Attachment I: Drug Trend Analysis Report & Methodology

February 2020

Background

The Centers for Medicare & Medicaid Services (CMS), in collaboration with the National Benefit Integrity Medicare Drug Integrity Contractor (NBI MEDIC), conducted a national proactive data-analysis project.

The goal was to analyze prescription drug event (PDE) records to detect sudden changes in specific drug utilization and total Medicare Part D drug spending for PDE records from second quarter (Q2) of 2019 to third quarter (Q3) of 2019.

Methodology

The PDE records were extracted from the Integrated Data Repository (IDR) using the SAS Enterprise Guide tool with an IDR service date from April 1, 2019, through September 30, 2019, and analyzed by Drug Enforcement Administration (DEA) class, therapeutic class, and National Drug Code (NDC) over each quarter to identify trends and outliers. Once identified, a clinical pharmacist review was completed to determine important trends with respect to fraud, waste and abuse (FWA) to the Medicare program.

Analysis and Findings

A review of these PDE records identified a 0.35% increase in total Medicare Part D drug spending and a 0.51% increase in PDE record counts. Also noted was a decrease of 0.16% in total Medicare Part D drug spending per PDE record, and a 0.32% decrease in total Medicare Part D drug spending per beneficiary.

Medicare Part D enrollment has risen from 45.6 million beneficiaries in 2019Q2 to 46.0 million beneficiaries in 2019Q3.[1] Changes identified in specific drug utilization may not always be attributed to any particular cause. See Table 1 for additional information on DEA drug class changes.

[1] Centers for Medicare & Medicaid Services, U.S. Department of Health & Human Services. Medicare Advantage/Part D Contract and Enrollment Data. https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/MCRAdvPartDEnrolData/Monthly-Enrollment-by-Contract.html. Accessed January 10, 2020.

DEA Class Summary

Table 1. DEA Drug Class by Total Medicare Part D Drug Spending[a] and PDE Record Growth Rate for 2019Q2-2019Q3

DEA Class Code	Period 1 Total Part D Spent	Period 1 Part D PDE Record Count	Period 2 Total Part D Spent	Period 2 Part D PDE Record Count	PDE Record Count Growth	Beneficiary Count Growth	Total Part D Spent Growth
0	$41,120,537,914.47	343,476,527	$41,570,046,589.83	345,371,984	0.55%	0.68%	1.09%
2	$678,729,752.16	12,909,903	$660,444,057.58	12,864,404	-0.35%	-1.35%	-2.69%
3	$300,501,987.77	1,698,469	$298,664,895.49	1,730,356	1.88%	0.47%	-0.61%
4	$245,289,920.33	15,846,322	$250,918,438.04	15,846,042	0.00%	-0.99%	2.29%
5	$891,860,961.16	1,703,494	$606,792,242.71	1,722,500	1.12%	1.59%	-31.96%
Totals	**$43,236,920,535.89**	**375,634,715**	**$43,386,866,223.65**	**377,535,286**	**0.51%**	**0.66%**	**0.35%**

[a] Total Medicare Part D Drug Spending includes the Covered Plan Paid Amount, Non-Covered Plan Paid Amount, Low-Income Cost-Sharing Subsidy Amount, Patient Liability Reduction due to Other Payer Amount, Patient Paid Amount, and Other True Out-Of-Pocket Amount. *Note:* Chart does not include IDR Unknown.

Schedule II Controlled Substances

- Schedule II drugs in the drug subclass opiate agonists exhibited a 0.54% decrease in PDE record utilization, a 1.51% decrease in beneficiary count, and a 3.04% decrease in total Medicare Part D drug spending. The top five Schedule II controlled substances by total Medicare Part D drug spending in 2019Q3 are all opioid analgesics and four of them showed decreases in PDE record count compared to the previous quarter. All five drugs showed decreases in total Medicare Part D drug spending, and four of five drugs displayed decreases in total beneficiaries for 2019Q3. This trend appears to show that CMS initiatives to promote the safe and effective use of opioids, while curbing misuse and abuse, are having a positive impact.

