

The transdermal fentanyl patch is a long-acting controlled release preparation of a potent short-acting, lipophilic opioid. The amount of fentanyl released per hour is proportional to the surface area of the patch (25 mcg/h per 10 cm²). The patch comes in five sizes: 12.5, 25, 50, 75, and 100mcg/h. After patch application, a depot of fentanyl accumulates in the upper skin layers resulting in a slowly increasing serum level over 12 to 18 hours. Peak serum concentrations of fentanyl generally occur between 24 and 72 hours after initial application. Therefore, after initial patch application, supplemental analgesia must be provided with a short-acting opioid. After patch removal, serum fentanyl concentrations decline gradually due to ongoing absorption of the drug remaining in the skin, falling about 50% in approximately 17 hours (range 13-22h).

| Dose (mcg/h) | Size (cm ²) | Fentanyl Content (mg) |
|--------------|-------------------------|-----------------------|
| 12.5 | 5 | 1.25 |
| 25 | 10 | 2.5 |
| 50 | 20 | 5 |
| 75 | 30 | 7.5 |
| 100 | 40 | 10 |

The transdermal fentanyl patch is a rectangular transparent unit consisting of a protective liner and four functional layers including a copolymer membrane that controls the rate of fentanyl delivery to the skin surface. Caution should be used when patients switch between patches from different manufacturers as absorption rates may be different.

| Oral Morphine Equivalent Dose mg/24h | Transdermal Fentanyl Dose mcg/h |
|--------------------------------------|---------------------------------|
| 60-134 | 25 |
| 135-224 | 50 |
| 225-314 | 75 |
| 315-404 | 100 |
| 405-494 | 125 |
| 495-584 | 150 |
| 585-674 | 175 |
| 675-764 | 200 |
| 765-854 | 225 |
| 855-944 | 250 |
| 945-1034 | 275 |
| 1035-1124 | 300 |

Equianalgesic Conversion: There are two methods to calculate a starting dose: 1) the manufacturer recommends basing the initial dose on the previous 24 hour oral morphine dose (see box insert). Note, the dose ranges of morphine are very broad; 50% of patients will be under-dosed when this conversion table is used; or 2) use a 2:1 ratio of mg oral morphine sulfate/24h:mcg transdermal fentanyl/hr. For example, 100mg oral morphine/24h would be approximately equivalent to a 50mcg patch changed every 72h. Choose the lower end of the dosage range for the elderly and anyone with renal impairment as they are at greater risk of retaining drug and experiencing sedation/respiratory depression. When in doubt, start low and go slow; use PRN breakthrough doses of a short-acting opioid for interim analgesia. The maximal recommended dose of transdermal fentanyl is 300mcg/h.

Other Important Points

- **Transdermal fentanyl should not be used for acute pain, acute postoperative pain or in opioid-naïve patients**, as these patients are at high risk of respiratory depression and the dosage cannot be adjusted quickly.
- Although the approved dosing interval for transdermal fentanyl is 72 hours, studies suggest that up to 25% of cancer patients may require more frequent administration; for some the duration of analgesia is only 48 hours.

- When titrating, the recommended upward dose titration interval should not be more frequent than every 72 hours.
- Place patches on non-irradiated, hairless skin. If needed, clip hair, don't shave, as shaving can cause micro abrasions which may affect drug absorption. If site needs to be washed, do so with clear water; soaps, lotions, alcohols and other agents can also affect drug absorption.
- With the recent addition of a 12.5mcg patch, use in pediatrics may increase. It is approved for use over the age of 2 years. The studies have found younger children may require proportionately higher doses, have longer time to steady state, shorter half-life and poor skin adhesion.
- Do not cut or otherwise damage, fold, or partially occlude patches with non-porous dressings; the manufacturers do not recommend such practices as they will interfere with the delivery system, and there is potential for overdose.
- Overdose may also occur if the application area is warmed/heated (avoid heating pads or heated water beds).
- There are data to suggest that transdermal fentanyl has fewer GI side effects than oral sustained-release morphine.
- Every fentanyl patch removed must have a witnessed and documented disposal per hospital policy.
- Fentanyl is metabolized by CYP 3A4. Therefore patients taking CYP 3A4 inhibitors may result in increased plasma concentrations of fentanyl and associated side effects. Patients on CYP 3A4 inhibitors should be monitored closely for side effects for an extended period of time and appropriate dosage adjustments should be made if warranted.

References:

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- Muijsers RBR, Wagstaff AJ. Transdermal fentanyl: an updated review of its pharmacological properties and therapeutic efficacy in chronic cancer pain control. *Drugs* 2001; 61: 2289-2307.
- Skaer TL. Practice guidelines for transdermal opioids in malignant pain. *Drugs* 2004; 64(23): 2629-2638.
- Zernikow B, Michel E, Anderson B. Transdermal fentanyl in childhood and adolescence: A comprehensive literature review. *The Journal of Pain*. 2007; 8(3): 187-207.
- US Food and Drug Administration. Important Information for the Safe Use of Fentanyl Transdermal System (Patch). Silver Spring, MD. US Food and Drug Administration, 2007.