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Reviewers: Sarah Kang, PharmD, MSP, BCPS
Division of Pharmacovigilance II (DPV II)

Tracy Pham, PharmD, Drug Utilization Analyst
Division of Epidemiology II (DEPI-II)

Medical Officer: Ivone Kim, MD, FAAP
DPV I

Team Leaders: Neha Gada, PharmD, BCPS
DPV II

Rajdeep Gill, PharmD
DEPI-II

Deputy Division Directors: Ida-Lina Diak, PharmD, MS
DPV II

Associate Director for Special Initiatives (Acting) LCDR Grace Chai, PharmD
Office of Surveillance and Epidemiology (OSE)

Product Name: Butrans (buprenorphine transdermal system)

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EXECUTIVE SUMMARY

This review from the Office of Pharmacovigilance and Epidemiology (OPE) evaluates FDA Adverse Event Reporting System (FAERS) reports and the utilization patterns for buprenorphine transdermal system (Butrans) in pediatric patients through age 17 years. OPE conducted this review in accordance with the Food and Drug Administration Amendments Act (FDAAA) Pediatric Research Equity Act (PREA). This review focuses on serious unexpected adverse events associated with buprenorphine transdermal system in pediatric patients.

The FDA approved Butrans on June 30, 2010 for management of moderate to severe chronic pain in patients requiring a continuous, around-the-clock opioid analgesic for an extended period of time. On April 16, 2014, Butrans' indication was updated to the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate in adult patients. Butrans was studied in the pediatric population in an open-label, multicenter, multiple-dose study of the safety and pharmacokinetics (PK) of Butrans in patients aged 7 through 16 years but it was not designed to assess efficacy. Given the small database size, there were not sufficient data to fully describe the safety profile of Butrans in pediatric patients. Therefore, the sponsor did not request a Butrans indication in the pediatric population.

We reviewed serious FAERS reports with buprenorphine transdermal system in the pediatric population through age 17 years during the period June 30, 2010 - June 26, 2019. We identified no new safety concerns for buprenorphine transdermal system. However, we identified one case of an unintentional exposure resulting in excessive blinking and unusual face/mouth movement in a patient for whom buprenorphine transdermal system was not indicated.

To provide context for the FAERS reports, we examined the pediatric utilization of buprenorphine transdermal system based on prescription dispensing data from U.S. outpatient retail pharmacies from July 2010 through June 2019. Our analyses showed that pediatric patients younger than 18 years of age accounted for 0.1% or less of total estimated number of patients who received prescriptions dispensed for buprenorphine transdermal system annually, throughout the study period. Cumulatively from July 2018 through June 2019, an estimated 70 pediatric patients received prescriptions dispensed for buprenorphine transdermal system.

Based on our findings of the one FAERS case and low utilization in pediatric patients, OPE recommends no regulatory action at this time and will continue to monitor all adverse events associated with the use of buprenorphine transdermal system.

1 INTRODUCTION

This review from the Office of Pharmacovigilance and Epidemiology (OPE) evaluates FDA Adverse Event Reporting System (FAERS) reports and the utilization patterns for buprenorphine transdermal system (Butrans) in pediatric patients through age 17 years. OPE conducted this review in accordance with the Food and Drug Administration Amendments Act (FDAAA) Pediatric Research Equity Act (PREA). This review focuses on serious unexpected adverse events associated with buprenorphine transdermal system in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Buprenorphine is a partial opioid agonist. FDA first approved buprenorphine transdermal system on June 30, 2010 for the management of moderate to severe chronic pain in patients requiring a continuous, around-the-clock opioid analgesic for an extended period of time. On September 10, 2013, FDA announced proposed class-wide safety labeling changes for extended-release (ER)/long acting (LA) opioid analgesic product.¹ On April 16, 2014, Butrans indication was updated to the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate in adult patients.^{2,3}

On September 14, 2017, FDA asked the Anesthetic and Analgesic Drug Products Advisory Committee (AADPAC) and the Drug Safety and Risk Management Advisory Committee (DSaRM) to discuss a supplemental application for Butrans evaluating a study in pediatric patients aged 7 through 16 years.⁴ The committees discussed the findings of the Butrans' clinical study conducted in pediatric patients, and how much detail from this post marketing requirement (PMR) study should be included in Section 8.4 of the labeling.⁴ Overall, the committees were concerned about the study because of inadequate sample size and the studied patient population was not representative of all those who would receive treatment in the clinical setting (e.g. palliative and oncology patients).⁴

