Orodispersible and Transmucosal Alternative Medications

For Symptom Control in Adults

Corresponding Author: Anna Sutherland; annasutherland@doctors.org.uk; Sir Michael Sobell House Hospice, Churchill Hospital, Old Road, Oxford OX3 7LE;

Co - Authors: Melinda Presland, Sir Michael Sobell House Hospice, Churchill Hospital, Old Road, Oxford OX3 7LE; E Harrop, Consultant in Paediatric Palliative Care & Medical Director, Helen & Douglas House, 37 Leopold Street, Oxford, OX4 1QT & Honorary Consultant Oxford University Hospitals NHS Trust Churchill Hospital, Old Road, Oxford OX3 7LE; Matthew Carey, Sir Michael Sobell House Hospice, Churchill Hospital, Old Road, Oxford OX3 7LE, ORCID ID 0000-0002-6092-2512; Mary Miller, Sir Michael Sobell House Hospice, Churchill Hospital, Old Road, Oxford OX3 7LE, ORCID ID 0000-0002-2026-6397; Ian C K Wong, Professor in Pharmacy Practice, Medicines Optimisation Research and Education (CMORE), Research Department of Practice and Policy, UCL School of Pharmacy and University College London Hospitals NHS Foundation Trust

Key words:

Word count (excluding title page, abstract, references, statements, figures and tables): 1714

Competing interest statement: None declared.

Number of supplementary files for online only publication: 0

Number of references: 22

Number of figures: 0

Number of tables: 30

Contributorship statement:

AS drafted the manuscript, undertaking the literature search and constructing the tables for each drug listed.

AS, MP, EH, MC, MM and IW jointly agree the drugs to include in the manuscript. MP, EH, MC, MM and IW had supervising input throughout the drafting the final manuscript.

Sources of Funding: None declared.

Ethical approval: None required.
Abstract

Background

Paediatric palliative care makes frequent use of orodispersible and transmucosal drug delivery routes. The limited published experience of this practice suggests that it enables the delivery of needle-free symptom relief, with the potential to train family carers in the community to administer anticipatory medications without reliance on trained health professionals.

Aims

To identify orodispersible and potential transmucosal alternatives that may be used in adults in the event of a patient having no oral or intravenous route and no access to subcutaneous injections.

Methods

The author panel identified medications through review of multiple drug formularies, review of the published evidence and their experience. Where possible, licensed alternatives were identified and any “off label” or unlicensed medications clearly highlighted.

Results

A practical list of 29 medications is provided which could be used either via the orodispersible or transmucosal alternative route for health care professionals delivering end of life care to consider in their practice when the licensed alternative routes are unavailable. All users of this guide are encouraged to use their professional judgement whenever selecting a medication for a patient, recognising that this review is neither a guideline nor a systematic review, and taking account of licensing considerations, adverse effects, potential unpredictability of time to effect, and contraindications.

Conclusion

Orodispersible and transmucosal medications offer the possibility of enabling rapidly delivered needle-free symptom relief. Should it be necessary to utilise these transmucosal alternatives then any experience gained should be reported either on www.palliativedrugs.com or in the format of published articles. Combined with further research, this experience offers the possibility of reducing injection frequency and inherent delays in medication administration, particularly in the community setting during the Covid-19 pandemic.
Aim

Our aim in writing this guide is to provide a resource from which healthcare professionals can select medications to control symptoms when in patients do not have an oral route and when injectable medications are not available. This will enable high quality needle-free palliative care, particularly in the community. We aim to summarise the evidence available regarding the transmucousal route, how transmucosal medications are administered, why they’re effective and how transmucosal medications might be integrated into clinical practice.

Background

Transmucosal drug administration utilises the mucous membranes to deliver medication and is particularly beneficial when a patient cannot swallow tablets or liquids but does not have access to injectable medications or where the patient prefers to avoid injections. The mucosal membranes absorb lipophilic drugs rapidly, minimising first pass metabolism and therefore frequently leading to a rapid onset of effect. For these reasons transmucosal drug administration lends itself to use for rapid management of breakthrough symptoms. [1] The utilisation of transmucosal routes of administration is widely established in paediatrics.[2]

Prior to consideration of the transmucosal route it is important that every effort is made to utilise other available routes. In particular it is important to consider alternative formulations, such as, liquids in order to optimise the oral route before switching to a transmucosal alternative.

Examples of medications licenced and commonly used in the adult palliative population which utilise the transmucosal route include: nasal administration of fentanyl for pain; buccal administration of prochlorperazine for nausea and vomiting; orodispersible lansprazole for acid reflux; and rectal paracetamol for fever.

We defined methods of transmucosal drug administration as including buccal, sublingual, orodispersible, nasal and rectal routes. A pre-requisite to the use of transmucosal medications is that the mucosal membrane must be moist. There are several important general principles for transmucosal drug administration, which include:

1) Only soluble drug molecules can be readily absorbed via mucosal membrane. Therefore liquid preparations are preferable such as injection, concentrated solution or spray.

2) If chewable or oro-dispersible tablets are used it is critical to ensure sufficient saliva is available to dissolve the tablets or alternatively tablets may be dissolved prior to administration. Buccal hydration may be improved by 2 hourly ice chips, biotene oral gel or AS Orthna (contains porcine mucin).

3) To promote buccal or sublingual absorption keep the liquid in the mouth as long as possible without swallowing. Where the patient is not able to hold liquid in the mouth the prescriber may choose to use a buccal tablet and gently massage the outside of the cheek following administration.
4) The bioavailability of drugs is likely to be higher via transmucosal route compared to oral route but lower than via parenteral routes. The effect of the drug will depend on how long it can be retained next to the mucosa and any gastrointestinal absorption if the drug is swallowed.

5) To supply the patient or care giver with clear instructions on what each drug is being used for, how frequently it may be administered and how to administer each drug to avoid any administration errors, as well as any adverse effects to be aware of.

6) Patients need to be monitored and assessed when switched to a transmucosal route and adjust the dose as necessary.

7) It is best practice that injections prepared for sublingual or buccal administration are drawn up through a filter needle to reduce the risk of any glass injury to oral mucosa.

Furthermore, care needs to be taken to identify whether patients are swallowing or spitting out a large proportion of orally administered medications as this may further affect its efficacy. Taste is a particularly important factor as an unpleasant taste may make patients less likely to retain the medication on the buccal mucosa long enough for it to be effective. Anderson observed that:

“Buccal and sublingual administration, where there is considerable drug swallowed, results in lower plasma concentrations if that drug has a high first-pass effect because bioavailability is reduced.” [3]

In general, however, there is very limited pharmacokinetic and pharmacodynamic data available such as time to maximum concentration, time to maximum effect, and half-life when using the mucosal route for off licensed drug administration. The lack of data regarding “concentration–response relationship for either the beneficial or adverse effects”[3] of drugs means that adjustment of dose and frequency of administration to maximise efficacy and yet minimise adverse effects is very challenging.

