Bulletin 132 | April 2016

PrescQIPP Community Interest Company

Immediate release fentanyl (DROP-List)

This is one of a number of bulletins providing further information on medicines contained in the PrescQIPP DROP-List (Drugs to Review for Optimised Prescribing). This bulletin focuses on immediate release fentanyl products and provides the rationale for new patients to be commenced on immediate release morphine and for current patients to be considered for a switch to immediate release morphine or one of the less costly immediate release fentanyl products. Information on clinical and safety issues to consider, as well as potential savings are provided. Further bulletins, including the DROP-List,[1] are available on the PrescQIPP website: www.prescqipp.info

Recommendations

- In line with NICE guidance, offer oral immediate release morphine for the first line rescue medication of breakthrough pain in patients on maintenance oral morphine treatment. Do not offer fast-acting fentanyl as first line rescue medication (a NICE Do Not Do Recommendation).
- Immediate release fentanyl may be considered for breakthrough pain in adult patients using opioid therapy for chronic cancer pain, when other short-acting opioids are unsuitable. Prescribing should be in line with local policy, e.g. formulary guidelines.
- The availability of a number of different formulations of immediate release fentanyl products with different dosage instructions and pharmacokinetic profiles creates potential for prescribing and dispensing errors.
  - » Products should be prescribed by brand to reduce this risk.
  - » Organisations may wish to restrict the number of products included on local formularies.
- An individual's circumstances should be considered carefully to ensure they fulfil the necessary requirements for use of a transmucosal product, e.g. current opioid dose, ability to access, use, store and dispose of the product reliably, etc.
- Patients receiving immediate release fentanyl who are suitable for immediate release morphine (and haven't had it first line) could be considered for a switch to immediate release morphine. There is no well-established method for converting between them, and immediate release morphine is usually dosed as a proportion of the background analgesia dose. Appropriate specialist input should be sought.
- Patients receiving the most costly immediate release fentanyl products (Actiq® lozenges, Instanyl® nasal spray) who can't be switched to immediate release morphine could be considered for a switch to a less costly immediate release fentanyl product. Immediate release fentanyl products are not interchangeable. Do not convert patients on a microgram per microgram basis from one to another; it is necessary to titrate the new formulation. Appropriate specialist input should be sought.
- Identify patients regularly using more than 2 - 4 doses of immediate release fentanyl for breakthrough pain/24 hours for review.
- Immediate release fentanyl products are licensed only for the management of breakthrough pain in adult patients using opioid therapy for chronic cancer pain. Use outside of the licence (e.g. for non-cancer pain or for patients not taking at least 60mg of oral morphine daily or equivalent) has safety implications and should be reviewed.

Background

The PrescQIPP DROP-List is an accumulation of medicines that are regarded as low priority, poor value for money or medicines for which there are safer alternatives. The DROP-List also includes medicines which could be considered for self care with the support of the community pharmacist, plus it now incorporates some of NICE's Do Not Do Recommendations. Immediate release fentanyl features on the DROP-List as an item that is poor value for money compared to immediate release morphine, and for which there is a NICE Do Not Do Recommendation. There are also a number of important safety considerations associated with its use.

In England and Wales, over £10.8 million is spent on immediate release fentanyl products over the course of a year (ePACT Oct - Dec 2015). Reducing the use of immediate release fentanyl by using immediate release morphine as the first line choice (and immediate release fentanyl only in limited circumstances where other short-acting opioids are unsuitable) has the potential to release significant saving. As with all switches, individual patient circumstances need to be borne in mind. However, with tight switching criteria, assistance from practice nurses, support from your local CCG prescribing teams and the input of relevant specialist teams where appropriate (e.g. palliative care), it is hoped that GPs will participate in realising the cost savings.

