



The Risk of Misuse and Diversion of Buprenorphine for Opioid Use Disorder in Medicare Part D Continues to Appear Low: 2022

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The Risk of Misuse and Diversion of Buprenorphine for Opioid Use Disorder in Medicare Part D Continues to Appear Low: 2022

Why OIG Did This Review

- Ensuring access to buprenorphine to treat individuals with opioid use disorder is a critical step in addressing the Nation's opioid crisis.¹
- Buprenorphine—the most common medication used to treat opioid use disorder—has been shown to decrease illicit opioid use and opioid-related overdose deaths. Yet, due to concerns that buprenorphine has the potential for misuse and is at risk for diversion, access to this medication has historically been restricted.
- The Office of Inspector General (OIG) recently conducted an evaluation examining the use of buprenorphine in Medicare Part D in 2021 and found that buprenorphine's risk of misuse and diversion appeared to be low.²
- This data brief provides updated information—based on prescription drug event data from 2022—on the use of buprenorphine in Medicare Part D and its risk for diversion.

What OIG Found

- As in 2021, almost all Medicare Part D enrollees who received buprenorphine for the treatment of opioid use disorder received the recommended amounts in 2022.
- Most enrollees received buprenorphine-naloxone combination products which are generally recommended to minimize the risk of misuse or diversion.
- Enrollees rarely received either very high amounts of buprenorphine or buprenorphine at the same time as they received high amounts of other opioids.

97 percent of Part D enrollees **received the recommended amounts** or less of buprenorphine for opioid use disorder in 2022.

What OIG Concludes

- The findings from 2022 are similar to the findings from 2021. Together, they suggest that the risk of misuse and diversion of buprenorphine in Medicare Part D continues to be low.
- These updated data provide important information about buprenorphine utilization that can assist the Centers for Medicare & Medicaid Services (CMS), the U.S. Department of Health and Human Services (the Department), and others as they continue to take steps to improve access to buprenorphine, while also ensuring that the risk of misuse and diversion remains low.

Primer – Buprenorphine for the Treatment of Opioid Use Disorder

- Opioid use disorder is a problematic pattern of opioid use that leads to clinically significant impairment or distress. About 1.1 million people enrolled in Medicare had a diagnosis of opioid use disorder in 2022.³
- Buprenorphine is a medication used to treat opioid use disorder.⁴ It suppresses withdrawal symptoms and relieves cravings.
- Buprenorphine and other medications used to treat opioid use disorder are commonly referred to as medications for opioid use disorder (MOUD).⁵ These medications have been shown to decrease illicit opioid use and opioid-related overdose deaths.⁶
- Buprenorphine is designated as a Schedule III controlled substance—meaning that it has the potential for abuse and is at risk for diversion, but has a lower risk than Schedule II controlled substances, such as oxycodone.⁷
- Until recently, to prescribe or administer buprenorphine in an office-based setting, a provider had to obtain a waiver from the Substance Abuse and Mental Health Services Administration (SAMHSA). This waiver was commonly referred to as the “DATA waiver” after the Drug Addiction Treatment Act (DATA) of 2000 that established the waiver program.⁸ It was also commonly referred to as the “X-waiver.”
- To qualify for this waiver, providers were generally required to complete approved training and have the capacity to refer patients to counseling and other ancillary services.⁹ Providers were limited in the number of patients whom they were allowed to treat.¹⁰
- In late December 2022, the waiver requirement was repealed.¹¹ In its place, all providers who apply for or renew their Drug Enforcement Administration (DEA) registration to prescribe controlled substances must take a one-time training on treating and managing patients with substance use disorders.¹²

FINDINGS

Ensuring access to buprenorphine while minimizing the risk of diversion is critical to addressing the opioid crisis.