Despite these caveats and considerations, transmucousal medications present the possibility of delivering needle free symptom control, something which is routinely employed in paediatric palliative care because “by and large, children hate needles.” [3]

Spathis and colleagues identified that this was an area of paediatric palliative care that had the potential to augment and enhance practice in adult palliative care:

“Family members can respond immediately to symptoms, without having to wait for the arrival of nursing staff. This approach could be of considerable value in adult community palliative care practice.” [4]

The Covid-19 pandemic raised concerns that availability of district nurses in the community to administer medications via the traditional subcutaneous route for adults approaching the end of their lives may be outstripped by the steep increase in demand for their services. Additionally, there is a need to ensure alternative medications are identified early so that this information is available to inform practice in the event of drug shortages.
Caution

All users of this guide are encouraged to use their professional judgement whenever selecting a transmucosal medication for a patient. The reader should note that this is neither a guideline nor a systematic review. Users must therefore consider their local and national guidelines, as well as considering the evidence base for the drug they elect to use, its licencing, contraindications to its use and adverse events. Any statements regarding a drug’s licencing relate to its use in the United Kingdom only and users are advised to check the relevant licencing requirements if they are practicing in other countries around the world.

Methods

During the initial phase of the Covid-19 pandemic local, regional and national symptom management guidelines were created. [5,6,7,8,9,10,11,12,13,14,15] These were hand searched to identify potential transmucosal alternatives that might be of use in the event of a patient having no oral or intravenous route and no access to subcutaneous injections.

Transmucosal alternatives used in paediatric palliative care practice, both in the UK and internationally were explored. The experiences of expert colleagues working in a range of countries, was sought, both through personal communication and published work.

Having identified potential therapeutic options a list of alternative transmucosal medications was compiled and cross referenced with the British National Formulary (BNF), the Palliative Care Formulary (PCF) and the Association of Paediatric Palliative Care (APPM) Formulary and the Enteral Drug Handbook as appropriate.[16,17,18,19]

The potential list of transmucosal medications were discussed and reviewed by the author panel until consensus was achieved.

Results

We identified 29 potential transmucosal alternative medications, listed below, and present the potential risks and benefits of each, their licensing status and costings, as listed in the BNF. We present an example table. See Tables 1-30.
## Alfentanil Buccal, Sublingual or Nasal

| **What is it?**          | Strong opioid analgesic – CD schedule 2 drug |
|--------------------------|---------------------------------------------|
| **Mechanism of action**  | Opioid having central agonist effect         |
| **Dose**                 | 10-16% of the total CSCI dose hourly prn    |
| **Time to onset of effect** | 5 minutes [17]                            |
| **Formulation**          | Nasal spray with attachment for buccal/SL use (5mg/5mL) bottle available as special order from Torbay Hospital Manufacturing Unit Tel: 01803 664707. Each ‘spray’ delivers 0.14 ml = 140 microgram alfentanil OR Injection preparation given via buccal, sublingual or nasal route. Two strengths available, 500microgram/mL and 5mg/mL |
| **Indication**           | Moderate to severe pain for the management of breakthrough, incident or procedural pain when eGFR <20 |
| **Common Adverse Effects** | Apnoea; chills; fatigue; hypertension; movement disorders; muscle rigidity; procedural complications [16] |
| **Contraindications**    | Avoid or use a reduced dose in hepatic failure[17] |
| **Licencing**            | Nasal spray is an unlicensed product Injection is licensed but a transmucosal route is “off label” |
| **Benefits**             | Rapidity of onset of action                  |
|                         | Ease of nasal administration                 |
| **Risks**                | Prescribing/administration error              |
|                         | Lack of familiarity with drug                 |
|                         | Lay carer administration                      |
|                         | Lack of availability                          |
|                         | Cost                                          |
|                         | Unrecognised hepatic failure                  |
| **Cost**                 | Special – Price on Application (POA)         |

Table 1. Alfentanil Buccal, Sublingual or Nasal
| **Aripiprazole Orodispersible** |  |
|--------------------------------|----------------------------------|
| **What is it?**                | Atypical antipsychotic            |
| **Mechanism of action**        | Aripiprazole is a dopamine D₂ partial agonist with weak 5-HT₁α partial agonism and 5-HT₂A receptor antagonism. |
| **Starting dose**              | 10mg                              |
| **Time to onset of effect**    | 3 – 5 hours [17]                  |
| **Formulation**                | Orodispersible tablet             |
| **Indication**                 | Agitated delirium                 |
| **Common Adverse Effects**     | Anxiety; abnormal appetite; diabetes mellitus; fatigue; gastrointestinal discomfort; headache; hypersalivation; nausea; visual disorders [16] |
| **Contraindications**          | CNS depression; cerebrovascular disease; comatose state; phaeochromocytoma [16] |
| **Caution**                    | Long half-life (75 – 145 hours)   |
|                                | Elderly                           |
|                                | Hepatic failure                   |
| **Licence**                    | Licensed product                  |
| **Benefits**                   | Licensed product                  |
| **Risks**                      | Long half life                    |
| **Cost**                       | £25 - £96 for 28x 10mg tablets    |

Table 2. Aripiprazole Orodispersible
| **Atropine Sublingual** |
|-------------------------|
| **What is it?** | Anticholinergic |
| **Mechanism of action** | Non selective Antimuscarinic |
| **Starting dose** | 4 drops (800 microgram – 1mg as size of drop varies) of 1% eye drops 4 hourly prn sublingually |
| **Time to onset of effect** | Uncertain (Half-life 2 – 2.5 hours) [17] |
| **Formulation** | 1% eye drops |
| **Indication** | Sialorrhoea |
| | Noisy rattling breathing |
| **Common Adverse Effects** | Constipation; dizziness; drowsiness; dry mouth; dyspepsia; flushing; headache; nausea; palpitations; skin reactions; tachycardia; urinary disorders; vision disorders; vomiting [16] |
| **Contraindications** | Acute myocardial infarction; arrhythmias; autonomic neuropathy; cardiac insufficiency; cardiac surgery; diarrhoea; elderly; gastro-oesophageal reflux disease; hypertension; hyperthyroidism; narrow angle-closure glaucoma; ileus; prostatic hyperplasia; pyrexia; ulcerative colitis; myasthenia gravis [16] |
| **Caution** | Elderly |
| **Licence** | Unlicensed use and route for a licensed product |
| **Benefits** | Small volume |
| | Established body of use in palliative care practice |
| **Risks** | Varying dose with different droppers |
| | Systemic absorption |
| **Cost** | £131.89 for 10ml 1% eye drops |

Table 3. Atropine Sublingual
| **What is it?** | Strong opioid analgesic |
|----------------|------------------------|
| **Mechanism of action** | Opioid having agonist and antagonist properties |
| **Starting dose** | 200 micrograms every 6–8 hours prn (Equivalent to 15mg Morphine 6–8 hourly) |
| **Time to onset of effect** | 10 – 20 minutes [17] |
| **Formulation** | Sublingual tablet – CD schedule 3 drug |
| **Indication** | Moderate to severe pain |
| **Common Adverse Effects** | Vomiting; Opioid adverse effects; constipation; dizziness; drowsiness; dry mouth [16] |
| **Contraindications** | Acute respiratory depression, comatose, head injury, raised intracranial pressure [16] |
| **Caution** | Those at risk of aspiration |
| | Severe hepatic impairment |
| **Licence** | Temgesic and Tephine are licensed products for pain |
| **Benefits** | May cause less constipation |
| | May cause less hyperalgesia |
| **Risks** | Systemic absorption |
| | Use complicated: Advise patients that tablets should be dissolved under the tongue, not to swallow for 2 minutes and not to consume food or drink for at least 5 minutes after administration |
| | Non registered carers will not be able to administer |
| **Cost** | £8.50 for 28x 200 microgram tablets |