Rationale for restricting the use of immediate release fentanyl

Breakthrough pain and immediate release fentanyl products

Breakthrough pain is a transient exacerbation of pain that occurs either spontaneously or in relation to a specific predictable or unpredictable trigger despite relative stable and adequately controlled background pain. It is a common and distinct component of cancer pain.[2]

Fentanyl is a strong μ-opioid receptor agonist (as is morphine). It is suitable for transmucosal administration as it has a relatively low molecular weight and, unlike morphine, is lipophilic. Fentanyl itself cannot be patented, but novel delivery systems can and a variety of preparations are currently available (see table 1). The pharmacokinetic characteristics of these products vary and they are not interchangeable.[3]

All of the immediate release fentanyl products are licensed for the management of breakthrough pain in adult patients (over 18 years) using opioid therapy for chronic cancer pain (except Actiq®, which is licensed from 16 years old).[4-10] Patients receiving maintenance opioid therapy are defined in the product literature as those who are taking at least 60mg of oral morphine daily, at least 25 micrograms of transdermal fentanyl per hour, at least 30mg of oxycodone daily, at least 8mg of oral hydromorphone daily or an equianalgesic dose of another opioid for a week or longer.[4-10] None of the available products are licensed for any other type of pain. Although anecdotally there has been interest in the use of transmucosal fentanyl for managing other types of non-cancer pain, e.g. refractory migraine or pain at dressing changes, there is very limited published evidence relating to these uses. This should be considered alongside the safety signals relating to immediate release fentanyl (including unlicensed use), which include reports of deaths in opioid non-tolerant patients given this treatment for headaches (see 'Safety' section).[11]

Unlike immediate release morphine, which is dosed as a proportion of the regular 24 hour dose of background analgesia, immediate release fentanyl doses are established by individual titration (see table 1). This is because the effective dose of immediate release fentanyl cannot be reliably predicted from the maintenance dose of opioid. More than two-thirds of patients find an effective and tolerable dose of immediate release fentanyl. Patients should be monitored closely during the initial (and subsequent) dose titration period.[3]

Table 1. Immediate release fentanyl products and selected prescribing information for adult doses[4-10]

Product	Presentation	Dose titration	Maximum frequency of use	Maximum dose per episode
Abstral® ProStrakan Pharmaceuticals Ltd	**Sublingual tablets** 100 micrograms 200 micrograms 300 micrograms 400 micrograms 600 micrograms 800 micrograms	Initially 100 micrograms repeated if necessary after 15-30 minutes; adjust dose according to response - consult product literature.	Maximum 4 episodes/24 hours. Minimum 2 hours apart*#	800 micrograms
Effentora® Teva UK Ltd	**Buccal tablets** 100 micrograms 200 micrograms 400 micrograms 600 micrograms 800 micrograms	Initially 100 micrograms repeated if necessary after 30 minutes; adjust dose according to response - consult product literature.	Maximum 4 episodes/24 hours. Minimum 4 hours apart#	800 micrograms
Recivit® Grünenthal Ltd	**Sublingual tablets** 133 micrograms 267 micrograms 400 micrograms 533 micrograms 800 micrograms	Initially 133 micrograms repeated if necessary after 15-30 minutes; adjust dose according to response - consult product literature.	Maximum 4 episodes/24 hours. Minimum time interval not stated*#	800 micrograms
Actiq® Teva UK Ltd	**Lozenges (buccal)** 200 micrograms 400 micrograms 600 micrograms 800 micrograms 1200 micrograms 1600 micrograms	Initially 200 micrograms (over 15 minutes) repeated if necessary 30 minutes after first dose was commenced; adjust dose according to response - consult product literature.	Maximum 4 episodes/24 hours. Minimum time interval not stated*#	At 1600 microgram dose a second dose is only likely to be required by a minority of patients.
Breakyl®, Meda Pharmaceuticals Ltd	**Buccal film** 200 micrograms 400 micrograms 800 micrograms	Initially 200 micrograms; adjust dose according to response - consult product literature.	Maximum 4 episodes/24 hours. Minimum 4 hours apart#	1.2 mg