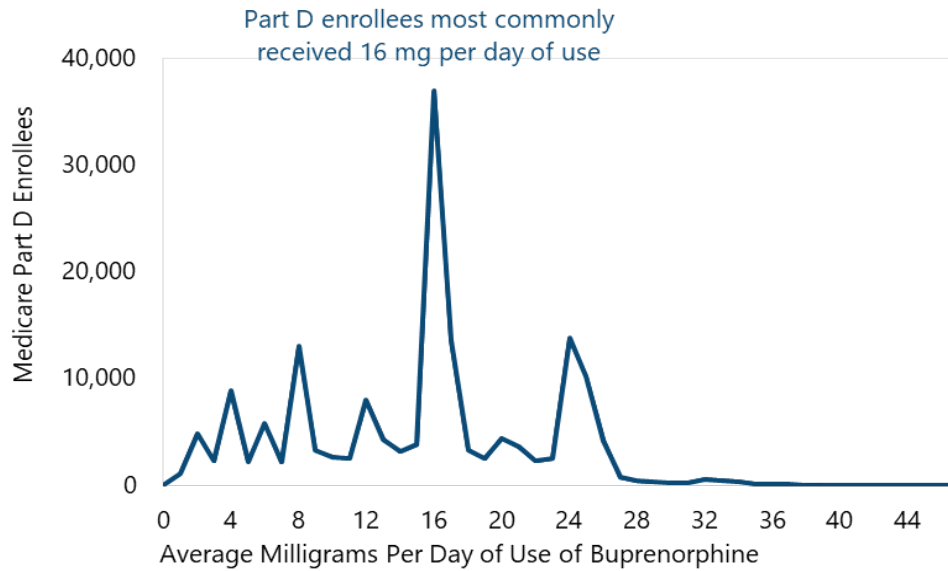
This data brief provides updated information from 2022 about Medicare Part D enrollees' use of buprenorphine. As we did in our prior work, to assess the risk of diversion, we determined the extent to which enrollees received the recommended amounts of buprenorphine; the extent to which enrollees received buprenorphine-naloxone combination products—which have a reduced risk of misuse or diversion; and the extent to which enrollees received very high amounts of buprenorphine or received buprenorphine at the same time as they received high amounts of opioids indicated for pain.

As in 2021, almost all Medicare Part D enrollees who received buprenorphine for the treatment of opioid use disorder received the recommended amounts in 2022

A total of 182,043 people enrolled in Medicare Part D received buprenorphine in 2022.¹³ Almost all of these enrollees—97 percent—received the recommended amounts or less of buprenorphine. See Exhibit 1. In general, buprenorphine products have a recommended daily dose range of 4 mg to 24 mg.¹⁴ The same percentage of enrollees received the recommended amounts or less of buprenorphine in 2021.¹⁵

Further, as in 2021, enrollees most commonly received an average daily dosage of buprenorphine of around 16 mg per day. Enrollees also commonly received dosages of around 24 mg per day, followed by 8 mg per day and then 4 mg per day. See Appendix A for more information about 2021 and 2022.

Exhibit 1: Most Part D enrollees received dosages of buprenorphine at or below the recommended range of 4 mg to 24 mg per day in 2022.



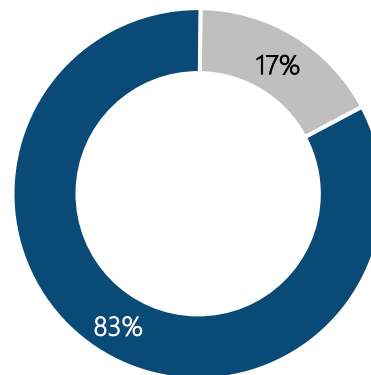
Source: OIG analysis of Medicare Part D data, 2023.

Most enrollees received buprenorphine-naloxone combination products which are generally recommended to minimize the risk of misuse or diversion

Medications that contain both buprenorphine and naloxone—i.e., buprenorphine combination products—are recommended for most individuals receiving buprenorphine for opioid use disorder. The addition of naloxone to the medication helps minimize the risk of misuse and diversion.¹⁶ These products are generally recommended for the treatment of opioid use disorder to minimize the risk of misuse or diversion.

In total, 83 percent—or 150,813 enrollees—received a combination product in 2022 through Part D.¹⁷ See Exhibit 2. This is very similar to the percentage of enrollees who received a combination product through Part D in 2021.¹⁸

Exhibit 2: 83 percent of enrollees received buprenorphine combination products.



Source: OIG analysis of Medicare Part D data, 2023.

The remaining 17 percent—or 31,230 enrollees—received medications that contain only buprenorphine—i.e., buprenorphine monoproducts. According to SAMHSA,

buprenorphine monoproducs should be reserved for patients such as pregnant patients, patients who are allergic to naloxone, and patients who cannot afford treatment if the combination product is required.¹⁹

Enrollees rarely received either very high amounts of buprenorphine or buprenorphine at the same time as they received high amounts of other opioids

A very small number of enrollees—1,409—either received very high average daily dosages of buprenorphine or received buprenorphine at the same time as they received high amounts of opioids indicated for pain in 2022.²⁰ These enrollees represent just 0.8 percent of all enrollees who received buprenorphine in 2022.²¹

Few enrollees received very high amounts of buprenorphine

Only 278 Part D enrollees received an average of more than 36 mg per day of buprenorphine, which is more than 50 percent higher than the maximum recommended daily dose. These enrollees received very high average daily dosages for more than 90 days.