Central Nervous System (CNS) Stimulants

- Schedule II CNS stimulants, which includes prescription drugs such as dextroamphetamine and methylphenidate, are typically prescribed for only a few health conditions, including attention-deficit hyperactivity disorder (ADHD), narcolepsy, and treatment-resistant depression. However, CNS stimulants can be misused on their own or in combination with opioids to combat fatigue and sedation caused by high daily doses of opioids. There has been an increase of 2.59% in PDE record utilization count for these medications in 2019Q3 compared to 2019Q2.

Schedule III-V Controlled Substances

- Schedule III-V controlled substances PDE record utilization increased by 0.26%, displayed a decrease in beneficiary count of 0.67%, and exhibited a 19.57% decrease in total Medicare Part D drug spending between 2019Q2 and 2019Q3.

- Schedule III-V opiate agonists exhibited a 0.31% decrease in PDE record utilization, a 1.13% decrease in beneficiary count, and a 3.42% increase in total Medicare Part D drug spending.

Belbuca® (Buprenorphine Products Used for Pain Management)

- Because Belbuca is only approved by the Food and Drug Administration (FDA) for pain,[2] it is important to monitor its increases in utilization, similar to other opioid analgesics, especially in light of the overall utilization in the opioid analgesic class decreasing. The Centers for Disease Control and Prevention (CDC) recommends against the calculation of a morphine milligram equivalent (MME) for buprenorphine products, such as Belbuca.[3] In the 2019 Final Call Letter,[4] CMS declared its expectations that all plan sponsors would implement an opioid care coordination edit at 90 MME per day. Plan sponsors were also provided the flexibility to implement hard safety edits and set the threshold at 200 MME or more and may include prescriber/pharmacy counts.

- Use of Belbuca, and other similar buprenorphine products, may be an avenue for beneficiaries to bypass MME based edits employed by plan sponsors. Plan sponsors can establish a separate safety edit or utilization management edit such as quantity limits for Belbuca (upon approval by CMS) based on the maximum recommended daily dose in the FDA label.

Table 2. Total Medicare Part D Drug Spending of Belbuca from 2017Q4-2019Q3

Quarter	PDE Record Count	Total Part D Spent	PDE Record Count Growth Compared to Previous Quarter	Total Part D Spent Growth Compared to Previous Quarter
2017Q4	6,060	$2,436,191.13	18.66%	25.12%
2018Q1	7,325	$3,288,579.35	20.72%	34.91%
2018Q2	10,760	$4,661,661.38	46.89%	41.73%
2018Q3	14,716	$6,430,552.86	36.73%	37.89%
2018Q4	19,963	$8,879,816.34	35.68%	38.09%
2019Q1	24,759	$11,883,583.93	23.97%	33.78%
2019Q2	30,877	$15,080,422.33	24.61%	26.84%
2019Q3	35,422	$17,053,784.05	14.53%	12.94%

Total Part D Spent refers to Total Medicare Part D Drug Spending.

Epidiolex®

- Epidiolex (cannabidiol) [CBD] oral solution is a Schedule V controlled substance approved for the treatment of seizures associated with two rare and severe forms of epilepsy, Lennox-Gastaut syndrome and Dravet syndrome, in patients two years of age and older. It was approved by FDA on June 25, 2018 and is the first FDA approved drug for the treatment of Dravet syndrome. It is also the first FDA approved drug that contains a purified substance derived from marijuana.

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[2] U.S. Food and Drug Administration, U.S. Department of Health & Human Services: Highlights of Prescribing Information for Belbuca. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/207932s008s009lbl.pdf. Updated September 2018. Accessed January 10, 2020.

[3] Centers for Disease Control and Prevention: Dosing and Titrating Opioids. https://emergency.cdc.gov/coca/transcripts/2016/call-transcript-081716.asp. Updated August 17, 2016. Accessed January 10, 2020.

[4] Centers for Medicare & Medicaid Services: Announcement of Calendar Year (CY) 2019 Medicare Advantage Capitation Rates and Medicare Advantage and Part D Payment Policies and Final Call Letter. Published April 2, 2018.

