Opioid Abuse and the Development of Abuse-Deterrent Drugs: Trends and Coverage in the Medicare Part D Program

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EXECUTIVE SUMMARY

Prescription opioid analgesics are among the most commonly prescribed treatments for pain relief in the United States. These products, which include medicines such as hydrocodone, oxycodone, morphine, and codeine are a significant component of outpatient pain management, and are prescribed more than 200 million times annually.[1] While prescription opioids serve an important role in treating patients suffering from chronic pain, abuse of these medications has increased significantly in the past few decades.[2] In 2013, over 16,000 Americans died from prescription opioid abuse, four times higher than in 1999.[3] The Medicare program has not been immune to this trend—according to the Substance Abuse and Mental Health Services Administration (SAMHSA), the number of seniors misusing pain relievers has nearly tripled between 2003 and 2013.[4] The Centers for Medicare & Medicaid Services (CMS) has, in response, taken initial steps to curb opioid misuse and abuse in Medicare that have shown preliminary success in slowing, but not eliminating abuse.[5]

In addition, stakeholders have identified a range of strategies to reduce prescription opioid abuse, including education, treatment, and prevention.[6] One such effort is to make opioids more difficult and less attractive to abuse. To date, the U.S. Food and Drug Administration (FDA) has approved abuse-deterrent labeling for four long-acting opioids and the agency has expressed its support of further development of these products. Most recently, in April 2015 the FDA finalized long-anticipated guidance on evaluation and labeling of abuse-deterrent opioids.[7]

The four products approved to date with abuse-deterrent labeling are branded drugs and the FDA guidance is also specific to branded drugs. To date, there are no generic opioids approved with abuse-deterrent labeling. While there has been significant media and political attention on the development and approval of new abuse-deterrent alternatives, there has been less consideration of the market incentives and patient access for such products.

In response to these trends and particular concern over prescription opioid abuse among Medicare beneficiaries, Avalere analyzed opioid coverage and utilization management[i] (UM) among Medicare Advantage prescription drug (MA-PDs) plans and standalone prescription drug plans (PDPs) between 2012 and 2015 in order to better understand the coverage of abuse-deterrent opioids in the Medicare Part D program. Avalere focused on coverage trends between 2012 and 2015 for OxyContin® (oxycodone HCl controlled-release) and Opana® extended release (ER) (oxymorphone HCl), each of which was subject to high-profile abuse-deterrent labeling decisions. OxyContin received abuse-deterrent labeling from the

i Utilization Management (UM) references procedures required by health plans or pharmacy benefit managers that govern consumer access to drugs. As referenced in this report, UM refers to Prior Authorization (PA), Quantity Limits (QL), and Step Therapy (ST). PA: Requirement that a health plan or pharmacy benefit manager reviews requests for certain medicines, on an individual patient basis, before granting coverage. QL: A limit on how much of a particular drug can be dispensed for a specific time period (days' supply). ST: Requirement that, before accessing a prescribed drug, patients try and "fail" on at least one alternative drug.

FDA, while Opana ER did not.[ii] In addition to Opana ER and OxyContin, Avalere analyzed the general landscape of coverage for long-acting branded and generic opioids (products without abuse-deterrent labeling from the FDA).

The results of Avalere's analysis show that long-acting opioid coverage rates[iii] have steadily declined between 2012 and 2015. In addition, despite FDA approval of abuse-deterrent labeling for OxyContin in 2013, Part D plan coverage of OxyContin decreased significantly in 2014 and 2015—potentially indicating a larger trend of Part D plans favoring lower-cost generic opioids. Specifically, Avalere found:

- Despite receiving abuse-deterrent labeling by the FDA in 2013, OxyContin's Part D plan coverage rate dropped from 61 percent in 2012 to 33 percent in 2015.
- One quarter of Part D plans require prior authorization (PA) for OxyContin in 2015.
- In comparison, the generic Oxycodone Hydrochloride (HCl) immediate release (IR) is covered by all Part D plans in 2015 and faces lower levels of utilization management—only 0.3 percent of plans require PA for Oxycodone HCl in 2015.
- Following the FDA's decision in 2013 not to grant abuse-deterrent labeling for Opana ER, Part D plan coverage declined from 71 percent in 2012 to 48 percent in 2015.
- Notably, Opana ER has a higher coverage rate than OxyContin, despite OxyContin's abuse-deterrent labeling.
- Overall, average Part D plan coverage rates for long-acting opioids decreased by 10 percentage points between 2012 and 2015. Part D plans may be narrowing the scope of coverage of opioids in response to growing utilization of these drugs.
- Proportionally, the rate of coverage among branded opioids decreased more significantly than generics.