Product	Presentation	Dose titration	Maximum frequency of use	Maximum dose per episode
Instanyl® Takeda UK Ltd	**Nasal spray** 50 micrograms 100 micrograms 200 micrograms	Initially 50 micrograms into one nostril, repeated once if necessary after 10 minutes; adjust dose according to response – consult product literature.	Maximum 4 episodes/24 hours. Minimum 4 hours apart#	400 micrograms
PecFent® Archimedes Pharma UK Ltd	**Nasal spray** 100 micrograms 400 micrograms	Initially 100 micrograms into one nostril; adjust dose according to response – consult product literature.	Maximum 4 episodes/24 hours. Minimum 4 hours apart#	800 micrograms

* The recommended interval between episodes is given in the table in accordance with the Summary of Product Characteristics. However, the Palliative Care Formulary (PCF) recommends that in general, a minimum interval between treatments of ≥4hours is appropriate, on the basis that it was used by most studies, and more frequent dosing than four hourly appears to increase the maximum plasma concentration achieved with the subsequent dose of fentanyl.[3]

Product information for immediate release fentanyl products generally states that a maximum of four breakthrough pain episodes/24hours can be treated; if more than four breakthrough pain episodes are experienced in 24 hours a review of the background analgesia is necessary. However, the BNF and the PCF suggest that regular daily use of breakthrough medication twice daily or more should prompt a review and possible increase in the dose of the regular strong opioid.[3,12]

National guidance

The NICE clinical guideline on opioids in palliative care (CG140) published in May 2012 states the following for first line treatment for breakthrough pain in patients who can take oral opioids:[13]

- Offer oral immediate release morphine for the first line rescue medication of breakthrough pain in patients on maintenance oral morphine treatment.
- **Do not** offer fast-acting fentanyl as first line rescue medication (a NICE Do Not Do Recommendation).
- If pain remains inadequately controlled despite optimising treatment, consider seeking specialist advice.

The guideline is aimed at patients with pain associated with advanced and progressive conditions including cancer, heart failure, chronic illness such as kidney, liver and respiratory disease, and neurodegenerative diseases.[13]

The Scottish Medicines Consortium have advised that Abstral® sublingual tablets, Effentora® buccal tablets, Instanyl® nasal spray and PecFent® nasal spray, should be restricted for use within NHS Scotland for the management of breakthrough pain in adult patients using opioid therapy for chronic cancer pain, when other short-acting opioids are unsuitable.[14-18]

The Palliative Care Formulary (PCF) suggests the following in patients with cancer taking regular strong opioids and experiencing cancer-related breakthrough pain:

Use oral immediate release strong opioids first line and titrate accordingly (include a trial of an oral solution if tablets not adequate); only when inadequate with regards to speed of onset of action or prolonged undesirable effects should the transmucosal products be considered.

A patient's circumstances should be considered carefully to ensure they fulfil the necessary requirements for use of a transmucosal product; e.g. current opioid dose, ability to access, use, store and dispose of the product reliably, etc.[3]

Clinical effectiveness

For NICE CG140, the guideline development group (GDG) considered data from one randomised controlled trial and two systematic reviews (including a Cochrane review) that compared immediate release morphine with immediate release fentanyl. The GDG was satisfied that there was limited evidence to suggest that fentanyl is more clinically effective than immediate release morphine (and immediate release oxycodone) for the management of breakthrough pain. However, it felt the cost impact of recommending fentanyl over immediate release morphine or oxycodone would be considerable and therefore could not be justified. Therefore, the GDG agreed to recommend that immediate release fentanyl is not offered (as first line rescue medication).[19]

Since this guideline was issued, NICE have published an evidence update on opioids in palliative care (Evidence Update 58, May 2014) which identified a 2013 Cochrane review assessing opioid analgesics for managing breakthrough pain in patients with cancer.[20,2] This was an update of the Cochrane review considered by the GDG and included 15 studies, however only two were considered to be of direct relevance to NICE CG140, and data from these studies had been considered in the original guideline;[20] they compared transmucosal fentanyl to immediate release morphine tablets. Both studies began with an open-label phase in which the dose of immediate release fentanyl was titrated to find a successful dose for each individual. Patients not titrated successfully in this phase were excluded. Meta-analysis of data from these two studies for pain intensity difference at 15 minutes reported a statistically significant difference favouring transmucosal fentanyl compared with morphine tablets (mean difference=0.37, 95% CI 0.00 to 0.73, p=0.048; 2 studies, n=154). Both the statistical and clinical significance of this finding have been questioned.[21] Statistical significance is not clear cut, with the lower boundary of the confidence interval touching 0.00 (i.e. the point of no difference). Clinicians also need to consider whether a 0.37 point difference on an 11 point pain intensity scale represents a difference that is clinically meaningful. In August 2015, after receiving feedback questioning the validity of the authors' conclusions, the Cochrane Editorial Unit withdrew this Cochrane review on the basis that it was misleading.[21]