- CBD is a chemical component of the cannabis sativa plant, more commonly known as marijuana. CBD is not known to cause the intoxication or euphoria that comes from tetrahydrocannabinol (THC). There are CBD products available over the counter, many of which are being offered as pain relief options. There has been an increase of 26.42% in PDE record utilization and a 20.00% increase in beneficiary count for Epidiolex in 2019Q3 compared to 2019Q2.

Opiate Agonists

There has been a decreased trend in MME per beneficiary since the first quarter of 2016 except for the slight increase in the first quarter of 2019. This appears to show that CMS initiatives to promote the safe and effective use of opioids, while curbing misuse and abuse, are having a positive impact. In each quarter, average MME per beneficiary is calculated as the average MME among beneficiaries receiving an opioid. Beneficiaries with cancer diagnoses, sickle cell diagnoses, or enrolled in hospice care during the quarter and one year prior were removed from consideration.

Figure 1. Opiate Agonist Utilization Quarterly Trend for 2016Q1-2019Q3

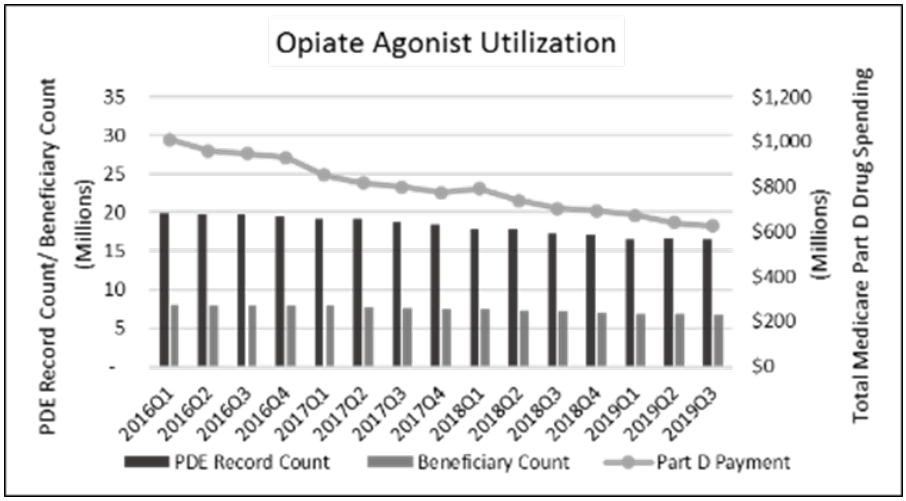
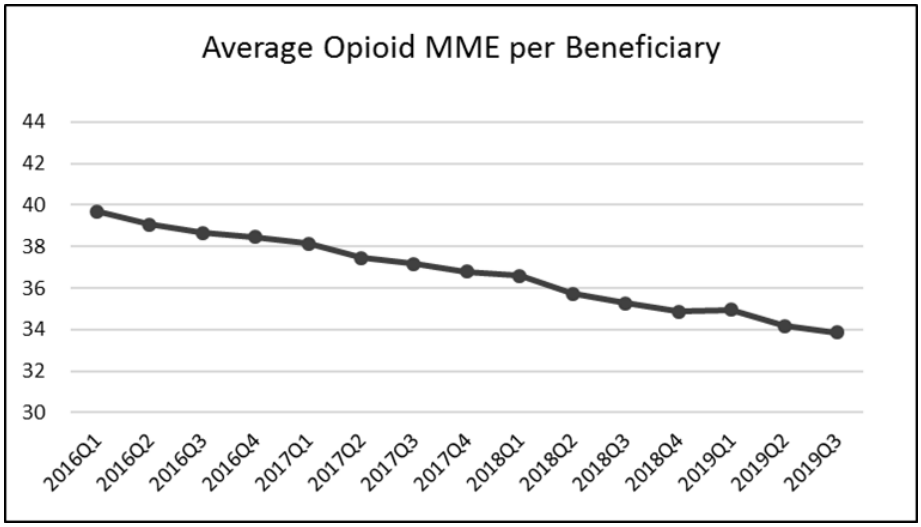


Figure 2. Average Opioid MME per Beneficiary Quarterly Trend for 2016Q1-2019Q3



Topical Drug Analysis

Several topical drugs have been targets of FWA through a telemarketing scheme. This telemarketing scheme typically involves beneficiaries receiving unsolicited phone calls inquiring if they have pain issues. Table 3 outlines topical drugs highly associated with telemarketing schemes.