The results of Avalere's analysis show that overall opioid coverage rates are decreasing and that, despite FDA's approval of abuse-deterrent labeling for OxyContin, Part D plans continue favoring non–abuse deterrent generics at high rates. As policymakers seek to limit opioid abuse, including encouraging more abuse-deterrent options, they will have to consider how to balance the desire for greater access and use of abuse-deterrent opioids with the potential costs of such medications to public programs, as well as private payers.

ii In addition to OxyContin, the FDA has approved three other long-acting opioids with abuse-deterrent labeling (Pfizer's Embeda® and Purdue Pharma's OxyContin, Targiniq™ ER, and Hysingla® ER). However, these three products were approved in the past year. As a result, data was not available to analyze these products.

iii Coverage Rate refers to the percentage of Part D plans (including Medicare Advantage-Prescription Drugs plans and standalone prescription drug plans) that include the drug on its list of formulary. Avalere used the proprietary DataFrame® database based on Medicare Part D public use files for this analysis.

THE RISE OF OPIOID ABUSE AND IMPLICATIONS FOR THE MEDICARE PROGRAM

From 1999 to 2013, the rate for drug poisoning deaths involving opioid analgesics, or pain medications, nearly quadrupled.[8] Between 2002 and 2010, chronic nonmedical use of opioids increased by around 75 percent and it is estimated that 4.5 million Americans abuse pain relievers.[9,10] In addition, rates of prescription-related emergency department (ED) visits also have grown, with 420,000 ED visits attributable to prescription opioids in 2011.[11] Declared epidemic by the Centers for Disease Control and Prevention,[12] prescription opioid abuse continues to attract the attention of lawmakers and public health experts. In this Congress, lawmakers have shown significant interest in strategies to reduce abuse. Most recently, the House Energy and Commerce Committee has held a number of hearings on opioid abuse.[13] Furthermore, members of Congress have introduced around a dozen bills in the House and Senate thus far in the 114th Congress that aim to address opioid or prescription drug abuse.

While the Centers for Medicare & Medicaid Services (CMS) has reported that the number of potential opioid overutilizers has decreased between 2011 and 2014,[14] prescription opioid use and abuse among Medicare beneficiaries has increased significantly since the early 2000s. According to the Substance Abuse and Mental Health Services Administration (SAMHSA), the number of seniors in 2013 misusing prescription pain relievers was estimated to be roughly 432,000—a nearly threefold increase from 2003 when that number was 149,000.[15]

Furthermore, the Medicare Payment Advisory Commission (MedPAC) found that among the 12.3 million Medicare Part D enrollees that filled at least one opioid prescription in 2012, 500,000 accounted for 70 percent of total opioid spending in the program. In addition, MedPAC found that these beneficiaries with very high opioid use filled, on average, 23 opioid prescriptions in 2012.[16]

In addition, the Government Accountability Office (GAO) conducted its own study of opioid prescribing patterns in Medicare Part D and found evidence of doctor shopping[iv] for 14 categories of prescription drugs with high incidence of abuse.[17] GAO found that, in 2008, approximately 1.8 percent of beneficiaries receiving one of the 14 categories of examined drugs received the same class of drug from five or more providers.

In response to growing concerns about opioid abuse, in 2013 CMS began requiring Part D plans to implement more effective concurrent and retrospective drug utilization review (DUR) programs and to enforce greater compliance with drug utilization management (UM)

iv Doctor shopping is defined as seeing multiple treatment providers, either during a single illness episode or to procure prescription medications illicitly (National Institutes of Health).

requirements. One of the goals of these efforts was to identify patients with questionable opioid utilization patterns and to intervene in situations when plans confirm problematic usage. In addition, the Part D Overutilization Monitoring System (OMS) was established to help CMS ensure that Part D sponsors implement sufficient drug UM programs that guard against opioid overutilization.[v,18] In its final Medicare Advantage and Part D Call Letter that includes policy changes for the 2016 plan year, the Agency highlighted initial results of these initiatives by stating that although the total number of Part D enrollees increased from 2011 through 2014, the number of potential opioid overutilizers decreased.[19] Despite this progress, CMS noted that Part D plan sponsors should take additional steps to reduce opioid overutilization.

