FENTANYL OROMUCOSAL FORMULATIONS FOR BREAKTHROUGH CANCER PAIN

HIGH RISK MEDICINES

NSW TAG NSW Therapeutic Advisory Group Inc.

This Advisory applies to ***rapid-acting buccal and sublingual formulations of fentanyl*** and is intended for use by health care professionals. (Intranasal fentanyl products are not discussed).

Deaths have occurred with the inappropriate dosing of these potent products in opioid-naïve patients

Appropriate selection of patient

USE **ONLY FOR BREAKTHROUGH CANCER PAIN (BTCP)** IN ADULTS WHO ARE:

- Opioid tolerant (i.e. **stabilised** for > 7 days on oral morphine daily doses ≥ 60 mg*); AND
- When other immediate release opioid formulations e.g. morphine and oxycodone are inadequate or unsuitable (e.g. dysphagia, intractable nausea/vomiting; poor absorption); AND
- Under the care of specialist palliative care clinician(s)

**Approximate daily dose equivalences:*
60 mg oral morphine = 30 mg oral oxycodone = 12 mg oral hydromorphone = 25 microgram/hour transdermal fentanyl

ALSO CONSIDER PATIENT-SPECIFIC RISK FACTORS: (for more details see full Product Information)

- Older age or frailty: greater susceptibility to adverse effects, especially in presence of co-morbidities/ polypharmacy or during acute illness e.g. infection or dehydration.
- Potential misuse, abuse, addiction and overdose: patient/family history or psychiatric history.
- Potential drug interactions: other sedative medicines, serotonergic medicines, CYP3A4 inhibitors and inducers.

Safe dosing & administration (details on following page)

- Document and communicate clearly the specific product and dosing information.
  - The various oromucosal fentanyl formulations are rapid-acting, however they **ARE NOT INTERCHANGEABLE. (Do NOT convert fentanyl products on a microgram: microgram basis,** including between oromucosal fentanyl products).
  - Numerous strengths of the various oromucosal fentanyl products are available.
  - Recommended maximum doses or frequencies should be stated and not exceeded.
  - Keep a record of supplied quantity and frequency of use.
- Frequently review adequacy of regular background opioid medication. If the dose of the regular opioid medication changes, re-titrate dose of oromucosal fentanyl product.
  - Dosing to treat and re-treat episodes of BTCP differ between the products.
- Tolerance to the analgesic effects but not adverse effects can develop quickly. Consider hyperalgesia, tolerance and progression of underlying disease if inadequate pain control.
- Monitor sedation and cardiorespiratory status of patient closely.

PATIENT/CARER COUNSELLING IS ESSENTIAL

- Discuss place in treatment plan, what to expect and specific instructions on use, possible side effects, what to do if side effects occur and provide a CMI and/or written information.

Appropriate storage, handling, recording & disposal

- Patients/carers should be educated about safe and appropriate storage and disposal.
- *KEEP OUT OF REACH OF CHILDREN* at all times as accidental exposure can be fatal.
- Never give a fentanyl product to another person for use.
- Record each formulation on its own separate page in the Schedule 8 register.
- In hospital, disposal in an appropriate, approved container and destruction of accountable medicines by healthcare workers requires witnessing, see NSW PD2017_026 and PD2013_043.

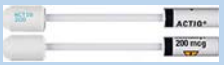
Key safety messages

- **Fentanyl must NOT be used in opioid-naïve patients: appropriate patient selection essential.**
- **Abstral®, Fentora® & Actiq® are NOT interchangeable.**
- **Provide explicit dosing instructions for management of breakthrough pain episodes and specify the maximum total dose in 24 hours.**
- **Always ask about breakthrough pain relief and confirm medicine, brand, strength, dosing instructions, circumstances and frequency of use.**
- **Ensure patients/carers are alert to signs of opioid overdose: sedation, respiratory depression, confusion.**
- **Extra precautions are required for safe use, storage and disposal of fentanyl products.**

Fentanyl Oromucosal Formulations
Important Dosing & Administration Information

HIGH RISK MEDICINES

*current brands available in Australia at the time of writing; BTCP = breakthrough cancer pain; mins = minutes