Table 4. Buprenorphine Sublingual
| **Carbamazepine Rectal** |  |
|--------------------------|---|
| **What is it?** | Analgesic – acting on neuropathic pain |
| **Mechanism of action** | Anti-epileptic sodium channel blocker |
| **Starting dose** | 125mg bd |
| **Time to onset of effect** | 4 to 8 hours [17] |
| **Formulation** | Suppository (125mg rectally is approximately equivalent to 100mg PO) |
| **Indication** | Neuropathic pain  
Seizures |
| **Common Adverse Effects** | Dizziness; drowsiness; dry mouth; eosinophilia; fatigue; fluid imbalance; gastrointestinal discomfort; headache; hyponatraemia; leucopenia; movement disorders; nausea; oedema; skin reactions; thrombocytopenia; vision disorders; vomiting; weight increased [16] |
| **Contraindications** | Acute porphyrias; AV conduction abnormalities (unless paced); history of bone-marrow depression; Cardiac disease; history of haematological reactions to other drugs; may exacerbate absence and myoclonic seizures; skin reactions; susceptibility to angle-closure glaucoma [16] |
| **Caution** | Hepatic impairment  
Bone marrow suppression |
| **Licence** | Licensed product for seizure control; “off label” for neuropathic pain |
| **Benefits** | Licensed product |
| **Risks** | Expensive  
Lack of familiarity with this use in palliative care |
| **Cost** | £120 for 5 x 125mg suppositories |

Table 5. Carbamazepine Rectal
| What is it?        | Antiemetic                          |
|-------------------|-------------------------------------|
| Mechanism of action | Antihistaminic antimuscarinic antiemetic |
| Starting dose     | 50 mg bd - tds                       |
| Time to onset of effect | 30 – 60 minutes [17]                |
| Formulation       | Injection given as a sublingual solution  |
|                   | Rectal suppository (Must be kept in fridge) |
| Indication        | Nausea related to raised intracranial pressure  |
|                   | Nausea related gastrointestinal obstruction  |
|                   | Nausea related to vestibular disorders  |
| Common Adverse Effects | Anticholinergic adverse effects; Movement disorders, potential for misuse / abuse of injections |
| Contraindications | Epilepsy; prostatic hypertrophy (in adults); pyloroduodenal obstruction; severe heart failure—may cause fall in cardiac output and associated increase in heart rate, mean arterial pressure and pulmonary wedge pressure; susceptibility to angle-closure glaucoma [16] |
| Caution           | Renal and hepatic impairment         |
| Licence           | Use of injection orally: “off label”  |
|                   | Use of suppositories: unlicensed product |
| Benefits          | Alternative routes of administration |
| Risks             | Delay to manufacture of suppositories |
| Cost              | Oral solution:  |
|                   | 50mg/ml ampoules for injection – £18.58 for 5  |
|                   | Suppository – a special order. Price of application (POA) |

Table 6. Cyclizine Sublingual or Rectal
| **What is it?** | Benzodiazepine |
|-----------------|----------------|
| **Mechanism of action** | GABA<sub>A</sub> modulator |
| **Starting dose** | 2.5mg (approximately equivalent to 1.25mg Midazolam)  10mg for seizure |
| **Time to onset of effect** | 30 minutes [17] |
| **Formulation** | Rectal tube |
| **Indication** | Agitated delirium  Anxiety  Seizures |
| **Common Adverse Effects** | Drowsiness; fatigue; muscle weakness; nausea; respiratory depression (particularly with high dose and intravenous use—facilities for its treatment are essential); sleep disorders; vertigo; vision disorders; withdrawal syndrome [16] |
| **Contraindications** | Coma; current alcohol abuse; current drug abuse; respiratory depression [16] |
| **Caution** | Hepatic impairment  Renal failure |
| **Licence** | Licensed for anxiety and seizures; “off label” for delirium |
| **Benefits** | Alternative route of administration |
| **Risks** | Greater evidence base with buccal midazolam than rectal diazepam |
| **Cost** | 2.5mg - £5.65 for 5  5mg - £6.49 for 5  10mg - £6.49 for 5 |

Table 7. Diazepam Rectal
### Diamorphine Intranasal or Sublingual

| **What is it?** | Strong opioid (CD Schedule 2) |
|-----------------|-------------------------------|
| **Mechanism of action** | Mu agonist |
| **Starting dose** | 1.25 – 2.5mg 4 hourly prn (Equivalent to 3.75 – 7.5mg Morphine PO) |
| **Time to onset of effect** | <5 minutes [17] |
| **Formulation** | Nasal spray (Ayendi(R)) OR Injection (powder for reconstitution) intranasal or sublingual routes |
| **Indication** | Moderate to severe pain |
| **Common Adverse Effects** | Vomiting; Opioid adverse effects; constipation; dizziness; drowsiness; dry mouth [16] |
| **Contraindications** | Acute respiratory depression, comatose, head injury, raised intracranial pressure [16] |
| **Caution** | Those at risk of aspiration; Severe hepatic and renal impairment |
| **Licencing** | Off license route of licensed injections Nasal spray (Ayendi(R)) licensed but not available in the UK at time of writing |
| **Benefits** | Rapidity of onset of action; Ease of nasal administration |
| **Risks** | Prescribing/administration error; Lack of familiarity with drug; Lay carer administration and difficulty making up the drug |
| **Cost** | £12.81 for 5 x 5mg ampoules for injection; Ayendi (R) POA |

Table 8. Diamorphine Intranasal or Sublingual
| **Diclofenac Rectal** |
|-----------------------|
| **What is it?**        | Non opioid analgesic |
| **Mechanism of action**| Non-steroidal anti-inflammatory selective Cox-2 inhibitor |
| **Starting dose**      | 50mg 8 - 12 hourly prn |
| **Time to onset of effect** | 30 minutes [17] |
| **Formulation**        | Rectal suppository |
| **Indication**         | Mild to moderate pain |
| **Common Adverse Effects** | Oedema; skin reactions; appetite decreased; diarrhoea; dizziness; gastrointestinal discomfort; gastrointestinal disorders; headache; nausea; rash (discontinue); vertigo; vomiting [16] |
| **Contraindications**  | Allergy to aspirin, cardiovascular disease, gastrointestinal bleeding or history of perforation [16] |
| **Caution**            | Hepatic impairment |
|                        | Renal failure [16] |
| **Licence**            | Licensed |
| **Benefits**           | Alternative route of administration |
| **Risks**              | Difficult to administer |
| **Cost**               | £1.24 for 10x 25mg or £2.04 for 10x 50mg suppositories |