Fewer than 300
enrollees averaged **more than 36 mg** per day of buprenorphine.

Enrollees with cancer or sickle cell disease; those receiving palliative care; and those in hospice care were not included in this analysis.

A similar number of enrollees—323—received very high amounts of buprenorphine in 2021. The low numbers in both 2021 and 2022 further suggest that misuse and diversion of buprenorphine are not widespread in Medicare Part D.²²

A small number of enrollees received buprenorphine and high amounts of opioids indicated for pain

The majority of Part D enrollees who received buprenorphine for opioid use disorder did not receive any opioids indicated for pain.²³ However, 1,135 enrollees received buprenorphine at the same time as they received high amounts of opioids indicated for pain, a similar number to that for 2021.²⁴ Each of these enrollees received opioids with an average morphine milligram equivalent (MME) of greater than 50 mg while they received buprenorphine for more than 90 days during the year. Receiving buprenorphine for opioid use disorder at the same time as opioids indicated for pain may indicate coordination-of-care issues or diversion.

Nonetheless, the small number of enrollees receiving buprenorphine and high amounts of opioids indicated for pain in 2021 and in 2022 further suggests that misuse and diversion of buprenorphine are limited in Medicare Part D.

CONCLUSION

The findings from 2022 are similar to the findings from 2021. Together, they suggest that the risk of misuse and diversion of buprenorphine in Medicare Part D continues to be low.

Further, this information about buprenorphine utilization can assist CMS, the Department, and others as they continue to take steps to improve access to buprenorphine, while also ensuring that the risk of misuse and diversion remains low. For example, the Department's Behavioral Health Care Coordinating Council can use these data when developing future Department guidelines related to buprenorphine prescribing.

Considering the magnitude of the opioid epidemic—with an estimated 83,894 deaths in 2022—it is critical that CMS and the Department use all of the tools at their disposal to address the crisis. As such, we continue to call upon CMS to implement the recommendations in our prior data brief, including to:

- inform providers about buprenorphine use and the low risk of diversion to encourage providers to treat more Part D enrollees who have opioid use disorder;
- take steps to inform providers about the availability of buprenorphine combination products in Part D, which can minimize the risk of misuse and diversion; and
- monitor the use of buprenorphine and share information, as appropriate, with Departmental partners.²⁵

In response to these prior recommendations, CMS concurred with the first two.²⁶ While CMS did not indicate whether it concurred with the last recommendation, it did indicate ongoing activity it felt was responsive. OIG is currently awaiting updates from CMS about actions it is taking to implement the three recommendations.

METHODOLOGY

We based this study primarily on five data sources: Medicare Part D Prescription Drug Event (PDE) records, the First Databank, the Medicare Enrollment Database, the National Claims History File, and Part C Encounter Data. We also used U.S. Food and Drug Administration (FDA) drug labels and the Centers for Disease Control and Prevention's (CDC's) Morphine Milligram Equivalent (MME) conversion file. We compared the results of this analysis to the results from the prior OIG data brief, *The Risk of Misuse and Diversion of Buprenorphine for Opioid Use Disorder Appears to Be Low in Medicare Part D* (OEI-02-22-00160), which used the same methodology to review data from 2021.

PDE records are for prescriptions that enrollees received through Part D. They do not include prescriptions paid for through other programs, prescriptions paid for in cash, or illicitly purchased drugs. Part D sponsors submit a PDE record to CMS each time a drug is dispensed to a person enrolled in their plans. Each record contains information about the drug and enrollee, as well as the identification numbers for the pharmacy and the prescriber. For the purposes of this study, we use the term "prescription" to mean one PDE record.

To obtain descriptive information about the drugs and enrollees, we matched PDE records to data from the First Databank, the National Claims History File, Part C Encounter Data, FDA drug labels, and CDC's MME conversion file. The First Databank contains information about each drug, such as the drug name, strength of the drug, and therapeutic class (e.g., medication for opioid use disorder). The National Claims History File contains claims data from Medicare Parts A and B, including diagnosis codes. Part C Encounter Data contain medical claims data, including diagnosis codes, for Medicare Advantage plan enrollees. FDA drug labels indicate dosing equivalents between buprenorphine products. CDC's MME conversion file contains information about each opioid drug's morphine milligram equivalence.