v The Annual 2015 Call Letter included more clarity from CMS about plan monitoring of overutilizers. CMS noted its concern about internal parameters that plan sponsors use to identify beneficiaries at risk for overutilization of opioids. Therefore, CMS clarified that CMS' threshold for targeting beneficiaries at risk of overutilization of opioids (120 mg morphine equivalent doses [MED] daily over at least 90 days) should be used by plan sponsors as a minimum step. Sponsors may use lower MED and/or consecutive day thresholds to be more inclusive and may vary other criteria including the number of prescribers and pharmacies.

EFFORTS TO COMBAT PRESCRIPTION DRUG ABUSE AND THE ROLE OF ABUSE-DETERRENT OPIOIDS

Policymakers in Congress, federal and state governments, as well as advocates have identified a range of potential solutions to this epidemic. Responsible for coordinating the nation's strategy, the Office of National Drug Control Policy (ONDCP) crafted a prescription drug abuse prevention plan including education, drug monitoring, proper disposal, and enforcement.[20] In addition, the plan highlights efforts to support the development of abuse-deterrent opioids.

Intended to deter the product manipulation (i.e., crushing or dissolving in water in order to inhale, smoke, or inject) that often accompanies opioid abuse, abuse-deterrent opioids can contain various versions of opioid antagonists released upon manipulation of the pill to counter the euphoric effects of the drug, or they may contain a physical barrier that minimizes the extraction potential of an opioid when manipulated (e.g., hard coating or gel substance when dissolved in water). These properties include, but are not limited to: physical/chemical barriers, agonist/antagonist combinations, aversion substances, and delivery system alterations.[21] The objectives of these technologies are to make manipulation of the product more difficult and to prevent the abuser from achieving a rapid euphoric effect.

Although abuse-deterrent opioids may reduce adverse events related to abuse of these products, the most common type of abuse of these medications remains taking higher-than-recommended doses orally.[22] No technology presently available would prevent this type of abuse. That said, the Drug Enforcement Administration[23] and members of Congress[24] have made clear their view that such incremental innovation is of immediate value because of its role in reducing overdose deaths from abuse through inhalation or injection.

As awareness and interest in this issue continued to mount, two companies were among the first to seek regulatory approval for new opioid formulations. In 2010, Purdue Pharma LP reformulated its original OxyContin (oxycodone HCl controlled-release), while Endo Pharmaceuticals Inc. reformulated its original Opana ER (oxymorphone HCl) to include abuse-deterrent properties.[25] On April 16, 2013, the FDA approved abuse-deterrent labeling for OxyContin after concluding "the physical and chemical properties of the reformulated product are expected to make the product difficult to inject and to reduce abuse via snorting."[26,27] Separately on May 10, 2013, the FDA determined that Opana ER would not receive abuse-deterrent labeling after concluding that it could "be readily prepared for injection" and "be compromised when subjected to other forms of manipulation, such as cutting, grinding, or chewing, followed by swallowing."[28,29]

Since that time, the FDA has remained under pressure from Congress to finalize its January 2013 abuse-deterrent opioid evaluation and labeling guidance and to establish a clear pathway for the review and approval of branded and generic abuse-deterrent opioids. This pressure came to a head in H.R.83, the "Consolidated and Further Continuing Appropriations Act, 2015," which would have redirected $20 million in FDA funding if the Agency did not issue final guidance by June 30, 2015.[30] The FDA finalized this guidance in April 2015.[31] To date, the FDA has approved four long-acting opioid products with abuse-deterrent labeling: Pfizer's Embeda® and Purdue Pharma's OxyContin, Targiniq™ ER, and Hysingla® ER. Looking forward, FDA has also indicated that that it intends to issue draft guidance on testing requirements for generic opioids in 2015.[32]

EVOLUTION OF PART D PLAN COVERAGE OF LONG-ACTING OPIOID ANALGESICS, 2012-2015

While there has been a great deal of attention on the regulatory pathway for the approval and labeling of abuse-deterrent opioids, there has been significantly less consideration of what happens after a product with abuse-deterrent labeling has been brought to market. As noted previously, in 2013 the FDA granted abuse-deterrent labeling to OxyContin and denied abuse-deterrent labeling for Opana ER. This is important because, according to the FDA, "including information about a product's abuse-deterrent properties in labeling is important to inform health care professionals, the patient community, and the public about a product's abuse potential."[33] Moreover, drug manufacturers are generally limited to communicating information that is included on the label when marketing a product.