Table 9. Diclofenac Rectal
| **Docusate Rectal** |
|---------------------|
| **What is it?** | Laxative |
| **Mechanism of action** | Faecal softener with some stimulant effect |
| **Starting dose** | 120mg |
| **Time to onset of effect** | 30 minutes [17] |
| **Formulation** | Rectal enema |
| **Indication** | Constipation |
| **Common Adverse Effects** | Abdominal discomfort, anorectal irritation, incontinence [16] |
| **Contraindications** | Bowel perforation [16] |
| **Caution** | Proctitis |
|  | Intestinal obstruction |
| **Licence** | Licensed |
| **Benefits** | Alternative route of administration |
| **Risks** | Difficult to administer |
| **Cost** | £28.00 for 6x 120mg enemas |

Table 10. Docusate Rectal
## Domperidone Orodispensible

| What is it?               | Antiemetic                                      |
|--------------------------|------------------------------------------------|
| Mechanism of action      | Prokinetic D₂ antagonist                        |
| Starting dose            | 10mg prn tds                                    |
| Time to onset of effect  | 30 minutes [17]                                 |
| Formulation              | 10 mg orodispersible tab                         |
| Indication               | Nausea and vomiting                             |
| Common Adverse Effects   | Dry mouth; anxiety; asthenia; breast abnormalities; diarrhoea; drowsiness; headache; lactation disorders [16] |
| Contraindications        | QT abnormality                                   |
|                          | Prolactinoma [16]                               |
| Caution                  | Patients > 60                                   |
| Licence                  | Orodisperible tablet unlicensed product          |
| Benefits                 | Alternative route of administration              |
| Risks                    | Extrapyramidal adverse effects                  |
| Cost                     | Orodispersible tablet – special POA              |

Table 11. Domperidone Orodispensible
| What is it?         | Strong opioid (CD Schedule 2) |
|--------------------|--------------------------------|
| Mechanism of action| Mu agonist                    |
| **Starting Dose**  | 50 (Instanyl) to 100 micrograms (Pecfent, Abstral and Efentora)  
|                    | A further 50 or 100 micrograms after 15–30 minutes if required  
|                    | Maximum 2 doses per pain episode  
|                    | Dose titration as per manufacturer’s guidance |
| **Time to onset of effect** | 15 - 20 minutes [17] |
| **Formulation**   | Pecfent® nasal spray  
|                    | Instanyl® nasal spray  
|                    | Abstral® sublingual tablet  
|                    | Efentora® buccal tablet |
| **Indication**    | Moderate to severe pain for the management of breakthrough, incident  
|                    | or procedural pain |
| **Common Adverse Effects** | Acute respiratory depression, comatose, head injury, raised intracranial pressure |
| **Contraindications** | Those at risk of aspiration |
| **Licence**       | Licensed product |
| **Benefits**      | Rapidity of onset of action  
|                    | Ease of nasal administration |
| **Risks**         | Lack of familiarity with drug  
|                    | Lay carer administration  
|                    | Mucositis when using buccal or sublingual products |
| **Cost**          | Abstral - £49.99 for 10x 100microgram sublingual tablets;  
|                    | Effentora - £139.72 for 28x100microgram buccal tablets;  
|                    | Instanyl - £35.70 for 6x doses nasal spray 100micrograms/dose;  
|                    | Pecfent - £36.48 for 8 x doses nasal spray 100micrograms/dose. |

Table 12. Fentanyl Nasal, Buccal or Sublingual
| **What is it?** | Anticholinergic |
|----------------|----------------|
| **Mechanism of action** | Antimuscarinic |
| **Starting dose** | 200mcg 8 hourly prn sublingual |
| **Time to onset of effect** | 30 – 40 minutes [17] |
| **Formulation** | Oral solution OR Injection |
| **Indication** | Drooling Noisy rattling breathing Medical management of malignant bowel obstruction Paraneoplastic fevers and sweating |
| **Common Adverse Effects** | Constipation; dizziness; drowsiness; dry mouth; dyspepsia; flushing; headache; nausea; palpitations; skin reactions; tachycardia; urinary disorders; vision disorders; vomiting [16] |
| **Contraindications** | Tachycardia >100 Cardiac conduction disorders [16] |
| **Caution** | Elderly Renal impairment – may need to reduce dose |
| **Licence** | Oral solution “off label” use in adults and “off label” route (however licensed for oral administration in children >3 years to adolescents with neurological disorders) Injection is a licensed product but “off label” route |
| **Benefits** | Small volume |
| **Risks** | Risk of glass ampoule when administering |
| **Cost** | £91 for 150ml x 200microgram/ml oral solution £76.80 for 60mls x 400mcg/ml oral solution £9.95 for 10x 200microgram/ml ampoules for injection |

Table 13. Glycopyrronium Sublingual
**Haloperidol Buccal or Sublingual**

| What is it? | Butyrophenone antipsychotic |
|-------------|----------------------------|
| Mechanism of action | D₂, alpha-adrenergic and sigma receptor antagonist |
| Starting dose | 0.5mg – 1.5mg 6 – 8 hourly |
| Time to onset of effect | 1 hour if give PO (buccal / sublingual may be faster) [17] |
| Formulation | Oral solution |
| Indication | Delirium, Nausea and vomiting, Hiccups, Psychosis |
| Common Adverse Effects | Extra pyramidal effects, altered liver function tests, dizziness, sedation, visual disturbance, depression, hypotension [16] |
| Contraindications | Parkinson’s disease, Lewy body dementia, cardiac disorders, QTc prolongation, recent myocardial infarction, decompensated heart failure, heart failure [16] |
| Caution | Dementia, stroke risk, epilepsy, renal and hepatic impairment, cardiac disease [16] |
| Licence | Off licence use of licensed product |
| Benefits | Alternative route of administration of an antipsychotic |
| Risks | Time to effect unknown when used sublingually |
| Cost | Price varies widely by product: £4.45 for 100ml of Haldol 2mg/mL oral solution |

Table 14. Haloperidol Buccal or Sublingual
| **What is it?** | Antimuscarinic |
|-----------------|----------------|
| **Mechanism of action** | Antisecretory with smooth muscle relaxant properties |
| **Starting dose** | 150 microgram 4 hourly prn |
| **Time to onset of effect** | 10 – 15 minutes [17] |
| **Formulation** | Chewable tablets |
| **Indication** | Sialorrhea  
Drooling  
Smooth muscle spasm  
Paraneoplastic fevers and sweating |
| **Common Adverse Effects** | Constipation; dizziness; drowsiness; dry mouth; dyspepsia; flushing; headache; nausea; palpitations; skin reactions; tachycardia; urinary disorders; vision disorders; vomiting [16] |
| **Contraindications** | Tachycardia >100  
Cardiac conduction disorders [16] |
| **Caution** | Crosses blood brain barrier so may cause sedation  
Elderly  
Renal and hepatic impairment  
May prefer to use transdermal patch |
| **Licence** | “off label” use of a licensed product |
| **Benefits** | Chewable alternative |
| **Risks** | Aspiration |
| **Cost** | £1.67 for 12x 150mg Kwells  
£1.99 for 12x 150 microgram Joy-rides tablet |