Identifying Medicare Part D Enrollees with Buprenorphine

Using the PDE records, we first identified people enrolled in Medicare Part D with at least one prescription for buprenorphine indicated for the treatment of opioid use disorder with a date of service in 2022.²⁷ We did not include prescriptions for buprenorphine indicated for pain in this study. For the purposes of this study, we use the term "buprenorphine" to mean buprenorphine indicated for the treatment of opioid use disorder.

Average Daily Dosage of Buprenorphine Analysis

Next, we determined the amount of buprenorphine that each Part D enrollee received in 2022 by calculating each enrollee's average daily dosage of buprenorphine.²⁸

To do this, we first calculated the total number of milligrams of buprenorphine in each prescription.²⁹ We standardized buprenorphine products with higher bioavailability in order to sum dosages across different buprenorphine products.³⁰ We then determined the milligrams per day of buprenorphine for each prescription by dividing the total number of milligrams by the total days supply.

Next, we summed each enrollee's milligrams of buprenorphine for each day of the year on the basis of the dates of service and days supply on each PDE record.

We then calculated the days of use of buprenorphine for each enrollee. Each calendar date in 2022 with a day supply of buprenorphine is considered a day of use. For example, an enrollee who received a day supply for each date in 2022 had 365 days of use.

We then divided the total milligrams of buprenorphine over the year by the total number of days of use to get the average daily dosage of buprenorphine per day of use in 2022.

Next, we identified the recommended range of buprenorphine. To do this, we reviewed FDA-approved drug labels of buprenorphine and buprenorphine-naloxone products indicated for the treatment of opioid use disorder.

Buprenorphine Combination Product and Monoproduct Analysis

Next, we identified which buprenorphine prescriptions were buprenorphine-naloxone combination products and which were buprenorphine-only monoproducts in 2022.

Using this information, we determined the percentage of Part D enrollees who received at least one buprenorphine combination product in 2022 and the percentage who only received monoproducts.

Identifying Part D Enrollees Who Received Very High Amounts of Buprenorphine

We considered enrollees to have received very high amounts of buprenorphine if their average daily dosage of buprenorphine was more than 36 mg for more than 90 days in 2022. This analysis excluded enrollees who had a diagnosis of cancer or sickle cell disease; had a hospice stay; or received palliative care at any point in 2022.

Identifying Part D Enrollees Who Received Buprenorphine and High Amounts of Opioids Indicated for Pain

We identified enrollees who received buprenorphine indicated for the treatment of opioid use disorder at the same time as they received opioids indicated for pain in 2022.³¹

Next, we determined the amount of opioids that each of these enrollees received in 2022. To do this, we calculated each enrollee's average daily morphine milligram equivalent (MME) dose.³² The MME converts opioids of different ingredients, strengths, and forms into equivalent milligrams of morphine. It allows us to sum dosages of different opioids to determine an enrollee's daily opioid level.

To calculate each enrollee's average daily MME, we first calculated the MME for each prescription.³³ We used the following equation:

$$MME = \frac{(Strength\ per\ unit) \times (Quantity\ dispensed) \times (MME\ conversion\ factor)}{(Days\ supplied)}$$

Next, we summed each enrollee's MME for each day of the year based on the dates of service and days supply on each prescription.

For each enrollee, we then calculated the number of days on which they had both buprenorphine and other opioids.

We then calculated each enrollee's average MME over these days of overlap. We divided the total MME for the days of overlap by the total days of overlap for each enrollee.

Lastly, we identified the enrollees who received buprenorphine and high amounts of opioids indicated for pain. We considered enrollees to have received buprenorphine and high amounts of opioids indicated for pain if their opioids had an average daily MME of greater than 50 mg over the days of overlap and had more than 90 days of overlap. This analysis excluded enrollees who had a diagnosis for cancer or sickle cell disease; had a hospice stay; or received palliative care at any point in 2022.