The PCF includes commentary on some of the active comparator studies of transmucosal fentanyl products. The authors remark on how well oral morphine actually performs in these studies, noting that unlike the fentanyl product, the oral morphine was not optimized in a titration phase and was given as tablets rather than as a solution, which is absorbed and acts more quickly.[3]

Since the Cochrane review was published, two further randomized controlled trials comparing immediate release fentanyl to an active comparator for breakthrough cancer pain have been identified. One compared two different formulations of fentanyl nasal spray.[22] The other compared sublingual fentanyl to oral morphine solution.[23] Although this study reported a statistically significant difference between treatments favouring sublingual fentanyl, the study size (n=40) and methodological limitations (including lack of proper randomization) mean that further studies addressing this question are needed.

Safety

In response to a number of deaths and patient safety incidents associated with opioid dosing errors, the National Patient Safety Agency (NPSA) produced a Rapid Response Report on opioid medicines in 2008. The aim of the guidance was to ensure that all health professionals involved in the prescribing, dispensing or administration of opioids were aware that they have the responsibility to check that an intended opioid dose is safe and appropriate for that patient. They must also be familiar with the characteristics, e.g. dosing increments and side effects, of the opioid being used.[24]

In 2007, after reports of serious overdoses and deaths in the USA, the Food and Drug Administration issued a safety warning about the use of Fentora® (Effentora®). Factors which contributed to the adverse drug events included improper:

- Patient selection, e.g. non-opioid tolerant, acute (non-cancer) pain
- Dosing, e.g. wrong dose prescribed, exceeding recommended maximum use
- Product substitution, e.g. like for like swap from Actiq® to Fentora®.

The importance of the product being prescribed by health professionals fully aware of the prescribing information, the need for correct patient selection and the lack of interchangeability of the different products was emphasised.[11,3]

Fentanyl is metabolised by CYP3A4. Hepatic metabolism is reduced by grapefruit juice and a number of medications including macrolide antibiotics, azole antifungals and some protease inhibitors. Consult the product literature for details of interactions, contraindications and precautions.[4-10]

As with all opioids, risk of addiction and misuse should be borne in mind. The British Pain Society have stated that clinical experience suggests immediate release preparations are more associated with tolerance and problem drug use. They advise that, where possible, modified release opioids administered at regular intervals should be used to manage persistent pain. They do recognise that in some circumstances, including when background pain is well controlled with modified release preparations but the patient has infrequent, short-lived episodes of increased pain, the use of immediate release preparations may be justified.[25]

The availability of a number of different formulations of immediate release fentanyl products with similar strengths but different dosage instructions and pharmacokinetic profiles creates potential for prescribing and dispensing errors. Products should be prescribed by brand to reduce this risk and organisations may wish to restrict the number of products included on local formularies.

Safe storage and disposal of products is essential. They must be kept out of reach of children; accidental deaths have occurred.[3]

Patient factors

Fentanyl is metabolised by the liver to inactive and non-toxic metabolites, and may therefore be preferred to morphine and several other opioids when renal function is impaired. However not all renal impairment necessitates a switch in opioid, and in some cases a dose reduction or increase in the dosing interval may be sufficient to continue with the first line opioid.[26]

The patient's circumstances need careful consideration to ensure they fulfil the necessary requirements for use of a transmucosal product. This will include their current opioid dose and their ability to access, use, store and dispose of the product reliably.[3]

When the decision to use an immediate release fentanyl product has been made, consideration should be given to which type of transdermal fentanyl product may be more suitable for an individual:

