

Drug Utilization Evaluation: Transdermal Fentanyl

Fentanyl, a synthetic opioid, available for transdermal application, provides pain relief especially useful for patients with swallowing and other gastro-intestinal difficulties aggravated by oral drugs.¹ It is employed primarily in persistent moderate to severe chronic pain, malignant or non-malignant pain, which is not neuropathic.² Transdermal fentanyl provides convenience, high potency and up to three days of pain relief.

Previous DUR Board analyses indicated that transdermal fentanyl is frequently used in combination with other long-acting opioids.³ Other reported problems with fentanyl transdermal range from difficult dose conversions to unintended overdoses of patients or caregivers. The Drug Abuse Warning Network estimates 8,000 visits to ER during 2004 involved fentanyl.⁴ These visits were prompted both by abuse and accidental exposure, such as discarded patches that retain 28% to 85% of fentanyl after 72 hours.

Since approved in 1990 there have been 120 reported deaths associated with fentanyl patches. Periodically, the FDA has issued additional safety warnings about prescribing, use, and disposal, lengthening the black box warnings.^{5, 6, 7} Transdermal fentanyl is contraindicated in non-opioid tolerant patients, the management of acute pain or in patients who only require temporary analgesia, the management of post-operative pain, management of mild pain, management of intermittent pain. Opioid tolerance is defined by at least 60 mg of morphine daily, 30 mg of oral oxycodone, 8 mg of oral hydromorphone, or equianalgesic dose of another drug.

Questions:

- 1) What proportion of patients newly started on transdermal fentanyl have a previous history of opioid analgesic use?
 - a) What is the previous opioid dose for these patients?
 - b) What type of previous opioid are these patients using – long-acting, short acting, both
- 2) What is the initial fentanyl patch dose and approximately how often are patches changed?

Methods:

- Identify a cohort of transdermal fentanyl users between 1/1/06 and 6/30/06 with a minimum of 6 months FFS eligibility prior to index fill.
- Characterize cohort demographics
- Identify which patients have exposure to an opioid analgesic within 30 days index fill of transdermal fentanyl.
- Quantify the average equipotent dose of the previous opioid analgesic.
- Quantify the name and type (long versus short acting) of opioid used prior to new fentanyl start.
- Quantify the starting patch strength, if more than one patch strength is used, and approximately how often patch is replaced (e.g. Q72, Q48, Q24 hours).

Table 1 - Dose Conversion^{8,9}

Drug	Equianalgesic dose
Morphine	30
Hydrocodone	30
Hydromorphone	7.5
Levorphanol	1
Meperidine	300
Methadone	4
Oxycodone	20
Codeine	200
Propoxyphene	100

Results

During the study period 411 unique individuals had a claim for transdermal fentanyl. After excluding those with insufficient eligibility, 101 unique individuals were identified for analysis. The demographics of all users and the analysis cohort are described in the tables below. Based on these data, it appears as though the analysis group is similar to the overall population.

Table 2: Age

	Analysis Cohort		All Users	
n	101		408	
Average Age	47.3		49.1	
Age Category	count	%	count	%
<19	1	1.0%	2	0.5%
>=19 and <30	8	7.9%	27	6.6%
>=30 and <50	49	48.5%	184	45.1%
>=50	43	42.6%	195	47.8%

Table 3: Sex

	Analysis Cohort		All Users	
Sex	count	%	count	%
Female	73	72.3%	285	69.9%
Male	28	27.7%	123	30.1%

Table 4: Race

	Analysis Cohort		All Users	
Race	count	%	count	%
White	91	90.1%	369	90.4%
American Indian	6	5.9%	17	4.2%
Hispanic	2	2.0%	9	2.2%
Unknown	1	1.0%	3	0.7%
Asian	1	1.0%	4	1.0%
African American	0	0.0%	6	1.5%

Table 5 shows a break down of previous opioid use in the 101 patients in the analysis group. A total of 15 patients (15%) had no history of a long or short-acting opioid (opioid naive) 30 days prior to their initial fentanyl fill. Only 5 patients (5%) used another long-acting opioid prior to their initial fentanyl prescription. The majority, 67% of patients had a previous treatment with a short-acting opioid. The reminder, or 13%, had both a long and short acting opioid prior to their first fentanyl prescription. Of the patients who had a history of opioid use, 36 were estimated to be using less than 60mg morphine equivalent per day, which is recommended in the fentanyl package insert as the minimum dose consumed prior to initiating fentanyl. Thus, more than 50% of patients starting fentanyl either had no previous opioid or appeared to be using less than the recommended opioid dose prior to starting.