Table 15. Hyoscine hydrobromide Chewable
**Ibuprofen Orodispersible or Chewable Capsule**

| What is it?         | Non opioid analgesic |
|---------------------|----------------------|
| **Mechanism of action** | Non-steroidal anti-inflammatory non-selective Cox inhibitor |
| **Starting dose**   | 200mg                |
| **Time to onset of effect** | 20-30 minutes onset [17] |
| **Formulation**     | Orodispersible tablets or chewable capsule |
| **Indication**      | Mild to moderate pain |
| **Common Adverse Effects** | Oedema; skin reactions; appetite decreased; diarrhoea; dizziness; gastrointestinal discomfort; gastrointestinal disorders; headache; nausea; rash (discontinue); vertigo; vomiting [16] |
| **Contraindications** | Allergy to aspirin or other NSAIDs, cardiovascular disease, gastrointestinal bleeding or history of perforation [16] |
| **Caution**         | Hepatic impairment   |
|                     | Renal failure        |
| **Licence**         | Licensed             |
| **Benefits**        | Licensed alternative route of administration |
| **Risks**           | Worsening COVID, GI bleeding |
| **Cost**            | £2.58 for 12x 200mg orodispersible tablets |
|                     | £3.23 for 12 x 100mg chewable capsule |

Table 16. Ibuprofen Orodispersible or Chewable Capsule
| **Ipratropium Nasal** |  |
|----------------------|---|
| **What is it?**       | Antimuscarinic |
| **Mechanism of action** | Antisecretory with bronchodilator properties |
| **Starting dose**     | 41 micrograms (2 sprays) 6 – 8 hourly prn |
| **Time to onset of effect** | 15 - 30 minutes [17] |
| **Formulation**       | Nasal spray |
| **Indication**        | Rhinorrhoea  
                        | Bronchial secretions  
                        | Respiratory secretions |
| **Common Adverse Effects** | Dizziness; dry mouth; headache; urinary disorders; vision disorders; vomiting; tachycardia; GI dysmotility; oropharyngeal irritation; bronchoconstriction [16] |
| **Contraindications** | Tachycardia >100  
                        | Cardiac conduction disorders [16] |
| **Caution**           | Narrow angle glaucoma  
                        | Bladder outflow obstruction  
                        | Cystic Fibrosis |
| **Licence**           | “off label” use of licensed product |
| **Benefits**          | Easy to use |
| **Risks**             | It is unknown whether sufficient systemic absorption is achieved via the intranasal route to improve bronchial and respiratory secretions |
| **Cost**              | £6.54 for 180 x 21 microgram/dose nasal spray |

Table 17. Ipratropium Nasal
**Levomepromazine Buccal or Sublingual**

| What is it?         | Anti-psychotic                                                                 |
|---------------------|-------------------------------------------------------------------------------|
| **Mechanism of action** | Central nervous system (CNS); receptors include adrenergic, dopamine, histamine, cholinergic and serotonin receptors |
| **Starting dose**    | 3mg-25mg once daily (or 6.25-12.5mg as required maximum three times in 24 hours) |
| **Time to onset of effect** | Not known (30 minutes via oral route) [17]                                     |
| **Formulation**      | oral tablet crushed, with water 6.25-25mg; OR 6mg tablets (Levinan®) 3mg (1/2 tablet) 4-6 hourly PRN (can be crush); OR injection 0.25-1ml sublingual |
| **Indication**       | second line for nausea and vomiting or delirium and agitation                  |
| **Common Adverse Effects** | postural hypotension; falls; “Asthenia; heat stroke” [16]                     |
| **Contraindications** | “CNS depression; comatose states; phaeochromocytoma”[16]                      |
| **Caution**          | Dementia, cardiac, prolonged QT, Parkinsonism, hypothyroidism, seizure, postural hyotension, myasthenia, renal and liver impairment [16] |
| **Licencing**        | oral tablet licensed; Levinan is an unlicensed preparation available on a named patient basis; off licence route for injectable levoempromazine |
| **Benefits**         | buccal administration of broad spectrum, long acting anti-psychotic*          |
| **Risks**            | injection concentration is 25mg/ml so challenging to administer 0.25ml, risk of injury from glass ampoule to lay carer |
| **Cost**             | £20.26 for 84 x 25mg tablets                                                                                     |
|                      | £20.13 for 10 x 25mg/ml ampoules for injection; 6mg tablets – special POA                                      |

Table 18. Levomepromazine Buccal or Sublingual

*Level of Evidence supporting its use (CBEM): Level 5; Authors EH and IW have clinical experience of its use.*
| **What is it?** | Anti-diarrheal agent |
|-----------------|----------------------|
| **Mechanism of action** | Opioid agonist effect on the large intestine |
| **Starting dose** | 2–4 mg as needed maximum 4 times a day |
| **Time to onset of effect** | 1 hour [17] |
| **Formulation** | Orodispersible tablets |
| **Indication** | Diarrhoea; colic |
| **Common Adverse Effects** | “Gastrointestinal disorders; headache; nausea” [16] |
| **Contraindications** | “Active ulcerative colitis; antibiotic-associated colitis; bacterial enterocolitis; conditions where abdominal distension develops; conditions where inhibition of peristalsis should be avoided” [16] |
| **Caution** | “Serious cardiovascular events (such as QT prolongation, torsades de pointes, and cardiac arrest)” [16] |
| **Licencing** | Licenced formulation |
| **Benefits** | a licenced orodispensible alternative for with good bioavailability in contrast to other alternatives such as hyoscine hydrobromide or glycopyrronium which have very low bioavailability when given via oral or buccal route |
| **Risks** | QT prolongation risk not yet widely recognised in clinical practice |
| **Cost** | £5.85 for 18 x 2mg orodispersible tablets |

Table 19. Loperamide Orodispensible
| **Lorazepam Sublingual** |
|--------------------------|
| **What is it?** | Anxiolytic |
| **Mechanism of action** | Benzodiazepine |
| **Starting dose** | 0.5-1mg |
| **Time to maximal effect** | 2.5 hours [17] |
| **Formulation** | Tablet - can be halved |
| **Indication** | anxiety, panic, agitation |
| **Common Adverse Effects** | “Apnoea; asthenia; coma; disinhibition; extrapyramidal symptoms; hypothermia; memory loss; speech slurred; suicide attempt” [16] |
| **Contraindications** | Severe hepatic failure, untreated sleep apnoea, myasthenia gravis, severe respiratory failure [16] |
| **Caution** | “Avoid prolonged use (and abrupt withdrawal thereafter); debilitated patients (reduce dose) (in adults); elderly (reduce dose) (in adults); history of alcohol dependence or abuse; history of drug dependence or abuse; myasthenia gravis; personality disorder (within the fearful group—dependent, avoidant, obsessive-compulsive) may increase risk of dependence; respiratory disease” [16] |
| **Licencing** | Off license route of a licensed formulation |
| **Benefits** | sublingual benzodiazepine, widely used in usual practice |
| **Risks** | Common misconception that the sublingual route is licensed due to widespread use |
| **Cost** | £3.29 for 28 x 1mg tablets |