- Nasal products generally work quicker and are shorter lasting (less oral absorption) than the sublingual/buccal route. They may be preferred in the presence of severe dry mouth or mucositis.
- Sublingual/buccal may be preferred if the patient has nose bleeds.[3]
- Patients may have an individual preference. It has been reported anecdotally that experience with palliative care patients has found Effentora® takes longer to dissolve than Abstral®, feels uncomfortable and can leave a prolonged taste, and that patients tend to prefer Abstral® and Actiq® to Effentora®.[27]

Costs

There is a significant difference in cost between immediate release fentanyl products and other immediate release strong opioids such as morphine and oxycodone. Table 2 below illustrates the cost differences. Example morphine and oxycodone doses are included for comparison; the list is not exhaustive for the strengths available or the dosages used in practice and is for illustrative purposes only.

Table 2. Immediate release fentanyl, morphine and oxycodone products and price comparison[28,29]

Product	Cost per dose unit	Cost of 28 days treatment with three doses/day
Abstral® sublingual tablets (all strengths)	£4.99	£419.16
Effentora® buccal tablets (all strengths)	£4.99	£419.16
Recivit® sublingual tablets (all strengths)	£4.24	£356.16
Actiq® lozenges (all strengths)	£7.01	£588.84
Breakyl® buccal film (all strengths)	£4.99	£419.16
Instanyl® nasal spray (all strengths)	£5.95	£499.80
PecFent® nasal spray (all strengths)	£4.56	£383.04
Morphine sulphate tablets 10mg	£0.09	£7.56
Morphine sulphate tablets 20mg	£0.19	£15.96
Morphine sulphate oral solution 10mg/5ml 10mg dose	£0.09	£7.56
Morphine sulphate oral solution 10mg/5ml 20mg dose	£0.18	£15.12
Oxycodone 5mg capsules	£0.20	£16.80
Oxycodone 10mg capsules	£0.41	£33.60
Oxycodone oral solution 5mg/5ml5mg dose	£0.19	£15.96
Oxycodone oral solution 5mg/5ml10mg dose	£0.39	£32.63

Prescribing review and switching options

Local policy should outline the circumstances in which immediate release fentanyl can be considered, which products can be prescribed and who can prescribe them. Any review of prescribing should reflect local as well as national guidelines.

- New patients should be commenced on immediate release morphine for breakthrough pain unless there is a compelling case for avoiding morphine or for using an alternative.[13]
- Patients receiving immediate release fentanyl who are suitable for immediate release morphine (and haven't had it first line) could be considered for a switch to immediate release morphine. There is no well-established method for converting between them, and immediate release morphine is usually dosed as a proportion of the background analgesia dose.[12,3] Appropriate specialist input should be sought.
- Patients receiving the most costly immediate release fentanyl products (Actiq® lozenges, Instanyl® nasal spray) who can't be switched to immediate release morphine could be considered for a switch to a less costly immediate release fentanyl product (see table 2 for prices). Immediate release fentanyl products are not interchangeable. Do not convert patients on a microgram per microgram basis from one to another; it is necessary to titrate the new formulation.[3-10] Appropriate specialist input should be sought.

- On switching, review the person's laxative and anti-emetic treatment to ensure side-effects are being effectively managed.[13]
- Patients regularly using more than 2-4 doses of immediate release fentanyl for breakthrough pain/24 hours should be reviewed by an appropriate person and an increase of background analgesia considered.[3-10]
- All strengths of each brand of immediate release fentanyl product cost the same.[29] Therefore, once the maintenance dose is reached (i.e. after titration) avoid prescribing doses as multiple dose units (unless this is essential to get the required dosage) as this increases the cost of treatment.
- Immediate release fentanyl should be prescribed by brand for safety reasons; any generic prescribing should be reviewed.
- Immediate release fentanyl products are licensed only for the management of breakthrough pain in adult patients using opioid therapy for chronic cancer pain.[4-10] Use outside of the licence (e.g. for non-cancer pain or for patients not taking at least 60 mg of oral morphine daily or equivalent) has safety implications and should be reviewed. Where such use is deemed to be appropriate, consider if it would be more appropriate for the relevant specialist to prescribe and manage it.

