possible. Patients/carers should monitor for increased corticosteroid effects (moon face, weight gain and hyperglycaemia).</td></tr></table> See BNFC for complete list of interactions.
Reminder to ask patient about specific problems	Ask the patient whether they have any symptoms of oropharyngeal candida infection.

Section 6: Contra-indications, Cautions and Special Recommendations

Please list

1. MHRA advice regarding risk of central serious chorioretinopathy for any corticosteroid therapy. Patients should be advised to report any blurred vision or other visual disturbance and may require ophthalmologic assessment
2. Contra-indications: Hypersensitivity to budesonide, sucralose or to any of the excipients listed.
3. Cautions: Congestive heart failure, diabetes mellitus, history of tuberculosis, hypertension, infection (particularly untreated), osteoporosis, peptic ulcer, long-term oral or high dose inhaled corticosteroids (see BNFC for complete list)
4. Live vaccines can be administered as topical corticosteroids are not known to cause substantial systemic immunosuppression and are therefore are not contraindicated.

Section 7: Advice to the patient

Advice for prescribing clinician to inform patient

Instructions for patient:

1. The nebules should be detached from the strip. Twist open the plastic top of the nebules
2. Squeeze out the contents of required nebules into a mortar or suitable container.
3. Measure the amount of granulated Splenda® required and gradually add the Splenda® to the budesonide to form a slurry.
4. Give the slurry with a spoon orally
5. The patient must not brush their teeth, eat, drink or take medication at least 30 minutes following administration.

Section 8: Responsibilities for Secondary Care

Core responsibilities

1. Initiating treatment and prescribing for the first three months
2. Undertaking the clinical assessment and monitoring for the first three months.
3. Communicate details of the above in 1 and 2 to GP within the first month of treatment. This information should be transferred in a timely manner.
4. Refer patients to GP and provide information of further action where appropriate e.g. blood test is due.
5. To provide advice to primary care when appropriate.
6. Review concurrent medications for potential interaction prior to initiation of Budesonide.

7. Stopping treatment where appropriate or providing advice on when to stop. 8. Reporting adverse events to the MHRA. 9. Reminder to ask patients about particular problems see section 5.
Other specific to drug
1. Click here to enter details

Section 9: Responsibilities for Primary Care

Core responsibilities 2. Responsible for taking over prescribing after the first three months 3. Responsible for the clinical assessment and monitoring after the first three months 4. Review of any new concurrent medications for potential interactions. 5. Reporting adverse events to the MHRA. 6. Refer for advice to specialist where appropriate. 7. Reminder to ask patients about particular problems see section 5.
Other specific to drug
1. Click here to enter details

Section 10: Contact Details

Name	Organisation	Telephone Number	E mail address
Paediatric GI secretary	Bristol Royal Hospital for Children	0117 3429450	Click here to enter details
Paediatric Medicine Pharmacist	Bristol Royal Hospital for Children	0117 3427042	Click here to enter details
A.Wiskin	Bristol Royal Hospital for Children	01173429451	a.wiskin@nhs.net

Section 11: Document Details

Date prepared	January 2018 (Minor amendment November 2019)
Prepared by	Anthony Wiskin (Consultant Paediatric Gastroenterologist) and Rachel Crampton (Paediatric Pharmacist for Medicine) Minor amendment November 2019 – Jane Hutchinson-Jones (Paediatric Pharmacist for Medicine)
Date approved by JFG	April 2018
Date of review	April 2020

Document Identification: Version	Version 1.1

Section 12: Collaboration

Specialists in any one discipline are encouraged to collaborate across the health community in preparing shared care guidance. Please give details

1. Click here to enter details

Section 13: References

Please list references

1. Baxter, K. Stockley's Drug Interactions [online]. London: Pharmaceutical Press. Accessed at: http://www.medicinescomplete.com/accessed on 12.01.17
2. BNF for Children (BNFC 2017-2018). Accessed at: www.medicinescomplete.com (accessed on 10.01.2018)
3. Budesonide (AstraZeneca) Summary of Product Characteristics. Accessed at: https://www.medicines.org.uk/emc/medicine/193. Last updated: (accessed on 10.01.18)
4. Department of Health, The Green Book. Chapter 6: Contraindications and special considerations (last updated 26 October 2017). Available at: https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book#the-green-book (accessed on 10.01.18)
5. Gan, C et al. Oral viscous Budesonide for Eosinophilic Esophagitis in Children. Great Ormond Street Hospital Guideline (June 2015).
6. Guandalini, S et al. Textbook of Paediatric Gastroenterology, Hepatology and Nutrition: A Comprehensive Guide to Practice. Springer, 2015 page 99
7. MHRA, Corticosteroids: rare risk of central serous chorioretinopathy with local as well as systemic administration. Accessed at: https://www.gov.uk/drug-safety-update/corticosteroids-rare-risk-of-central-serous-chorioretinopathy-with-local-as-well-as-systemic-administration (accessed on 09.07.18)
8. Papadopoulou, A et al (for the ESPGHAN Eosinophilic Esophagitis Working Group and Gastroenterology Committee). Management Guidelines of Eosinophilic Esophagitis in Childhood. JPGN 2014;58: 107-118
9. Jorveza (Dr. Falk Pharma UK Ltd) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/9446 [Accessed 12.11.2019]

Please email completed shared care protocol to emilyknight1@nhs.net or Natasha.mogford@nhs.net