Table 5: Previous Opioid Use in 30 day prior to Initial Fentanyl Fill

Long-acting	Short-acting	Count	%	Average Total Dose (mg MSO4)	Count <60mg/day	%
no	no	15	14.9%		15	14.9%
no	yes	68	67.3%	69.6	36	35.6%
yes	no	5	5.0%	508.8	0	
yes	yes	13	12.9%	374.8	0	

Table 6 shows a breakdown of the frequency for which new users of fentanyl were changing their patches. The product is formulated to last approximately 72 hours, however, the package insert recognizes the need in some patients to reduce the interval to 48 hours if analgesia is not sufficient. In this analysis over 20% of new users of fentanyl appear to be changing their patches every 48 hours or less. The most frequent patch dose started was the 25 mcg/hr (48%) and 50 mcg/hr (30%) strength. Although this was a cohort of newly started patients, we found that 10 (10%) were using a concurrent long-acting opioid. This may reflect a conversion period of another long-acting opioid to fentanyl.

Table 6: Estimate of number of days between patch changes

Days per Patch	count	%
3	79	78.2%
2	18	17.8%
1	3	3.0%
other	1	1.0%

Discussion and Recommendations

In this analysis of prescription drug claims for transdermal fentanyl, 15% of new users appear to be beginning this potent medication without having previous exposure to shorter acting, less potent opioids. Another 36% of patients may be on lower than recommended doses of opioid prior to beginning fentanyl. Finally, close to 20% of new starts were prescribed the patches at a frequency of change ≤ 48 hours, perhaps without a sufficient trial period on the standard 72 hour cycle.

While these figures are subject to all of the limitations associated with dealing with administrative data, they do suggest the need for closer oversight of the use of this potentially dangerous and expensive medication.

It is recommended transdermal fentanyl be added as a recurrent RetroDUR criteria for review. The criteria for a patient profile review will be:

- Newly started patients without evidence of opioid use
- Newly started patients with evidence that they are replacing patches less than every 72 hours.

¹ Kornick CA et al. Benefit-Risk Assessment of Transdermal Fentanyl for the Treatment of Chronic Pain. Drug Safety. 2003. 26(13):951-973.

² Skaer TL. Practice Guidelines for Transdermal Opioids in Malignant Pain. Drugs. 2004. 64(23): 2629-2638.

³ DUE: Duplicate Long-Acting Opioids, Oregon DUR Board Meeting, September 7, 2006.

⁴ U.S. Dept. of Health & Human Services. Substance Abuse & Mental Health Services Administration. Drug Abuse Warning Network, 2004: National Estimates of Drug-Related Emergency Department Visits. Available at: <http://DAWNinfo.samsha.gov>.

⁵ FDA Public Health Advisory. Safety Warnings Regarding Use of Fentanyl Transdermal (Skin) Patches. July 15, 2005. <http://www.fda.gov/cder/drug/advisory/fentanyl.htm>.

⁶ Janssen, Important Drug Warning on changes in prescribing information for Duragesic. June 2005.

⁷ Janssen. Duragesic full prescribing information. 2003. Approved by FDA 2-4-2005.

⁸ CareOregon OPIOIDS AND CHRONIC NON-MALIGNANT PAIN: A CLINICIAN'S HANDBOOK. Available at: <http://www.careoregon.org/provider/documents/Opioids.pdf>.

⁹ Conversion between opioid analgesics – a practical guide from the University of Alberta. Available at: www.med.ualberta.ca/uofapain/opioidconversion.htm.