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Analysis of the Abuse and Diversion of the Buprenorphine Transdermal Delivery System

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Abstract: Prescription opioid abuse and diversion are major causes of morbidity and mortality in the United States. The buprenorphine transdermal delivery system (BTDS) is indicated for the treatment of moderate to severe chronic pain and provides a continuous dose of 5, 7.5, 10, 15, or 20 μg/h buprenorphine for 7 days. Quarterly rates of abuse and diversion of BTDS were compared with 4 comparator groups: 1) other buprenorphine products, 2) fentanyl patches, 3) extended-release (ER) opioid tablets/capsules, and 4) ER tramadol. Data were obtained from the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS) System Poison Center, Drug Diversion, Treatment Programs Combined (Opioid Treatment and Survey of Key Informants' Patients Programs), and College Survey Programs. Rates were calculated using case counts per population and mentions per prescriptions filled. Poisson regression analysis was used to compare mean rates over time across drug groups after allowing for drug group-specific dispersion parameters. Population adjusted abuse rates were low for BTDS in all of the RADARS System programs compared with the other comparator groups. Findings were similar for the prescription adjusted rates, with BTDS reported at the lowest rates in all programs. Route of abuse differed slightly for BTDS and the comparator groups depending on the program. BTDS was abused and diverted at low rates compared with the other opioid groups in 5 programs of the RADARS System using either population-based rates or prescription dispensed rates.

***Perspective:** Data from the RADARS System show the BTDS is abused and diverted at low rates compared with other opioid groups including other forms of buprenorphine, fentanyl patches, ER opioid formulations, and ER tramadol.*

***Key words:** Buprenorphine, Butrans, opioid abuse, opioid diversion, RADARS.*

Prescription drug abuse is a substantial burden on the United States. According to the 2011 National Survey on Drug Use and Health nearly 2 million individuals met criteria for abuse or were dependent on prescription opioid analgesics.[18] Death rates from prescription opioid abuse and misuse increased more than threefold from 1999 to 2006 and emergency department visits because of prescription drug overdose

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doubled from 2004 to 2010.[8,19,21] Overdose fatality rates have now surpassed those from motor vehicle accidents and are now the number one cause of accidental death in the United States.[12]

Not all opioids are associated with the same risk for abuse. Some opioids are associated with a higher risk for nonmedical use and diversion than other opioids.[6,22] However, even products with the same active ingredient may have varying degrees of risk dependent upon dosage strength and form. Previous analysis has shown, for example, that tamper-resistant formulations of extended-release (ER) oxycodone are associated with less abuse, misuse, and diversion than the original formulations of this product.[16] Postmarketing surveillance and analysis involving abuse, misuse, and diversion then plays a critical role in informing the process of safe prescribing.

The buprenorphine transdermal delivery system (BTDS), marketed in the United States under the brand name Butrans (Purdue Pharma, Stamford, CT) was approved by the U.S. Food and Drug Administration in August, 2010 and released to the market on January 20, 2011. It is a schedule III partial opioid agonist product indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.[2,23] BTDS is designed to deliver 5, 7.5, 10, 15, or 20 μg/h buprenorphine. Transdermal delivery of buprenorphine is associated with a low risk of adverse effects. According to the product insert, the most common adverse effects are local skin reactions to the patch or systemic effects typical of treatment with opioids such as vomiting or constipation. In one large multicenter noninterventional postmarketing study involving transdermal administration of buprenorphine for moderate to severe chronic pain, adverse effects occurred in 0.8% of patients.[13]

Investigations assessing the diversion and abuse of BTDS have not been previously reported. We used the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS) System to provide the first postmarketing data on the abuse and diversion of BTDS compared with other prescription opioid drug groups. The RADARS System provides postmarketing surveillance of prescription medication misuse, abuse, and diversion to regulatory agencies, policy making organizations, health care providers, and pharmaceutical companies.

Methods

We compared event rates for abuse, diversion, and endorsements of BTDS with 4 comparator groups: 1) other buprenorphine products, 2) fentanyl patches, 3) ER opioid tablets/capsules, and 4) ER tramadol. The drugs included in each of the comparator groups and the reasons for their use in comparison are detailed in Table 1.

The RADARS System uses several unique populations to address the entire spectrum of drug abuse.[3,5,7,8,14,15,24] Data from the following RADARS System programs were included: 1) Poison Center Program, 2) Drug Diversion Program, 3) Treatment Center Programs Combined (Opioid Treatment Program and the Survey of Key Informants' Patients Program combined), and 4) College Survey Program. BTDS was approved by the U.S. Food and Drug Administration in August, 2010 and first released for prescription on January 20, 2011. The reporting period of January 1, 2011 through December 31, 2013 was chosen using the date of first availability by prescription and first BTDS surveillance through the most recent quarter of surveillance. However, BTDS was added to the Treatment Center Programs surveys on July 1, 2011, so the time period for these programs is July 1, 2011 to December 31, 2013. The Treatment Center Programs do not collect information on ER tramadol, so this comparator group was not included in the analyses for these programs.

The Poison Center Program obtains data from the general population seeking advice after an exposure to a potentially toxic substance, including exposures to prescription analgesic drugs. In 2013, the Poison Center Program received data from 49 regional U.S. Poison Centers in 46 states (91.5% of total U.S. population). Standardized data fields and systematic data collection processes are used to record case data (demographic and exposure characteristics, substances involved, exposure reason, medical outcome, etc) for exposures to prescription medications.

The Drug Diversion Program provides surveillance data on prescription drug diversion from municipal police

Table 1. Drugs Included in Each Comparator Group and Reason for Comparison

Comparator Group	Drugs Included and Reason for Comparison*
BTDS	Buprenorphine (transdermal patches only)
Other buprenorphine	Buprenorphine (single ingredient buprenorphine tablets, combination buprenorphine tablets, combination buprenorphine oral films) *Included for comparison because buprenorphine has same active ingredient
Fentanyl patches	Fentanyl (transdermal patches only) *Included for comparison because similar product form/drug delivery system
ER opioid tablets/capsules	Oxycodone (ER tablets/capsules) Hydrocodone (ER tablets/capsules) Hydromorphone (ER tablets/capsules) Oxymorphone (ER tablets/capsules) Tapentadol (ER tablets/capsules) Morphine (ER tablets/capsules) Methadone (tablets/capsules) *Included for comparison because of the same indication and has been previously compared with regard to abuse and diversion potential
ER tramadol	Tramadol (ER tablets) *Included for comparison because a similar volume of prescriptions dispensed