Brand* & Form	Abstral® Tablet	Fentora® Orally Disintegrating Tablet	Actiq® Lozenge on handle
Route	Sublingual 	Absorbed buccally (or sublingually) 	Buccal 
Dosing (Adults) These products are NOT registered for use in patients less than 18 years of age. These products are rapid-acting, however, they are **NOT INTERCHANGEABLE**. **DO NOT convert on a microgram per microgram basis** to other fentanyl products including converting between oromucosal fentanyl products.	**Start at** 100 micrograms; after 30mins, if required, give another 100 microgram tablet and consider increasing the tablet strength for the first dose of the next episode of BTCP. **Titrate** upwards as necessary through the range of available dosage strengths (100, 200, 300, 400, 600, 800 micrograms) **Maximum** 800 micrograms per BTCP episode. Wait at least 2 hours between treatment of BTCP episodes. If >4 BTCP episodes occur per day for 4 days, consider increasing the dose of the regular background opioid.	**Start at** 100 micrograms; after 30mins, if required, give another 100 microgram tablet and consider increasing the tablet strength for the first dose of the next episode of BTCP. **Titrate** upwards as necessary through the range of available dosage strengths (100, 200, 400, 600, 800 micrograms) **Maximum** 800 micrograms per BTCP episode. Wait at least 4 hours between treatment of BTCP episodes. If >4 BTCP episodes occur per day for several consecutive days, or 2 doses are needed to treat several consecutive episodes, consider increasing the dose of the regular background opioid.	**Start at** 200 micrograms; after 30mins, if required, give another 200 microgram lozenge and consider increasing the tablet strength for the first dose of the next episode of BTCP. **Titrate** upwards as necessary through the range of available dosage strengths (200, 400, 600, 800, 1200, 1600 micrograms) **Usual maximum** is 1600 micrograms per BTCP episode. (A second dose of 1600mcg is rarely needed). Wait at least 4 hours between treatment of BTCP episodes. If >4 BTCP episodes occur per day for 4 days, or 2 doses are needed to treat several consecutive episodes, consider increasing the dose of the regular background opioid.

Prescribing practice principles:

- initiate therapy with the lowest dose available
- aim to relieve an episode of BTCP with a single dose and minimal opioid adverse effects
- attempt to only use a maximum of 2 doses per BTCP episode
- preferably treat no more than 4 BTCP episodes/day (review and increase the dose of regular background opioid, if required)
- **always re-titrate** any oromucosal fentanyl at the recommended starting dose if:
  - the regular background opioid dose is increased; OR
  - changing brands (Note: patients should only be prescribed one brand of rapid release fentanyl at any one time).

Administration & key counselling points			
• If mouth is dry, moisten mouth with water before using. • Do not remove from packaging until required. • Do not eat or drink anything until dose is finished. • Fentanyl's activity is significantly reduced if swallowed.	Place tablet well under the tongue; do not swallow the tablet; allow it to dissolve completely without biting, chewing or sucking. • Once under the tongue, tablet falls apart almost immediately into small particles which dissolve resulting in release of fentanyl. • Onset of pain relief commences at approximately 10mins.	Place tablet between the cheek and gum near the back molar teeth (if using more than one tablet at a time, place tablets on each side of the mouth); alternatively, a tablet can be placed well under the tongue. Allow it to disintegrate without biting, chewing or sucking. • Allow 30mins for absorption, then if there are any bits of tablet left, patient can swallow them with a glass of water. • Onset of pain relief commences in 10-15mins.	Place lozenge in the mouth against the cheek and move it around the mouth using the handle. Allow it to dissolve without biting, chewing or sucking. • Optimal pain relief achieved if lozenge is dissolved over 15mins (not sooner). • Onset of pain relief commences within 15mins. • Lozenge resembles a lollipop. **DO NOT LEAVE IN REACH OF OTHERS** • If there is any lozenge left, dispose safely as per policy for Schedule 8 medicines. • Ensure good dental hygiene as the lozenge contains sugar.

References

- Australian Medicines Handbook, 2019. Adelaide: Australian Medicines Handbook Pty Ltd.
- CareSearch, 2016. *PHARMACY PROFILE: Oromucosal Fentanyl Preparations (Abstral® tablet, Actiq® lozenge and Fentora® tablet).* [Online] Available at: https://www.caresearch.com.au/caresearch/Portals/0/Documents/PROFESSIONAL-GROUPS/Nurses%20Hub/NHN_Pharmacy_Nov2016.pdf [Accessed 29 April 2019].
- TIRF REMS Access, 2012. *Transmucosal Immediate Release Fentanyl (TIRF) Products Risk Evaluation and Mitigation Strategy (REMS) Education Program for Prescribers and Pharmacists.* [Online] Available at: https://www.tirfremsaccess.com/TirfUI/rems/pdf/education-and-ka.pdf [Accessed 29 April 2019].

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