To assess the market's reaction to these decisions and identify considerations for future coverage of abuse-deterrent opioids, Avalere conducted an analysis of coverage and UM of long-acting opioid analgesics in the Medicare Part D market. Given the FDA's divergent abuse-deterrent labeling decisions in 2013 regarding Opana ER and OxyContin, Avalere assessed the market reaction across the two years before these decisions (2012 and 2013) and the two years following these decisions (2014 and 2015). The analysis explored coverage and UM of these two products, in addition to the coverage landscape for prescription opioids more broadly, in order to determine whether FDA's abuse-deterrent labeling decisions impacted plan coverage decisions.

Avalere used its proprietary DataFrame® database to assess coverage[vi] of both generic and branded long-acting opioids products by standalone prescription drug plans (PDPs) and Medicare Advantage prescription drug (MA-PDs) plans from 2012 to 2015. Specifically, Avalere focused its analysis on eight long-acting opioids, as well as OxyContin.[vii,viii]

Findings

Long-Acting Opioid Drug Coverage Rate Declining

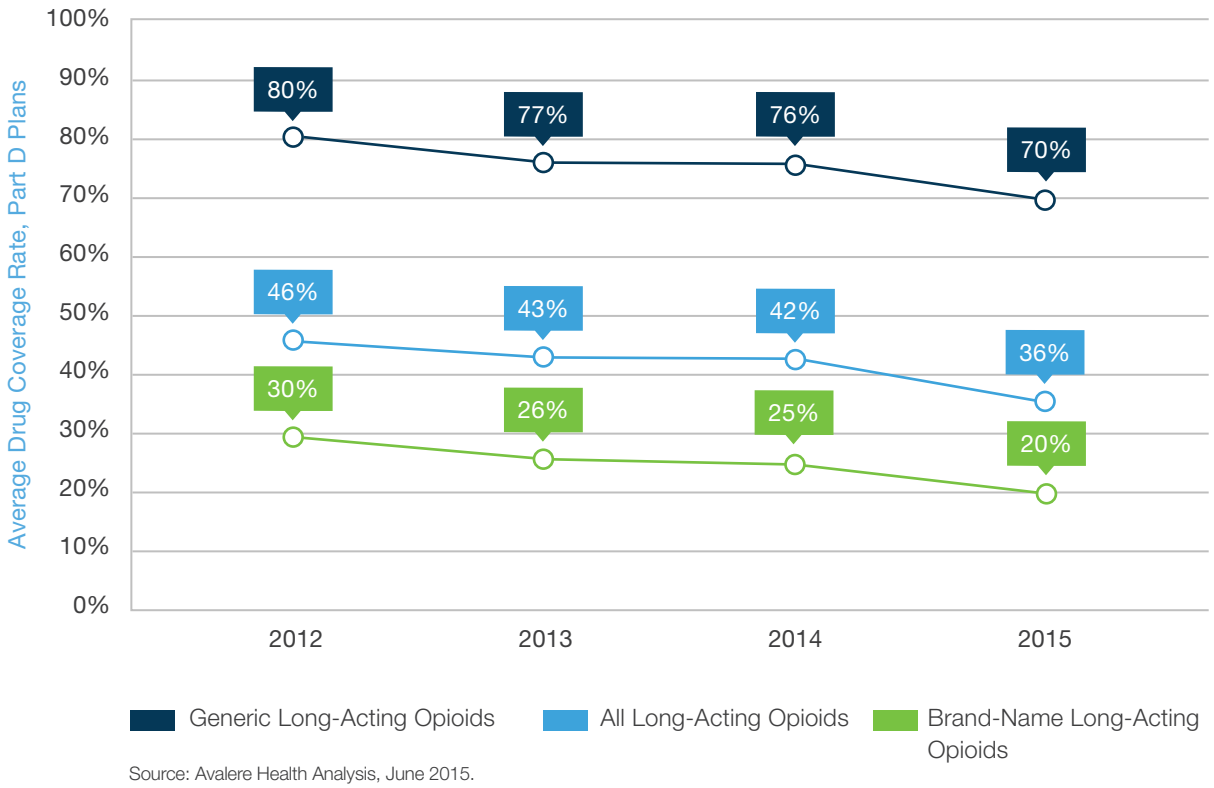
Part D plan coverage of all long-acting opioids has steadily declined between 2012 and 2015. After peaking at 46 percent of plans in 2012, long-acting opioids have a Part D coverage rate, on average, of 36 percent of plans in 2015 (**Figure 1**). This decline is even more significant among brand-name long-acting opioids. Branded opioid coverage rates have decreased proportionally by one-third and have a 20 percent average coverage rate in 2015. By