Limitations

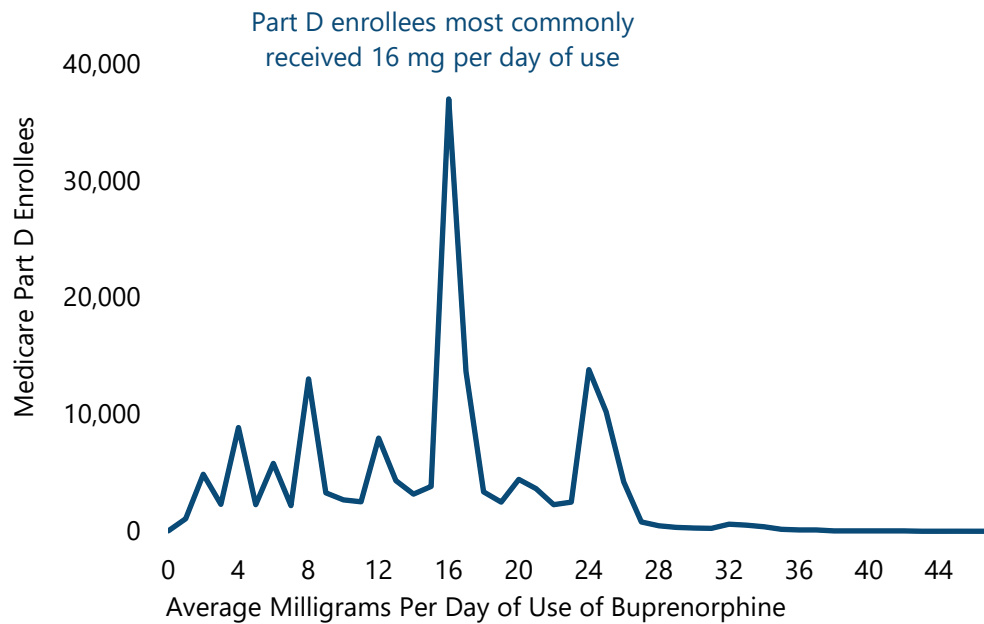
This analysis is based on Medicare claims data. We did not review medical records or independently verify the accuracy of the Medicare claims data for this study. The analysis does not include data on buprenorphine or opioids that enrollees may have received from sources other than Medicare Part D.

Standards

We conducted this study in accordance with the *Quality Standards for Inspection and Evaluation* issued by the Council of the Inspectors General on Integrity and Efficiency.

APPENDIX A

Exhibit A1: Most Part D enrollees received dosages of buprenorphine at or below the recommended range of 4 mg to 24 mg per day in 2021.



Source: OIG analysis of Prescription Drug Event data, 2023.

Exhibit A2: Number of Medicare Part D enrollees receiving buprenorphine for opioid use disorder, by average milligrams of buprenorphine per day, 2022

Average milligrams per day	Enrollees	Average milligrams per day	Enrollees
< 0.5	37	32	675
1	1,200	33	559
2	5,688	34	383
3	2,516	35	132
4	10,012	36	118
5	2,450	37	76
6	6,665	38	53
7	2,268	39	35
8	14,101	40	28
9	3,498	41	19
10	2,718	42	14
11	2,630	43	14
12	8,311	44	5
13	4,389	45	3
14	3,317	46	3
15	3,755	47	2
16	38,590	48	14
17	13,563	49	9
18	3,457	50	10
19	2,659	51	7
20	4,927	52	2
21	3,790	53	3
22	2,520	54	1
23	2,606	55	1
24	16,004	58	1
25	11,196	59	1
26	4,369	62	1
27	821	68	3
28	484	69	1
29	358	73	2
30	290	77	1
31	224	99	1

Source: OIG analysis of Medicare Part D data, 2023.

Note: For more information about these calculations, see the Methodology. To calculate the averages across different buprenorphine products, we standardized buprenorphine products with higher bioavailability.

ACKNOWLEDGMENTS AND CONTACT

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This report was prepared under the direction of Jodi Nudelman, Regional Inspector General for Evaluation and Inspections in the New York Regional Office, and Nancy Harrison and Meridith Seife, Deputy Regional Inspectors General.

Contact

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ENDNOTES

¹ Increasing access to buprenorphine to treat opioid use disorder is a goal of the Administration. See Office of National Drug Control Policy, *The Biden-Harris Administration's Statement of Drug Policy Priorities for Year One*, 2021. Accessed at https://www.whitehouse.gov/wp-content/uploads/2021/03/BidenHarris-Statement-of-Drug-Policy-Priorities-April-1.pdf?fbclid=IwAR2TBk34U_XRqIqK_pAYnUd_9f7zY3IbCQI9KxI6S5eYeRjDfzI9B09hZ84 on October 30, 2023.