Table 3. Eleven Topical Drugs Highly Associated With Telemarketing Scheme by PDE Record Count, Beneficiary Count, and Total Medicare Part D Drug Spending for 2019Q2-2019Q3

Drug Name	Period 1			Period 2			Growth Rate		
	PDE Record Count	Beneficiary Count	Total Part D Spent	PDE Record Count	Beneficiary Count	Total Part D Spent	PDE Record Count	Beneficiary	Total Part D Spent
DICLOFENAC GEL 1%	928,470	659,099	$49,134,436.72	1,131,274	797,788	$57,184,480.06	21.84%	21.04%	16.38%
CALCIPOTRIENE CRE 0.005%	48,936	34,474	$24,855,889.69	44,528	32,012	$19,644,604.11	-9.01%	-7.14%	-20.97%
DICLOFENAC DIS 1.3%	9,212	6,151	$5,855,427.78	19,232	13,059	$13,887,192.73	108.77%	112.31%	137.17%
DIFLORASONE DIACETATE CRE/OIN 0.05%	4,299	3,187	$5,778,528.35	5,146	3,583	$8,007,797.28	19.70%	12.43%	38.58%
DOXEPIN HCL CRE 5%	7,304	4,535	$7,956,680.66	4,763	3,273	$5,216,365.64	-34.79%	-27.83%	-34.44%
PIMECROLIMUS CRE 1%	7,933	7,020	$3,196,475.92	10,988	9,395	$4,333,084.41	38.51%	33.83%	35.56%
ACYCLOVIR CRE 5%	2,857	2,425	$2,717,071.02	3,104	2,596	$2,886,066.76	8.65%	7.05%	6.22%
ZTLIDO PAD 1.8%	4,311	2,879	$1,794,021.07	6,128	4,055	$2,589,889.47	42.15%	40.85%	44.36%
DESOXIMETAS CRE 0.05%	3,660	2,877	$1,352,026.01	4,402	3,617	$1,976,892.14	20.27%	25.72%	46.22%
HYDROCORTISO LOT 0.1%	1,557	1,120	$1,120,096.97	2,494	1,619	$1,653,425.05	60.18%	44.55%	47.61%
FLURANDRENOL LOT 0.05%	1,833	1,476	$1,012,516.62	1,624	1,145	$1,099,738.70	-11.40%	-22.43%	8.61%

Total Part D Spent refers to Total Medicare Part D Drug Spending.

- The telemarketing scheme appears to evolve. As plan sponsors implement tighter controls on one drug, the fraud scheme then moves to a new drug. There were large increases in ZTLido patches, diclofenac epolamine 1.3% patches, diclofenac gel 1%, pimecrolimus cream 1%, and hydrocortisone lotion 0.1% this quarter.

Foot Baths/Nasal Rinses/Mouthwashes

The use of antibiotics and antifungals in foot baths is a recently identified trend similar to the topical telemarketing scheme. This scheme has also evolved to include nasal rinse and mouthwash preparations that include antibiotics, antifungals, and steroids. These programs are promoted as a preventative measures, and not for treatment of an active disease.