On October 13, 2017, Butrans' sponsor, Perdue Pharma, fulfilled the PMR to examine pediatric pharmacokinetics (PK) and safety in pediatric patients 7 through 16 years old through the completion of study BUP3031. Of note, the sponsor did not seek a pediatric indication due to limited data available. BUP3031 was an open-label, multicenter, multiple-dose study of the safety and pharmacokinetics of Butrans in patients aged 7 through 16 years, who required around-the-clock opioid analgesia for moderate-to-severe persistent pain. Two patients in BUP3031 developed QT prolongation at doses of 10 micrograms. QT prolongation is already labeled under Warnings and Precautions, and "the overall data did not suggest a new safety signal."⁵ FDA revised the Pediatric Use section of the labeling, incorporating the results of study BUP3031. This pediatric labeling change triggered this PREA review. Safety and efficacy data reflected in the pediatric labeling change for Butrans are described below:⁶

The safety and efficacy of Butrans in patients under 18 years of age has not been established. Butrans has been evaluated in an open-label clinical trial in pediatric patients. However, definitive conclusions are not possible because of the small sample size.

Although buprenorphine transdermal system use in children was discussed during the AADPAC and DSaRM AC meeting held on September 14, 2017, buprenorphine transdermal system has not been presented before the Pediatric Advisory Committee previously.

1.2 RELEVANT LABELED SAFETY INFORMATION

WARNING: ADDICTION, ABUSE, and MISUSE; RISK EVALUATION AND MITIGATION STRATEGY (REMS) LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL EXPOSURE; NEONATAL OPIOID WITHDRAWAL SYNDROME; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

See full prescribing information for complete boxed warning.

- Butrans exposes users to risks of addiction, abuse, and misuse, which can lead to overdose and death. Assess patient's risk before prescribing, and monitor for these behaviors and conditions. (5.1, 10)
- To ensure that the benefits of opioid analgesics outweigh the risks of addiction, abuse, and misuse, the Food and Drug Administration (FDA) has required a Risk Evaluation and Mitigation Strategy (REMS) for these products. (5.2)
- Serious, life-threatening or fatal respiratory depression may occur. Monitor closely, especially upon initiation or following a dose increase. Instruct patients on proper administration of Butrans to reduce the risk. (5.2)
- Accidental exposure to Butrans, especially in children, can result in fatal overdose of buprenorphine. (5.2)
- Prolonged use of Butrans during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated. If prolonged opioid use is required in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available. (5.3)
- Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing for use in patients for whom alternative treatment options are inadequate; limit dosages and durations to the minimum required; and follow patients for signs and symptoms of respiratory depression and sedation. (5.4, 7)

-----CONTRAINDICATIONS-----

- Significant respiratory depression (4)

- Acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment (4)
- Known or suspected gastrointestinal obstruction, including paralytic ileus (4)
- Hypersensitivity to buprenorphine (4)

-----**WARNINGS AND PRECAUTIONS**-----

- Life Threatening Respiratory Depression in Patients with Chronic Pulmonary Disease or in Elderly, Cachectic, or Debilitated Patients: Monitor closely, particularly during initiation and titration. (5.6)
- Adrenal Insufficiency: If diagnosed, treat with physiologic replacement of corticosteroids, and wean patient off of the opioid. (5.7)
- Risk of Prolonged QTc Interval: Avoid in patients with Long QT Syndrome, family history of Long QT Syndrome, or those taking Class IA or Class III antiarrhythmic medications. (5.8, 12.2)
- Severe Hypotension: Monitor during dose initiation and titration. Avoid use of Butrans in patients with circulatory shock (5.9)
- Risks of Use in Patients with Increased Intracranial Cranial Pressure, Brain Tumors, Head Injury, or Impaired Consciousness: Monitor for sedation and respiratory depression. Avoid use of Butrans in patients with impaired consciousness or coma. (5.10)

-----**ADVERSE REACTIONS**-----

Most common adverse reactions ($\geq 5\%$) include: nausea, headache, application site pruritus, dizziness, constipation, somnolence, vomiting, application site erythema, dry mouth, and application site rash. (6.1)

Section 8 USE IN SPECIFIC POPULATIONS, the *Pediatric Use* subsection includes the following information:

The safety and efficacy of Butrans in patients under 18 years of age has not been established. Butrans has been evaluated in an open-label clinical trial in pediatric patients. However, definitive conclusions are not possible because of the small sample size.