Table 20. Lorazepam Sublingual
| **Miconazole Buccal** |  |
|----------------------|----------------|
| **What is it?**       | Azole anti-fungal |
| **Mechanism of action** | Disrupts the fungal cell member by inhibiting ergosterol synthesis |
| **Starting dose**     | 2.5ml four times a day oral gel; 50mg buccal tablet daily |
| **Time to effect**    | Uncertain [17] |
| **Formulation**       | Oral gel or buccal tablet |

“Oral gel should be held in mouth, after food” [BNF]

Buccal tablet is indicated for the treatment of oropharyngeal candidiasis in immunocompromised adults, Loramyc(R) 50 mg muco-adhesive buccal tablets should be applied to the upper gum just above the incisor tooth once daily for 7-14 days.

| **Indication** | Oropharyngeal candidiasis |
|----------------|---------------------------|
| **Common Adverse Effects** | “Skin reactions...dry mouth; nausea; oral disorders; vomiting” [16] |
| **Contraindications** | Pregnancy due to teratogenicity |
| **Caution** | CYP3A4 inhibitor; “Avoid in acute porphyrias” [16] |
| **Licencing** | Oral gel licenced and available to buy over the counter; muco-adhesive buccal tablet not yet listed in the BNF, not recommended by Scottish Medicines Consortium |
| **Benefits** | Over the counter, simple administration, licensed product |
| **Risks** | Choking is listed as a side effect in children, adults with compromised swallow may therefore also be at risk of choking, may not fully clear thrush if oesophageal involvement** |
| **Cost** | £4.38 for 80g x 20mg/g oromucosal gel; Loramyc(R) – special POA |

**Level of Evidence supporting its use:** “Miconazole muco-adhesive buccal tablets were shown to be non-inferior to another locally-acting miconazole preparation in the treatment of oropharyngeal candidiasis in patients with cancer of the head and neck who had received radiotherapy. There are no data comparing miconazole buccal tablets to treatments currently used in practice in NHS Scotland. The manufacturer did not present a sufficiently robust analysis to gain acceptance by SMC. The licence holder has indicated their intention to resubmit.” [21]
| What is it? | Opioid analgesic |
|------------|-----------------|
| Mechanism of action | Mu opioid receptor antagonist |
| Starting dose | IR suppository 10mg PR As Required, maximum 2 hourly; conversion oral 1:rectal 1 |
| Time to effect | 45-60 minutes [17] |
| Formulation | Immediate release - suppositories are available as a specials order; when prescribing “Both the strength of the suppositories and the morphine salt contained in them must be specified by the prescriber.” [16] |
| | Modified release - Morphine MST Continus® tablets given rectally |
| Indication | moderate to severe pain, breathlessness |
| Common Adverse Effects | “appetite decreased; asthenic conditions; gastrointestinal discomfort; insomnia; neuromuscular dysfunction” [16] |
| Contraindications | “Acute abdomen; delayed gastric emptying; heart failure secondary to chronic lung disease; phaeochromocytoma” [16] |
| Caution | See Direct.gov.uk for Drug Driving advice |
| Licencing | suppository licensed; rectal use of modified release tablets is an off licence use |
| Benefits | a transmucosal alternative to oral or subcutaneous morphine |
| Risks | unpredictability of bioavailability when rectal route used, “Delayed absorption of rectal morphine has contributed to respiratory arrest in infants.” [3] |
| Cost | £19.45 for 12 x 10mg suppositories; £5.20 for 60 x 10mg modified release tablets |

Table 22. Morphine Rectal
| **Morphine Sublingual** |
|-------------------------|
| **What is it?** | Opioid analgesic |
| **Mechanism of action** | Mu opioid receptor antagonist |
| **Starting dose** | 2.5mg given as drops, up to hourly |
| **Time to effect** | Uncertain (16-60 minutes oral, but drug not lipophilic therefore likely to be significantly longer) [17] |
| **Formulation** | 20mg/1ml oral solution, designed for oral administration, risk of unpredictable absorption OR injection |
| **Indication** | pain, breathlessness |
| **Common Adverse Effects** | “appetite decreased; asthenic conditions; gastrointestinal discomfort; insomnia; neuromuscular dysfunction” [16] |
| **Contraindications** | “Acute abdomen; delayed gastric emptying; heart failure secondary to chronic lung disease; phaeochromocytoma” [16] |
| **Caution** | See Direct.gov.uk for Drug Driving advice |
| **Licencing** | “off label” route of licensed oral solution; “off label” route of licensed injection |
| **Benefits** | a transmucosal alternative to oral or subcutaneous morphine |
| **Risks** | best avoided due to unpredictability of bioavailability when buccal route used, likely lower than oral due to solution not being lipophilic, likely no advantage over oral administration |
| **Cost** | £19.50 for 120ml x 20 mg/ml oral solution; £11.47 for 10 x 10mg/ml ampoules for injection |

Table 23. Morphine Sublingual
### Olanzapine Orodispersible

**What is it?**  
Anti-psychotic

**Mechanism of action**  
Antagonist to: D1, D2, D3, D4, 5HT(2A, 2C, 3, 6, 7), α1 and α2; anti-cholinergic

**Starting dose**  
2.5mg -10mg prn ON initially, can be increased to BD

**Time to onset of effect**  
Hours to days [17]

**Formulation**  
orodispersible tabs (placed on the tongue & allowed to dissolve, or can be dissolved in small volume water/juice)

**Indication**  
nausea and vomiting (low dose) or delirium and terminal agitation (higher dose)

**Common Adverse Effects**  
“Anticholinergic syndrome; appetite increased; arthralgia; asthenia; eosinophilia; fever; glycosuria; oedema; sexual dysfunction” [16]

**Contraindications**  
“Bone-marrow depression; hypereosinophilic disorders; low leucocyte count; low neutrophil count; myeloproliferative disease; paralytic ileus” [16]  
Narrow angle glaucoma [17]

**Caution**  
Fatalities when injected due to over sedation or cardiorespiratory depression. Increased risk of this is co-administered with midazolam.