vi Avalere's analysis examines trends in coverage and therefore correlation. The analysis did not seek to determine a cause of changing coverage levels.

vii Included in this analysis are 54 opioids in the long-acting opioid analgesics U.S. Pharmacopeial Convention (USP) class, including 37 branded drugs and 17 generic drugs. Part D coverage rates include Medicare Advantage (MA Prescription Drug Plans (PDPs) and standalone PDPs.

viii Avalere's analysis includes 3,046 plans in 2012, 3,199 in 2013, 3,210 in 2014, and 3,136 in 2015. The analysis excludes 69 plans in 2012, 130 in 2013, 185 in 2014, and 31 in 2015 because CMS suppresses formulary data for sanctioned plans. These plans suppress formulary data on CMS' public use formulary files. These suppressed plans account for 3.4 million enrollees in 2012, 9.5 million enrollees in 2013, 12.2 million enrollees in 2014, and 11.8 million enrollees in 2015.

Figure 1: Average Drug Coverage Rate Among Part D Plans, Long-Acting Opioids, 2012-2015



Source: Avalere Health Analysis, June 2015.

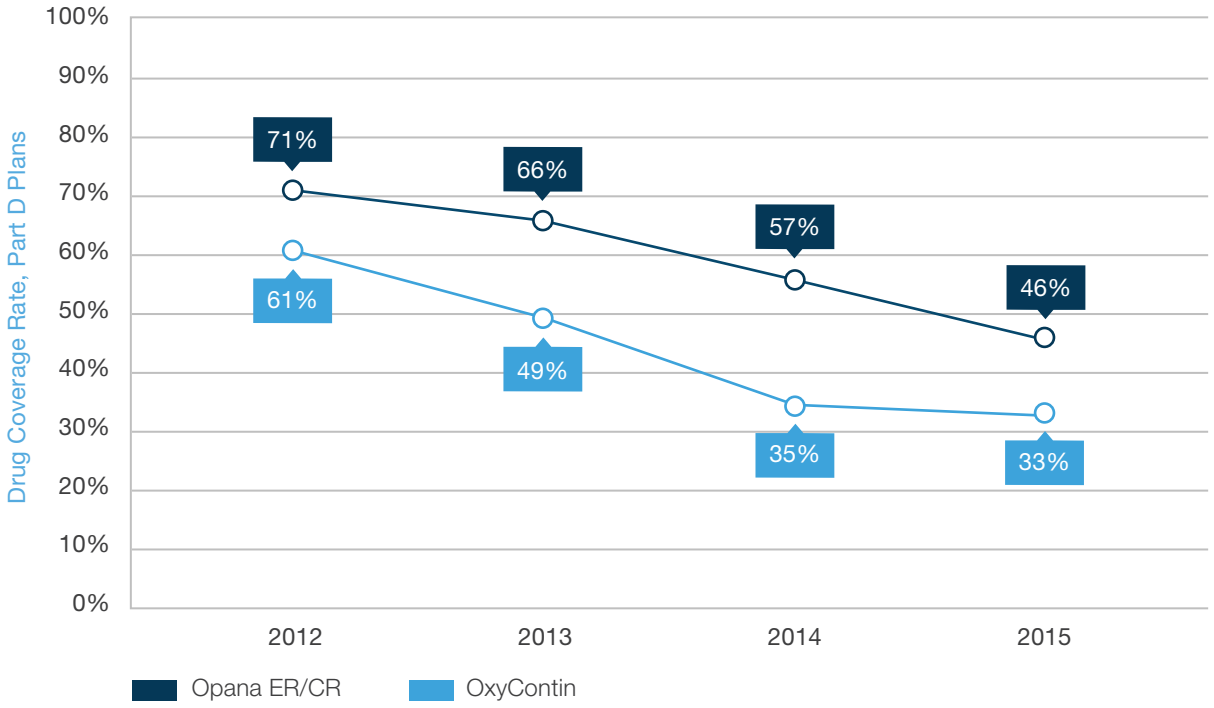
contrast, coverage of generic long-acting opioids decreased proportionally by 13 percent and generic opioids have a 70 percent Part D coverage rate in 2015, on average.