2 METHODS AND MATERIALS

2.1 FAERS SEARCH STRATEGY

DPV searched the FAERS database with the strategy described in **Table 1**.

Table 1. FAERS Search Strategy*		
	Search #1	Search #2
Date of Search	June 27, 2019	June 27, 2019
Time Period of Search	June 30,2010 [†] - June 26, 2019	June 30,2010 [†] - June 26, 2019
Search Type	Quick Query, Product- Manufacturer Reporting Summary	Quick Query, Product- Manufacturer Reporting Summary

	Search #1	Search #2
Product Terms	Product names- Butrans, buprenorphine transdermal system	Product Active Ingredient- buprenorphine
MedDRA Search Terms (Version 22.0)	All Preferred Terms (PTs)	All PTs
Other Criteria	N/A	transdermal route, narrative text search “transdermal”

* See **Appendix A** for a description of the FAERS database.
† U.S. approval date

2.2 DRUG UTILIZATION

We used proprietary databases available to the FDA to conduct the drug utilization analyses in this review. See Appendix B for full database descriptions and limitations.

We used the IQVIA National Sales Perspectives™ (NSP) database to determine the primary settings of care for the utilization of buprenorphine transdermal system (including Butrans and its generic products) based on the estimated number of boxes of buprenorphine transdermal system sold from manufacturer to various U.S. settings of care in 2018.

We also used the IQVIA Total Patient Tracker™ (TPT) database to provide the annual estimated number of patients who received prescriptions dispensed for buprenorphine transdermal system from U.S. retail pharmacies, stratified by patient age (0 - <18, and ≥ 18 years), from July 2010 through June 2019.

3 RESULTS

3.1 FAERS

Table 2 presents the number of adult and pediatric FAERS reports from June 30, 2010 - June 26, 2019 with buprenorphine transdermal system.

	All reports (U.S.)	Serious† (U.S.)	Death (U.S.)
Adults (≥ 18 years)	5255 (4554)	992 (750)	157 (77)
Pediatrics (0 - <18 years)‡	22 (17)	12 (7)	1 (0)

* May include duplicates and transplacental exposures, and have not been assessed for causality

Table 2. Total Adult and Pediatric FAERS Reports* Received by FDA from June 30, 2010 - June 26, 2019 with Buprenorphine Transdermal System

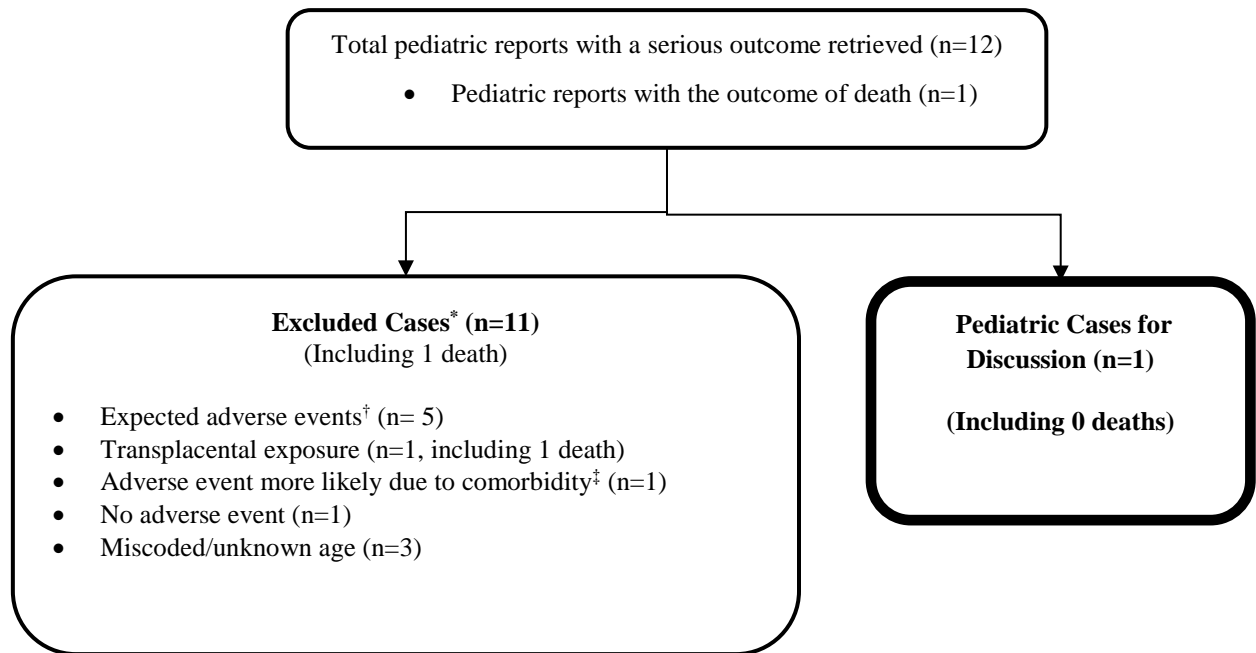
	All reports (U.S.)	Serious [†] (U.S.)	Death (U.S.)
[†] For the purposes of this review, the following outcomes qualify as serious: death, life- threatening, hospitalization (initial or prolonged), disability, congenital anomaly, required intervention, and other serious important medical events.			
[‡] Butrans labeling under Section 8.4 notes the safety and efficacy in patients under 18 years of age has not been established.			