Table 4. Antibiotic and Antifungal Drugs of Note for 2019Q2-2019Q3

Drug Name	Period 1 Total Part D Spent	Period 2 Total Part D Spent	PDE Record Count Growth	Beneficiary Count Growth	Total Part D Spent Growth
OXICONAZOLE NT 1% CR	$7,642,337.30	$7,881,382.37	12.45%	5.37%	3.13%
KETOCONAZOLE CRE 2%	$21,695,034.32	$22,029,526.39	7.31%	5.93%	1.54%
CLINDAMYCIN SOL 1%	$5,698,835.11	$6,071,220.41	6.42%	5.58%	6.53%
VANCOMYCIN 125MG CP	$14,127,900.08	$13,840,083.30	6.12%	6.01%	-2.04%
VANCOMYCIN 250MG CP	$21,581,160.54	$20,348,765.54	3.67%	1.83%	-5.71%
NYSTATIN SUSP 100000	$4,882,968.35	$4,875,590.82	3.93%	2.47%	-0.15%
NYSTATIN POW 100000	$4,747,887.29	$4,458,512.16	-6.33%	-7.65%	-6.09%
MUPIROCIN OIN 2%	$8,052,796.35	$8,290,583.04	7.15%	6.56%	2.95%
ERYTHROMYCIN OIN 5MG/GM	$1,541,280.25	$2,193,084.19	41.03%	38.52%	42.29%
CLOTRIM/BETA CRE	$8,855,331.51	$9,615,651.45	5.95%	5.74%	8.59%
TOBRADEX OIN 0.3-0.1%	$4,497,856.78	$5,922,848.58	36.99%	38.94%	31.68%
KETOROLAC SOL 0.5%	$4,737,407.97	$5,707,479.57	1.76%	1.88%	20.48%

Total Part D Spent refers to Total Medicare Part D Drug Spending.

- There appears to be a shift from the foot bath drugs to those utilized for the nasal rinses and mouthwashes. The nasal rinse and mouthwash preparations typically utilize ophthalmic products, which had larger increases this quarter.

Other Drugs of Note

Arikayce® (Amikacin Liposome Inhalation Solution)

- The FDA approved Arikayce on September 28, 2018, for the treatment of lung disease caused by a group of bacteria, mycobacterium avium complex (MAC) in a limited population of patients with the disease who did not respond to conventional treatment. Arikayce is the first drug to be approved under the Limited Population Pathway for Antibacterial and Antifungal Drugs (LPAD) pathway, which advances the development and approval of antibacterial and antifungal drugs to treat serious or life-threatening infections in a limited population of patients with unmet need.

- As required for drugs approved under the LPAD pathway, labeling for Arikayce includes certain statements to convey that the drug has been shown to be safe and effective only for use in a limited population. Included in the product labeling, is the following information on its limited population: "ARIKAYCE is an aminoglycoside antibacterial indicated in adults who have limited or no alternative treatment options, for the treatment of mycobacterium avium complex (MAC) … As only limited clinical safety and effectiveness data for ARIKAYCE are currently available, reserve ARIKAYCE for use in adults who have limited or no alternative treatment options…"

- The NBI MEDIC along with the Investigations MEDIC (I-MEDIC) have received complaints that the manufacturer of Arikayce has been promoting off label uses of the medication. In 2019Q3 the total spend on the medication was $22,344,375.83, which is an increase of 34.39% from the previous quarter.

Metformin HCL-ER

- Metformin oral tablets are used in combination with diet and exercise to treat high blood sugar levels caused by type 2 diabetes. The NBI MEDIC and I-MEDIC have recently received multiple complaints on these metformin extended release (ER) products including billing for services not rendered and pharmacies dispensing the osmotically released generic but billing for the gastric released product. This is due to the average wholesale price (AWP) being significantly different between the two products. The AWP for the osmotically released generic is approximately $17.22 per tablet, where the AWP for the gastric released product is approximately $120.22 per tablet.

- In 2019Q3, there were 20,813 PDE records for the osmotic release generic with a total cost of $17,409,027.27 for the quarter. However, that is compared to the gastric release product, in which there 23,265 PDE records associated with a total cost of $60,980,394.42.

Additional Analysis

This section outlines drugs CMS and the NBI MEDIC have identified that plan sponsors may have had difficulty in determining whether a PDE record is appropriately paid under the Part D benefit. Areas such as medications being authorized for a non-medically accepted indication (MAI), incorrect benefits assignment (i.e., Part B versus Part D), and incorrect units billed have been an issue.

The following drugs have been identified for inclusion in the third Quarter of 2019 Drug Trend Report. PDE records were extracted from the IDR for the selected drugs using the SAS Enterprise Guide tool with a service date from January 1, 2017, through September 30, 2019.