**Licencing**  
“off label” use of licensed drug if used for nausea and vomiting

**Benefits**  
improves mood, appetite, sleep as well as nausea and vomiting, and delirium ***

**Risks**  
hyper somnolence, if used long term patients will require blood monitoring – lipids, FBC, BM

**Cost**  
£6.86 for 28 x 5mg orodispersible tablets sugar free – those containing sugar are much more expensive

| Table 24. Olanzapine Orodispersible |
|-------------------------------------|

***Level of Evidence supporting its use as an anti-emetic (CBEM): 1a (multiple meta-analyses)***

Number Needed to Treat to Benefit: 5; Number Needed to Treat to Harm: 19 [22]
**Ondansetron Orodispensible or Rectal**

| What is it?          | Anti-emetic          |
|----------------------|----------------------|
| **Mechanism of action** | Anti-serotonin 5HT3   |
| **Starting dose**    | buccal 4mg prn, max 16mg in 24 hours; rectal 16mg suppositories |
| **Time to onset of effect** | Uncertain (<30 minutes with oral route) [17] |
| **Formulation**      | orodispersible film 4mg OR orodispersible tablets 4mg 6-8 hourly PRN max 16mg/24hr OR 16mg suppositories only dose available |
| **Indication**       | nausea and vomiting   |
| **Common Adverse Effects** | “Constipation; feeling hot; headache; sensation abnormal” [16] |
| **Contraindications** | “Congenital long QT syndrome” [16] Serious drug interaction with metoclopramide due to combined QT prolongation effect [17] |
| **Caution**          | May reduce efficacy of tramadol and paracetamol [17] |
| **Licencing**        | Licensed formulation for an “off label” indication in palliative care |
| **Benefits**         | licenced oro dispersible and rectal alternative anti-emetic |
| **Risks**            | constipation, more costly than other alternatives such as olanzapine |
| **Cost**             | £28.50 for 10 x 4mg or £57 for 10 x 8mg oro dispersible films; £43.38 for 10 x 4mg or £85.43 for 10 x 8mg oro dispersible tablets; £14.39 for 1 x 16mg suppository |

Table 25. Ondansetron Orodispensible or Rectal
### Oxycodone Sublingual

| **What is it?** | Opioid analgesic |
|----------------|------------------|
| **Mechanism of action** | Mu opioid agonist |
| **Starting dose** | 1.25-2.5mg given as drops, maximum 1 hourly |
| **Time to effect** | Uncertain (20-30 minutes with oral route) [17] |
| **Formulation** | OxyNorm® Concentrate 10mg/ml oral solution |
| **Indication** | pain, breathlessness |
| **Common Adverse Effects** | “Anxiety; bronchospasm; depression; diarrhoea; dyspnoea; gastrointestinal discomfort; hiccups; mood altered; tremor” [16] |
| **Contraindications** | “Acute abdomen; chronic constipation; cor pulmonale; delayed gastric emptying” [16] |
| **Caution** | See Direct.gov.uk for Drug Driving advice |
| **Licencing** | “off label” route of licensed oral solution |
| **Benefits** | a transmucosal alternative to oral or subcutaneous morphine |
| **Risks** | unpredictability of bioavailability when sublingual or buccal route used, likely lower than oral due to solution not being lipophilic |
| **Cost** | £46.63 for 120ml x 10mg/ml oral solution |

Table 26. Oxycodone Sublingual
| **Paracetamol Orodispensible or Rectal** |
|-------------------------------|----------------------------------|
| **What is it?**               | Non-opioid analgesic              |
| **Mechanism of action**      | Weak COX2 and peroxidase inhibitor |
| **Starting dose**            | 500mg -1000mg, maximum four times a day |
| **Time to onset of effect**  | Uncertain (15-30 minutes with oral route) [17] |
| **Formulation**              | Paracetamol FasTab 250mg oradispersible tablets (2-4 tablets per dose, dependent on weight and liver function) Paracetamol suppositories 1g; n.b. bioavailability is 60% compared with oral administration[3] |
| **Indication**               | pain, fever                       |
| **Common Adverse Effects**   | rectal “anorectal erythema” with rectal preparation [16] |
| **Contraindications**        | severe liver dysfunction, 500mg QDS maximum if weight less than 50Kg |
| **Caution**                  | Old age, poor nutritional state, fasting, anorexia, weight <50kg, chronic alcohol use [17] |
| **Licencing**                | both are licensed formulation      |
| **Benefits**                 | transmucosal alternatives for managing fever |
| **Risks**                    | ensuring correct number of orodispersible are used; ensuring that dose is reduced to 500mg QDS if weight less than 50kg or liver function tests severely deranged |
| **Cost**                     | £4.12 for 24 x 250mg orodispersible tablets (Fastmelts - would need 4 tablets per 1g dose); £59.50 for 10 x 1g suppositories |

Table 27. Paracetamol Orodispensible or Rectal
| What is it?    | Anti-emetic |
|--------------|-------------|
| Mechanism of action | Antagonist to: D2, 5HT (2A and 2C), H1 and α1, and muscarinic receptors |
| Starting dose | 3mg to 6mg every 12 hours [17] |
| Time to maximal effect | 8 hours (4 hours with regular dosing) |
| Formulation | 3mg orodispersible tablets (Buccastem) |
| Indication | dizziness, nausea |
| Common Adverse Effects | “Agitation; amenorrhoea; arrhythmias; constipation; dizziness; drowsiness; dry mouth; erectile dysfunction; galactorrhoea; gynaecomastia; hyperprolactinaemia; hypotension (dose-related); insomnia; leucopenia; movement disorders; neutropenia; parkinsonism; QT interval prolongation; rash; seizure; tremor; urinary retention; vomiting; weight increased” [16] |
| Contraindications | “CNS depression; comatose states; phaeochromocytoma” [16] |
| Caution | Photosensitivity |
| Licencing | Licensed formulation |
| Benefits | buccal alternative anti-emetic, widely used in clinical practice |
| Risks | oral and skin reactions possible, constipating |
| Cost | £27.61 for 50 x 3mg buccal tablets |

Table 28. Prochlorperazine Buccal
| **Risperidone Orodispensible** |  |
|---|---|
| **What is it?** | Anti-psychotic |
| **Mechanism of action** | “Risperidone is a dopamine D2, 5-HT2A, alpha1-adrenoceptor, and histamine-1 receptor antagonist.” [BNF] |
| **Starting dose** | 0.5mg OD (can be increased to BD if needed) |
| **Time to effect** | Hours to days |
| **Formulation** | Orodispensible tablet |
| **Indication** | Delirium, terminal agitation |
| **Common Adverse Effects** | Anaemia; anxiety; appetite abnormal; asthenia; chest discomfort; conjunctivitis; cough; depression; diarrhoea; dyspnoea; epistaxis; fall; fever; gastrointestinal discomfort; headache; hyperglycaemia; hypertension; increased risk of infection; joint disorders; laryngeal pain; muscle spasms; nasal congestion; nausea; oedema; oral disorders; pain; sexual dysfunction; skin reactions; sleep disorders; urinary disorders; vision disorders; weight decreased” [16] |
| **Contraindications** | Hypersensitivity to the active substance or to any of the excipients |
| **Caution** | “Avoid in Acute porphyrias; cataract surgery (risk of intra-operative floppy iris syndrome); dehydration; dementia with Lewy bodies; prolactin-dependent tumours” [16] Seizure, Parkinsonism, renal and liver failure, old age [16] |
| **Licencing** | “off label” use of a licensed formulation |
| **Benefits** | Orodispensible alternative anti-psychotic |
| **Risks** | Narrower spectrum of action than olanzapine, currently not widely use outside of psychiatry |
| **Cost** | £18.28 for 28 x 500micrograms oro dispersible tablets |