² *The Risk of Misuse and Diversion of Buprenorphine for Opioid Use Disorder Appears to Be Low in Medicare Part D* (OEI-02-22-00160) May 16, 2023.

³ *The Consistently Low Percentage of Medicare Enrollees Receiving Medication to Treat Their Opioid Use Disorder Remains a Concern* (OEI-23-00250) forthcoming.

⁴ Buprenorphine products indicated for pain are different from buprenorphine products indicated for the treatment of opioid use disorder.

⁵ Methadone and naltrexone are also approved by the Food and Drug Administration (FDA) for the treatment of opioid use disorder.

⁶ SAMHSA, *Treatment Improvement Protocol 63: Medications for Opioid Use Disorder*, 2021. Accessed at https://store.samhsa.gov/sites/default/files/SAMHSA_Digital_Download/PEP21-02-01-002.pdf on November 1, 2023.

⁷ For more information about controlled substance scheduling, see DEA, *Drug Scheduling*. Accessed at <https://www.dea.gov/drug-information/drug-scheduling> on November 1, 2023.

⁸ The Drug Addiction Treatment Act of 2000 was enacted under Title XXXV of the Children's Health Act of 2000, P.L. No. 106-310.

⁹ Prior to April 2021, all providers were required to complete approved training and have the capacity to refer patients to counseling and other ancillary services. The Department of Health and Human Services (HHS) released new practice guidelines in 2021 that exempted eligible providers from these requirements if they are treating 30 or fewer patients. See 86 F.R. 22439. Congress has since repealed the need for a waiver. See 21 U.S.C. § 823(g)(2)(B)(iii)(I)-(II), repealed by Consolidated Appropriations Act, 2023, § 1262, P.L. No. 117-328 (Dec. 29, 2022).

¹⁰ Before late December 2022, with a waiver, practitioners could treat up to 100 patients with buprenorphine in the first year, although most qualified practitioners were limited to treating up to 30. In subsequent years, a practitioner could treat up to 275 patients. See 42 CFR § 8.610. In December 2022, Congress repealed the need for a waiver. See 21 U.S.C. § 823(g)(2)(B)(iii)(I)-(II), repealed by Consolidated Appropriations Act, 2023, § 1262, P.L. No. 117-328 (Dec. 29, 2022).

¹¹ P.L. No. 117-328 § 1262.

¹² P.L. No. 117-328 § 1263.

¹³ These data are based on an analysis of Medicare Part D prescription drug event records for buprenorphine indicated for the treatment of opioid use disorder. We did not include buprenorphine indicated for pain.

¹⁴ Most buprenorphine products have recommended daily dosages ranging from 4 mg per day to 24 mg per day, based on their FDA-approved manufacturer labels. See SAMHSA, *Treatment Improvement Protocol 63: Medications for Opioid Use Disorder*, 2021. In addition, some buprenorphine products have higher bioavailability, meaning that they enter into the bloodstream more quickly, allowing for lower dosages. For this analysis, we standardized buprenorphine products with higher bioavailability to have the same recommended range as other buprenorphine products have. In addition, to accommodate

early refills of prescriptions, we considered an enrollee's average daily dosage to be about 24 mg per day of use if it did not exceed 26 mg per day.

¹⁵ In 2021, a total of 170,408 people enrolled in Medicare Part D received buprenorphine. Almost all of these enrollees—97 percent—received the recommended amounts or less of buprenorphine. *The Risk of Misuse and Diversion of Buprenorphine for Opioid Use Disorder Appears to Be Low in Medicare Part D* (OEI-02-22-00160) May 16, 2023.

¹⁶ Daily buprenorphine monoproduts carry a higher risk of diversion than do buprenorphine combination products. SAMHSA, *Buprenorphine*, 2023. Accessed at <https://www.samhsa.gov/medication-assisted-treatment/medications-counseling-related-conditions/buprenorphine> on November 1, 2023. Also see SAMHSA, *Buprenorphine Quick Start Guide*. Accessed at <https://www.samhsa.gov/sites/default/files/quick-start-guide.pdf> on November 1, 2023. Separately, naloxone is a medication used to reverse opioid overdoses. See SAMHSA, *Naloxone*, 2023. Accessed at <https://www.samhsa.gov/medications-substance-use-disorders/medications-counseling-related-conditions/naloxone> on November 1, 2023.