Savings

In England and Wales, over £10.8 million is spent on immediate release fentanyl products over the course of a year (ePACT Oct - Dec 2015).

The table below illustrates the significant savings that could be made by reducing and optimising the use of immediate release fentanyl products.

	National figure	Per 100,000 patients
Annual savings if 10th percentile of cost per 1000 patients reached by all currently above it	£9,156,643	£15,118
Annual savings if 25th percentile of cost per 1000 patients reached by all currently above it	£6,846,382	£11,303
Annual saving if all Actiq® switched to alternative immediate release fentanyl product (with a cost of £4.99 or less per dose)	£1,676,317	£2,767

Summary

A number of immediate release fentanyl products licensed for the relief of breakthough pain for people with cancer are available. There is some limited evidence that immediate release fentanyl gives better pain relief at 15 minutes than immediate release morphine, however the clinical significance and the quality of the available data has been questioned. Nonetheless, for a minority of patients for whom morphine or other strong opioids are unsuitable they offer an alternative option. Careful patient selection by appropriately skilled clinicians is essential to ensure both safe and cost-effective use of these medicines.

References

1. PrescQIPP DROP-List. Bulletin available at www.prescqipp.info
2. Zeppetella G, Davies AN. Opioids for the management of breakthrough pain in cancer patients. Cochrane Database of Systematic Reviews 2013, Issue 10. Art. No.: CD004311. DOI: 10.1002/14651858.CD004311.pub3. Accessed via http://www.cochranelibrary.com on 28/6/15
3. Fentanyl (transmucosal) monograph. Palliative Care Formulary. Accessed via www.palliativedrugs.com on 30/6/15
4. Summary of Product Characteristics. Abstral® buccal tablets. ProStrakan Ltd. Date of revision of the text 4/4/14. Accessed via www.emc.medicines.org.uk July 2015
5. Summary of Product Characteristics. Effentora® 100 mcg sublingual tablets. Teva B.V. Date of revision of the text 25/2/15. Accessed via www.emc.medicines.org.uk July 2015
6. Summary of Product Characteristics. Recivit® sublingual tablets. Grünenthal Ltd. Date of revision of the text 9/1/15. Accessed via www.emc.medicines.org.uk July 2015
7. Summary of Product Characteristics. Actiq® 200 mcg lozenges. Teva Pharma B.V. Date of revision of the text 9/6/15. Accessed via www.emc.medicines.org.uk July 2015
8. Summary of Product Characteristics. Breakyl® 200 mcg buccal film. Meda Pharmaceuticals Ltd. Date of revision of the text 27/4/15. Accessed via www.emc.medicines.org.uk July 2015
9. Summary of Product Characteristics. Instanyl® 50, 100 and 200 mcg dose nasal spray. Takeda UK Ltd. Date of revision of the text 5/3/15. Accessed via www.emc.medicines.org.uk July 2015
10. Summary of Product Characteristics. PecFent® nasal spray. Archimedes Pharma UK Ltd. Date of revision of the text 30/3/15. Accessed via www.emc.medicines.org.uk July 2015
11. U.S. Food and Drug Administration (FDA). Information for Healthcare Professionals: Fentanyl Buccal Tablets (marketed as Fentora). FDA Alert [9/2007]. Accessed via www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm126082.htm on 28/6/15
12. Joint Formulary Committee. British National Formulary (online) London: BMJ Group and Pharmaceutical Press. Guidance on prescribing, Prescribing in palliative care. Accessed June/July 2015 via https://www.medicinescomplete.com/mc/bnf/current/
13. National Institute for Health and Care Excellence (NICE). Opioids in palliative care: safe and effective prescribing of strong opioids for pain in palliative care of adults (CG140). May 2012 https://www.nice.org.uk/guidance/cg140 Accessed 28/6/15
14. Scottish Medicines Consortium Fentanyl sublingual (Abstral) (No: 534/09). Advice issued 9/2/09. Accessed via www.scottishmedicines.org.uk on 30/06/15
15. Scottish Medicines Consortium Fentanyl buccal tablets (Effentora) (No: 510/08). Advice issued 9/2/09. Accessed via www.scottishmedicines.org.uk on 30/06/15
16. Scottish Medicines Consortium Fentanyl (Instanyl) (No: 579/09). Advice issued 9/11/09. Accessed via www.scottishmedicines.org.uk on 30/6/15
17. Scottish Medicines Consortium Fentanyl pectin nasal spray (PecFent) (No: 663/10). Advice issued 17/1/11. Accessed via www.scottishmedicines.org.uk on 30/06/15
18. Joint Formulary Committee. British National Formulary (online) London: BMJ Group and Pharmaceutical Press. 4.7.2. Opioid Analgesics, Fentanyl. Accessed June/July 2015 via https://www.medicinescomplete.com/mc/bnf/current/
19. National Collaborating Centre for Cancer (2012) Opioids in palliative care: safe and effective prescribing of strong opioids for pain in palliative care of adults. NICE guideline (CG140) (Full guideline) May 2012. Cardiff UK. Accessed via https://www.nice.org.uk/guidance/cg140/evidence/opioids-in-palliative-care-full-guideline-186485293 on 28/6/15
20. National Institute for Health and Care Excellence (NICE). Opioids in palliative care. Evidence Update 58, May 2014. Accessed via https://www.evidence.nhs.uk on 28/6/15
21. Zeppetella G, Davies AN. Opioids for the management of breakthrough pain in cancer patients. Cochrane Database of Systematic Reviews 2015, Issue 8. Art. No.: CD004311. DOI: 10.1002/14651858.CD004311.pub4. Accessed via http://www.cochranelibrary.com on 19/1/16