Table 29. Risperidone Orodispensible
| **Tramadol Orodispensible** |
|-----------------------------|
| **What is it?**             | opioid (CD Schedule 3) |
| **Mechanism of action**     | Mu opioid, SSRI, stimulate serotonin and noradrenaline |
| **Starting dose**           | 50mg maximum four times a day |
| **Time to effect**          | Uncertain (30-60 minutes with oral) [17] |
| **Formulation**             | orodispersible tablets |
| **Indication**              | pain |
| **Common Adverse Effects**  | “fatigue” [16]; hallucinations, delirium |
| **Contraindications**       | “Acute intoxication with alcohol; acute intoxication with analgesics; acute intoxication with hypnotics; acute intoxication with opioids; compromised respiratory function (in children); not suitable for narcotic withdrawal treatment; uncontrolled epilepsy” [16] |
| **Caution**                 | Increased risk of seizure and serotonin syndrome |
| **Licencing**               | Licensed formulation |
| **Benefits**                | licensed orodispersible opioid |
| **Risks**                   | seizures, hallucinations |
| **Cost**                    | £7.12 for 60 x 50mg orodispersible tablets |

Table 30. Tramadol Orodispensible
Discussion

Paediatric palliative has historically made greater use of oral transmucosal drug delivery for symptom relief in the community than adult palliative care. This practice offers an opportunity for rapid administration of needle-free symptom management in adults for whom transfer to hospital or hospice is not their preference or may be inappropriate, without delay inherent in subcutaneous medication administration by healthcare professionals in the community.

Use of licenced orodispersible medication in novel ways in adult palliative care has the potential to minimise the necessity for including “off license” or “unlicensed” products in the list above. Health care professionals should use licensed alternatives in preference to “off license” or “unlicensed” products. However, situations may arise where, due to the nature of a patients’ condition, symptom(s), or the complexity of the clinical situation (including drug and staff shortages), there are no licensed alternatives available. In these circumstances it is necessary to “give patients (or their carers) sufficient information about the medicines you propose to prescribe to allow them to make an informed decision”, answering any “questions from patients (or their carers) about medicines fully and honestly”. [20]

Therefore “off license” or “unlicensed” alternatives have been included above where the author panel agreed that there is sufficient evidence, clinical experience or expertise of their use.

Reporting of learning from the experience in using transmucosal drugs in adult palliative care in the literature is encouraged to inform future practice. If combined with further research this learning could lead to long-term changes in clinical practice, perhaps reducing the need for subcutaneous medication administration in the community in future.

Limitations

Due to the Covid-19 pandemic and the urgent need to generate a list of transmucosal medications there was insufficient time to undertake a rapid review of every medication listed above in order to establish an up to date evidence base for each.

It is outside the scope of this document to be able to offer guidance on the order of transmucosal drug selection to achieve symptom management, i.e. which drug would be first second or third line for any given symptom.

Unlicensed alternatives that have been reported in the literature but are not listed in the BNF, PCF or APPM are not included given that this list may be used by physicians who are not specialists in palliative medicine. Consequently, the list of transmucosal drugs in this article may not include all those which some specialist may elect to use.

Conclusion

Transmucosal medications offer the possibility of enabling rapidly delivered needle-free symptom relief in the community without the need to wait for a healthcare practitioner to visit.
A practical list of 29 medications have been identified and collated for health care professionals delivering care at the end of life to consider using in their practice. The list draws on existing knowledge of transmucosal delivery, in large part gained from clinical experience by colleagues in paediatric palliative care.

Should it be necessary to utilise this list of transmucosal drugs to deliver symptom management then any experience gained should be combined and reported either on www.palliativedrugs.com or in the format of published articles. Combined with further research, this experience offers the possibility of reducing injection frequency and inherent delays in medication administration, particularly in the community setting.

References

1. Kendall J, Maconochie I, Wong IC, Howard R, DIASAPE study; A novel multipatient intranasal diamorphine spray for use in acute pain in children: pharmacovigilance data from an observational study Emergency Medicine Journal, 2015 32(4):269-273
2. Lam JK, Xu Y, Worsley A, Wong IC, Oral transmucosal drug delivery for pediatric use, Advanced Drug Delivery Review. 2014 Jun 73:50-62
3. Anderson B, Goodbye to needles, Arch Dis Child 2013 98: 718-719
4. Spathis A, Harrop E, Robertshaw C, et al, Learning from paediatric palliative care: Lessons for adult practice, Palliative Medicine 2012 26: 777
5. COVID-19 management of End of Life symptoms – COMMUNITY SETTINGS, 24/3/2020 Version 1.3, Wessex Palliative Care Physicians 2020
6. Barnet Primary Care Guide During Covid-19 (Patient Age ≥ 12), Version 4.1: 25 March 2020
7. Community EOLC Alternative Meds Symptom Guidelines, March 2020, Oxfordshire, M Preslind
8. Clinical guide for symptom management using non-oral, non-parenteral routes of administration during the coronavirus pandemic, , March 2020, Oxfordshire, M Preslind
9. Symptom Control in the last days of life during COVID-19 pandemic, March 2020, Anonymous
10. Pre-emptive prescribing: COVID 19, Sheffield, March 2020, Anonymous
11. COVID-19 and Palliative, End of Life and Bereavement Care in Secondary Care Role of the specialty and guidance to aid care, 22 March 2020, Northern Care Alliance NHS Group and the Association for Palliative Medicine of Great Britain and Ireland by: Dr Iain Lawrie FRCP, MRCGP and Fiona Murphy MBE
12. Instruction sheet 3 for EMIS production, Anticipatory Meds Worksheet, V1.2, March 2020, SHFT/Solent NHS Trust
13. Non-injectable symptom control medication list, Palliative care team business continuity planning for Covid-19 March 2020, Anonymous
14. Supportive and Palliative Care Temporary Guideline, Additional Considerations During Pandemic Coronavirus Patients who are dying of causes other than Covid-19, March 2020 www.scottishpalliativecareguidelines.scot.nhs.uk, Accessed April 2020
15. EMERGENCY RESPONSE: Temporary End of LIFE CARE Symptom Control Guidance for Use in the COVID-19 crisis, Worcestershire and Herefordshire STP EOLC Emergency COVID 19 group 20 March 2020 Version 1, http://www.wmcares.org.uk/wmpcp/guide/, Accessed April 2020
16. British National Formulary (BNF) 79, BMJ Group and Pharmaceutical Press, March 2020
17. Palliative Care Formulary 6th Edition, Palliativedrugs.com Ltd, 2017
18. The Association of Paediatric Palliative Medicine Master Formulary (APPM) 5th edition, 2020www.appm.org.uk
19. Enteral Drug Handbook 3rd Edition, Pharmaceutical Press, 2015
20. Joint statement on community based prescribing for COVID-19 symptomshttps://content.govdelivery.com/accounts/UKCQC/bulletins/285a90b, Accessed 13.04.2020
21. Miconazole, https://www.scottishmedicines.org.uk/medicines-advice/miconazole-muco-adhesive-buccal-tablet-loramyc-fullsubmission-51708/, Accessed 03.04.2020
22. Sutherland A, Naessens K, Plugge E, et al, Olanzapine for the prevention and treatment of cancer-related nausea and vomiting in adults. Cochrane Database of Systematic Reviews 2018, Issue 9. Art. No.: CD012555