¹⁷ A total of 8,228 (5 percent) of Part D enrollees received both buprenorphine combination products and monoproduts.

¹⁸ In total, 84 percent—or 142,321 enrollees—received a combination product through Part D in 2021. *The Risk of Misuse and Diversion of Buprenorphine for Opioid Use Disorder Appears to Be Low in Medicare Part D* (OEI-02-22-00160) May 16, 2023.

¹⁹ SAMHSA, *Buprenorphine Quick Start Guide*. SAMHSA, *Treatment Improvement Protocol 63: Medications for Opioid Use Disorder*, 2021.

²⁰ Four enrollees received very high average daily dosages of buprenorphine and also received buprenorphine at the same time as they received high amounts of opioids indicated for pain in 2022.

²¹ A total of 1,245 enrollees either received very high average daily dosages of buprenorphine or received buprenorphine at the same time as they received high amounts of opioids indicated for pain in 2021. These enrollees represented just 0.7 percent of all enrollees who received buprenorphine in 2021. *The Risk of Misuse and Diversion of Buprenorphine for Opioid Use Disorder Appears to Be Low in Medicare Part D* (OEI-02-22-00160) May 16, 2023.

²² It is also noteworthy that, according to the National Institute on Drug Abuse, data suggest that the bulk of buprenorphine misuse (use without a prescription) is for the purpose of controlling withdrawal and cravings for other opioids and not to get high. See National Institute on Drug Abuse, *Medications to Treat Opioid Use Disorder Research Report*, December 2021. Accessed at <https://nida.nih.gov/publications/research-reports/medications-to-treat-opioid-addiction/what-treatment-need-versus-diversion-risk-opioid-use-disorder-treatment> on November 16, 2023.

²³ This analysis excluded buprenorphine indicated for the treatment of pain.

²⁴ In 2021, 927 enrollees received buprenorphine at the same time as they received high amounts of opioids indicated for pain. *The Risk of Misuse and Diversion of Buprenorphine for Opioid Use Disorder Appears to Be Low in Medicare Part D* (OEI-02-22-00160) May 16, 2023. Enrollees with cancer or sickle cell disease; those receiving palliative care; and those who were in hospice care were not included in this analysis in 2021 or 2022.

²⁵ *The Risk of Misuse and Diversion of Buprenorphine for Opioid Use Disorder Appears to Be Low in Medicare Part D* (OEI-02-22-00160) May 16, 2023.

²⁶ *Ibid.*

²⁷ Additional Medicare Part D enrollees may have also received buprenorphine. For instance, some enrollees may have received buprenorphine covered by Medicare Part B, such as through opioid treatment programs. Others may have paid out of pocket for buprenorphine to treat their opioid use disorder. Buprenorphine indicated for pain was not included in this analysis.

²⁸ We limited this analysis to oral buprenorphine products.

²⁹ We included buprenorphine dispensed in 2021 with days supply in 2022. This analysis excluded prescriptions for implant and injection buprenorphine.

³⁰ To account for buprenorphine products with higher bioavailability, we standardized the milligrams across all products to be equivalent to Suboxone. For example, according to the FDA drug label, one Zubsolv 5.7 mg buprenorphine/1.4 mg naloxone sublingual tablet provides equivalent buprenorphine exposure to that of one Suboxone 8 mg buprenorphine/2 mg naloxone sublingual tablet. Therefore, in our analysis we consider one of these Zubsolv tablets to have 8 mg of buprenorphine. For more information, see Orexo US, Inc., *Zubsolv: Highlights of Prescribing Information*, 2021. Accessed at https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/204242s019lbl.pdf on November 20, 2023.

³¹ We did not include buprenorphine indicated for pain in this analysis. We considered enrollees to have received buprenorphine at the same time as they received other opioids if, after the first day supply of buprenorphine in 2022, buprenorphine PDE and other opioid PDEs had days supply that fell on the same calendar day.

³² For more information on calculating opioid dosage, see CDC, *Calculating Total Daily Dose of Opioids for Safer Dosage*. Accessed at https://stacks.cdc.gov/view/cdc/38481/cdc_38481_DS1.pdf on October 30, 2023.

³³ We included opioids dispensed in 2021 with days supply in 2022. This analysis excludes prescriptions for injection, intravenous, and intrathecal opioids, as well as opioids indicated as medications for opioid use disorder.