3.1.1 Selection of Serious Pediatric Cases in FAERS

Our FAERS search retrieved 12 serious pediatric reports from June 30, 2010 - June 26, 2019 with buprenorphine transdermal system. We excluded 11 reports from the case series after review. We summarize the remaining one case in section 3.1.3 below.

Figure 1 presents the selection of cases for the pediatric case series.

Figure 1. Selection of Serious Pediatric Cases with Buprenorphine Transdermal System



* DPV reviewed and excluded these cases from further discussion for the reasons listed above.

[†] Expected events included somnolence, hallucination, constricted pupil, respiratory depression, QT prolongation, and headache. These events are well-described in the Butrans labeling for adult patients.

[‡] The case described a 13-year-old male with a medical history of sickle cell disease and eight previous hospitalizations for vaso-occlusive pain crisis who experienced another episode of vaso-occlusive pain crisis on the day Butrans was discontinued.

3.1.2 Summary of Fatal Pediatric Cases (N=0)

We did not include any fatal pediatric adverse event cases in our case series.

3.1.3 Summary of Non-Fatal Pediatric Serious Cases (N=1)

3.1.3.1 Unintentional exposure

FAERS case#10330986, version 1/Foreign/Expedited report:

A 3-year-old male “accidentally” put an unknown dose of Butrans transdermal patch on his chest after removing the patch belonging to his father from “the bin.” The patient was admitted into the hospital for a few days. On an unspecified date, the patient experienced adverse events described as, “eyes were constantly blinking and a lot of unusual movement around the face and mouth.” The patient recovered an unspecified time after hospitalization.

Reviewer’s comment:

This case represents an unintentional exposure to buprenorphine transdermal systems for an unapproved indication and age. The patient experienced excessive eye blinking and unusual face/mouth movement unspecified time after exposure to buprenorphine transdermal system. Butrans labeling includes muscle spasm and tremor, however, this case lacks sufficient information to assess the reported adverse events.

3.2 DRUG UTILIZATION DATA

Based on the sales distribution data, approximately 87% of buprenorphine transdermal system boxes were sold to the retail pharmacy settings in 2018, followed by the non-retail settings at 10% and the mail-order/specialty setting at 2%.⁷ Therefore, we examined the utilization of buprenorphine transdermal system in the retail pharmacy settings.

3.2.1 Patient Data

Throughout the study period from July 2010 through June 2019, pediatric patients younger than 18 years of age accounted for 0.1% or less of the total annual estimated number of patients who received prescriptions dispensed for buprenorphine transdermal system from U.S. retail pharmacy settings. From July 2018 through June 2019, an estimated 70 patients younger than 18 years of age received prescriptions dispensed for buprenorphine transdermal system. See **Table 3** below.