22. Mercadante S, Prestia G et al. Intranasal fentanyl versus fentanyl pectin nasal spray for the management of breakthrough cancer pain in doses proportional to basal opioid regimen. The journal of pain: official journal of the American Pain Society 2014;15(6):602-607
23. Velázquez Rivera I, Muñoz Garrido J et al. Efficacy of sublingual fentanyl vs. oral morphine for cancer-related breakthrough pain. Advances in therapy 2014;31(1):107-117
24. National Patient Safety Agency. Rapid Response Report: Reducing Dosing Errors with Opioid Medicines 2008. NPSA/2008/RRR05. Accessed via www.nrls.npsa.nhs.uk/resources/?EntryId45=59888 on 30/6/15
25. The British Pain Society 2010. Opioids for persistent pain: Good practice. A consensus statement. Accessed via www.britishpainsociety.org/british-pain-society-publications/professional-publications/ on 6/7/15
26. Crampton R, Beswick T. UKMi Q&A 402.2. Which opioids can be used in renal impairment? Date prepared 30/9/14. Accessed via https://www.evidence.nhs.uk on 28/6/15
27. London New Drugs Group APC/DTC Briefing. Fentanyl preparations for breakthrough cancer pain. August 2009. Accessed via https://www.evidence.nhs.uk on 28/6/15
28. Drug Tariff July 2015. Accessed via http://www.nhsbsa.nhs.uk/PrescriptionServices/4940.aspx on14/7/15
29. MIMS Accessed via http://www.mims.co.uk on 24/5/15

Additional PrescQIPP resources

 Briefing  Data pack  Implementation resources

Available here: https://www.prescqipp.info/resources/viewcategory/170-fentanyl

Information compiled by Lindsay Wilson, PrescQIPP Programme, March 2016 and reviewed by Katie Taylor, Senior Medicines Evidence Reviewer, April 2016

Non-subscriber publication August 2016.

Contact help@prescqipp.info with any queries or comments related to the content of this document.

This document represents the view of PrescQIPP CIC at the time of publication, which was arrived at after careful consideration of the referenced evidence, and in accordance with PrescQIPP's quality assurance framework.

The use and application of this guidance does not override the individual responsibility of health and social care professionals to make decisions appropriate to local need and the circumstances of individual patients (in consultation with the patient and/or guardian or carer). Terms and conditions