Central Nervous System (CNS) Stimulants

Schedule II CNS stimulants, which include prescription drugs such as dextroamphetamine and methylphenidate, are typically prescribed for only a few health conditions, including attention-deficit hyperactivity disorder (ADHD), narcolepsy, and treatment-resistant depression. However, CNS stimulants can be misused on their own or in combination with opioids to combat fatigue and sedation caused by high daily doses of opioids.

Table 5 provides a breakdown of potentially inappropriate claims for CNS stimulants from January 1, 2017, through September 30, 2019. In each year of the evaluation, less than 10% of the PDE records submitted for Schedule II CNS stimulants were associated with beneficiaries that did not have a documented MAI in Medicare Part A, Part B, or Part C claim data. This equates to over $79 million in potentially inappropriate payments.

Table 5. Yearly Comparison of Medicare Part D Spending on MAI and Non-MAI CNS Stimulants PDE Records

Year	# of PDE Records			Total Part D Payment		
	Non MAI	Total	% of Non MAI	Non MAI	Total	% of Non MAI
2017	277,706	2,941,491	9.44%	$27,334,450.95	$298,180,905.04	9.17%
2018	300,714	3,091,977	9.73%	$28,915,404.32	$308,654,412.86	9.37%
2019 (Q1 – Q3)	236,472	2,378,945	9.94%	$22,764,634.53	$233,906,334.18	9.73%

Of note, medications with the active ingredient being either methylphenidate or dexmethylphenidate had disproportionately higher share of non-MAI utilization by percentage. The percentage of PDE records not associated with an MAI in the Parts, A, B or C data were 11.44%, 11.57%, and 11.72% in each year between 2017 and 2019, which is 20% higher than the average Schedule II CNS stimulants.

Vancomycin (Oral)

Oral vancomycin is indicated for the treatment of Clostridioides difficile and enterocolitis caused by Staphylococcus aureus, including methicillin-resistant strains. It is currently not approved for topical use to treat any condition.

The use of antibiotics and antifungals in foot baths is a recently identified trend similar to the topical telemarketing scheme. Vancomycin 125mg and 250mg oral capsules have been associated with this foot bath scheme. This analysis reviews the potential for non-MAI use of these drugs in order to help educate plan sponsors as to the potential impact of inappropriate utilization.

Table 6 provides a breakdown of the utilization of vancomycin from 2017 through the third quarter 2019. There has been an increase in percentage of potentially inappropriate PDE records from 2017 to 2019Q3. In 2017, 11.32% of PDE records were not associated with an appropriate MAI, and in the first three quarters of 2019 that had increased to 23.09%. The Part D payment associated with those potentially inappropriate PDE records contributed 46.00% of the total Part D payment for vancomycin in the first three quarters of 2019.

Table 6. Yearly Comparison of Medicare D Spending on MAI and Non-MAI PDE Records for Vancomycin

Year	# of PDE Records			Total Part D Payment		
	Non MAI	Total	% of Non MAI	Non MAI	Total	% of Non MAI
2017	14,121	124,742	11.32%	$7,744,593.50	$70,314,715.82	11.01%
2018	26,061	184,420	14.13%	$14,794,666.89	$87,226,000.91	16.96%
2019 (Q1 – Q3)	38,171	165,279	23.09%	$45,976,172.32	$99,941,821.60	46.00%

Antifungals

Antifungals are another class of medications typically associated with the foot bath fraud scheme. Table 7 provides a breakdown of the utilization of antifungals from 2017 through the third quarter 2019. The percentage of PDE records submitted for beneficiaries with no MAI for antifungals decreased from 19.33% to 18.97% from 2017 to 2018 but increased to 19.54% in the first three quarters in 2019.

Table 7. Yearly Comparison of Medicare Part D Spending on MAI and Non-MAI PDE Records for Antifungals

Year	# of PDE Records			Total Part D Payment		
	Non MAI	Total	% of Non MAI	Non MAI	Total	% of Non MAI
2017	2,123,120	10,985,167	19.33%	$59,748,606.08	$471,817,393.70	12.66%
2018	2,174,224	11,462,825	18.97%	$60,393,770.79	$499,981,256.69	12.08%
2019 (Q1 – Q3)	991,238	8,854,190	19.54%	$49,059,163.99	$399,048,485.47	12.29%