Table 3. Annual Estimated Number of Patients Who Received Prescriptions Dispensed for Buprenorphine Transdermal System from U.S. Retail Pharmacies, Stratified by Patient Age, July 2010 through June 2019

	Time Period									
	July 2010 - June 2011		July 2011 - June 2012		July 2012 - June 2013		July 2013 - June 2014		July 2014 - June 2015	
	Patients	%	Patients	%	Patients	%	Patients	%	Patients	%
Buprenorphine Transdermal System	51,560	100.0%	130,894	100.0%	132,928	100.0%	147,184	100.0%	164,780	100.0%
0 - 17 years	46	0.1%	147	0.1%	133	0.1%	180	0.1%	203	0.1%
18+ years	50,243	97.4%	127,930	97.7%	129,564	97.5%	143,996	97.8%	162,692	98.7%
Unknown Age	1,760	3.4%	3,208	2.5%	4,798	3.6%	6,702	4.6%	3,664	2.2%
	July 2015 - June 2016		July 2016 - June 2017		July 2017 - June 2018		July 2018 - June 2019			
	Patients	%	Patients	%	Patients	%	Patients	%		
	Patients	%	Patients	%	Patients	%	Patients	%		
Buprenorphine Transdermal System	150,675	100.0%	145,085	100.0%	115,827	100.0%	109,930	100.0%		
0 - 17 years	115	0.1%	109	0.1%	116	0.1%	68	0.1%		
18+ years	150,964	100.2%	144,666	99.7%	115,919	100.1%	109,890	100.0%		
Unknown Age	140	0.1%	1,173	0.8%	398	0.3%	230	0.2%		

Source: IQVIA Total Patient Tracker™, July 2010 through June 2019. Data extracted January 2020.

*Of note, there was a change in the underlying data and methodology by IQVIA to manage prescription claims that are voided or reversed. Prescription volumes dispensed from the retail pharmacies have been historically adjusted back to January 2017, data prior to January 2017 have not been adjusted to the new methodology; therefore, there is a trend break and any changes over time must be interpreted in the context of the changes in methodology. In 2017, an estimated 6% of total prescription claims for buprenorphine transdermal system dispensed from U.S. retail pharmacies appeared to have been voided or reversed.

4 DISCUSSION

We reviewed all serious FAERS reports with buprenorphine transdermal system in the pediatric population through age 17 years during the period June 30, 2010 - June 26, 2019. We identified one case of an unintentional exposure resulting in excessive blinking and unusual face/mouth movement in a patient for whom buprenorphine transdermal system is not indicated.

Additionally, we examined the utilization patterns of buprenorphine transdermal system based on prescription dispensing data from the U.S. outpatient retail pharmacies. The drug utilization analyses showed that pediatric patients younger than 18 years of age accounted for 0.1% or less of total patients who received prescriptions dispensed for buprenorphine transdermal system annually, throughout the study period from July 2010 through June 2019. An estimated 70 pediatric patients received prescriptions dispensed for buprenorphine transdermal system from July 2018 through June 2019. Drug use findings should be interpreted in the context of the known limitations of the databases and methodology used. Patient estimates provided in this review are nationally projected based on a sample of outpatient retail prescription claims, and therefore have some degree of inherent sampling error. However, the data cannot be validated due to lack of access to medical records in the data source. In addition, projected pediatric patient estimates are based on small sample sizes, and therefore are not intended to be representations of exact enumerations and should be interpreted with caution.

5 CONCLUSION

Based on an examination of FAERS reports and drug utilization data, OPE did not identify any pediatric safety concerns for buprenorphine transdermal system at this time.

6 RECOMMENDATION

OPE recommends no regulatory action at this time and will continue to monitor all adverse events associated with the use of buprenorphine transdermal system.

7 REFERENCES

1. New Safety Measures Announced for Extended-release and Long-acting Opioids. In. <https://www.fda.gov/drugs/information-drug-class/new-safety-measures-announced-extended-release-and-long-acting-opioids>: U.S. Food & Drug Administration; September 10, 2013.
2. Butrans [Prescribing Information]. In. Stamford, CT: Purdue Pharma L.P.; April 2014.
3. Supplement Approval letter. In. *NDA 021306/S-018*.
https://www.accessdata.fda.gov/drugsatfda_docs/applletter/2014/021306Orig1s018ltr.pdf April 16, 2014.
4. Summary Minutes of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee Joint Meeting September 14, 2017. In. <https://www.fda.gov/media/108265/download>: Food and Drug Administration, Center for Drug Evaluation and Research; 2017.
5. Levin RA. Clinical Review: Butrans (buprenorphine transdermal system). In. *NDA 21306*.
<https://www.fda.gov/media/108804/download>. September 11, 2017.
6. Butrans [Prescribing Information]. In. Stamford, CT: Purdue Pharma L.P.; September 2018.
7. Source: IQVIA National Sales Perspectives™ 2018. Data extracted January 2020.

8 APPENDICES

8.1 APPENDIX A. FDA ADVERSE EVENT REPORTING SYSTEM

FDA Adverse Event Reporting System (FAERS)

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support the FDA's post-marketing safety surveillance program for drug and therapeutic biologic products. The informatic structure of the database adheres to the international safety reporting guidance issued by the International Conference on Harmonisation. Adverse events and medication errors are coded to terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. The suspect products are coded to valid tradenames or active ingredients in the FAERS Product Dictionary (FPD).

FAERS data have limitations. First, there is no certainty that the reported event was actually due to the product. FDA does not require that a causal relationship between a product and event be proven, and reports do not always contain enough detail to properly evaluate an event. Further, FDA does not receive reports for every adverse event or medication error that occurs with a product. Many factors can influence whether or not an event will be reported, such as the time a product has been marketed and publicity about an event. Therefore, FAERS data cannot be used to calculate the incidence of an adverse event or medication error in the U.S. population.

8.2 APPENDIX B. DRUG UTILIZATION DATABASE DESCRIPTIONS AND LIMITATIONS

IQVIA National Sales Perspectives™ (NSP)

The IQVIA National Sales Perspectives™ measures the volume of drug products, both prescription and over-the-counter, and selected diagnostic products moving from manufacturers into various outlets within the retail and non-retail markets. Volume is expressed in terms of sales dollars, eaches, extended units, and share of market. These data are based on national projections. Outlets within the retail market include the following pharmacy settings: chain drug stores, independent drug stores, mass merchandisers, food stores, and mail service. Outlets within the non-retail market include clinics, non-federal hospitals, federal facilities, HMOs, long-term care facilities, home health care, and other miscellaneous settings.

The manufacturer sales distribution data do not provide an estimate of direct patient use but do provide a national estimate of units sold from the manufacturer to various retail and non-retail settings of care. The amount of product purchased by these settings of care may be a possible surrogate for use if we assume that facilities purchase drugs in quantities reflective of actual patient use.

IQVIA Total Patient Tracker™ (TPT)

The IQVIA Total Patient Tracker (TPT) is a national-level projected service designed to estimate the total number of unique (non-duplicated) patients across all drugs and therapeutic classes in the retail outpatient setting from U.S. retail pharmacies. Data are available back to January 2002 and are available 20 days after the close of the month. TPT uses prescription activity as part of its projection and integrates information from pharmacies and payers to eliminate duplicate patients and multiple prescription fills, producing quick and reliable unique patient counts. IQVIA has 92% coverage and a sample of ~58,900 retail pharmacies. IQVIA captures about 3.8 billion transactions annually. TPT is projected to the known universe of retail pharmacies.

Due to the changing pharmaceutical marketplace, IQVIA has implemented changes to its prescription database, National Prescription Audit™ (NPA), to manage prescription voids, reversals, and abandonments that span multiple weeks. Beginning in January 2019, IQVIA has projected published prescription volumes dispensed from the retail pharmacies based on sold date, instead of date of adjudication (i.e., fill date). Because TPT patient data are derived from NPA prescription data, projected patient estimates have been adjusted and restated in the database back to January 2017, data prior to 2017 remain unadjusted. As a result, a trend break occurs between 2016 and 2017 patient estimates who received prescriptions dispensed from the retail pharmacies; any changes over time must be interpreted in the context of the changes in the underlying data and methodology.

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03/04/2020 09:49:13 AM

IVONE E KIM
03/04/2020 10:16:07 AM

RAJDEEP K GILL
03/04/2020 10:47:13 AM

MALLIKA L MUNDKUR on behalf of NEHA GADA
03/04/2020 12:52:20 PM

GRACE CHAI
03/04/2020 09:31:09 PM

IDA-LINA DIAK
03/04/2020 09:40:54 PM