Coverage Rate of OxyContin Declines Despite Abuse-Deterrent Labeling

The FDA's labeling decisions for OxyContin and Opana ER in 2013, and Part D plans' corresponding response, provide insight into how plans chose to cover and manage the two products. In light of the FDA's decisions, if plans reacted by awarding preferential coverage to opioids with abuse-deterrent labeling, then the Part D drug coverage rate for OxyContin might be expected to be higher than that of Opana's.

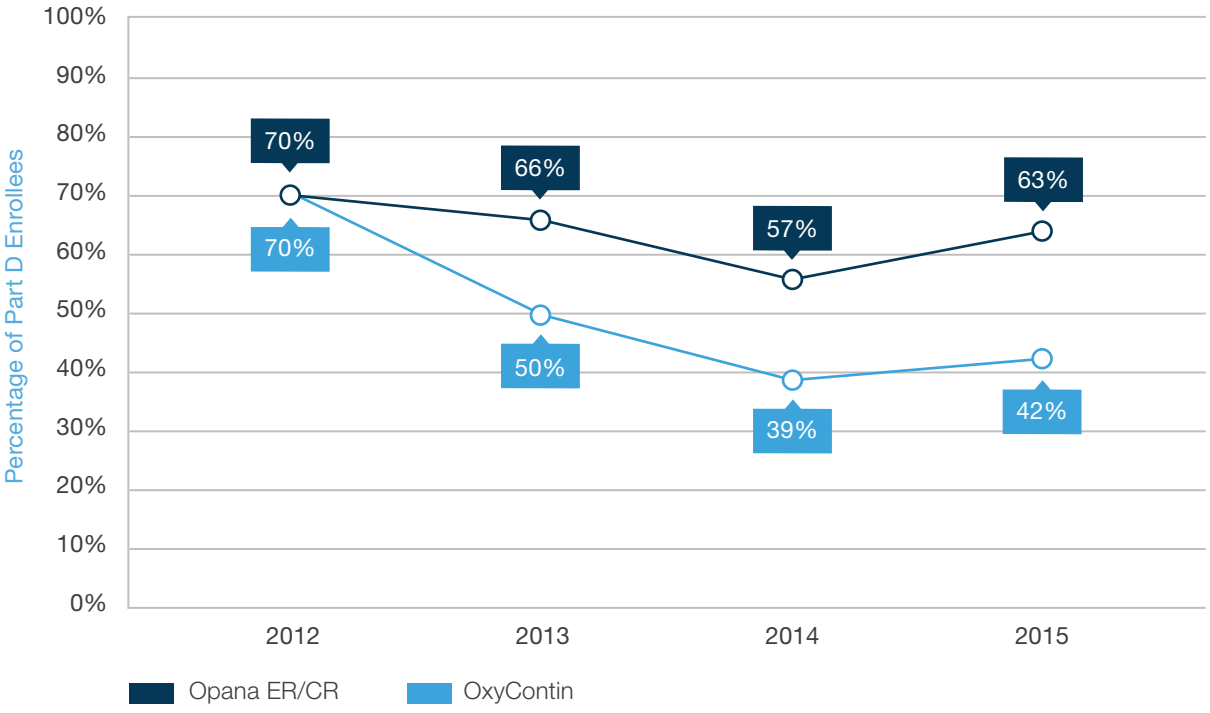
However, the results of Avalere's analysis show that while coverage rates for both Opana ER and OxyContin have reduced in line with the overall declining coverage rates of branded opioids, the rate of coverage for OxyContin is lower and has declined more sharply than that of Opana ER (**Figure 2**).

Figure 2: Opana and OxyContin Drug Coverage Rate Among Part D Plans, 2012-2015



Source: Avalere Health Analysis, June 2015.

Figure 3: Percentage of Part D Beneficiaries Enrolled in a Plan That Covers Opana and OxyContin, 2012-2015



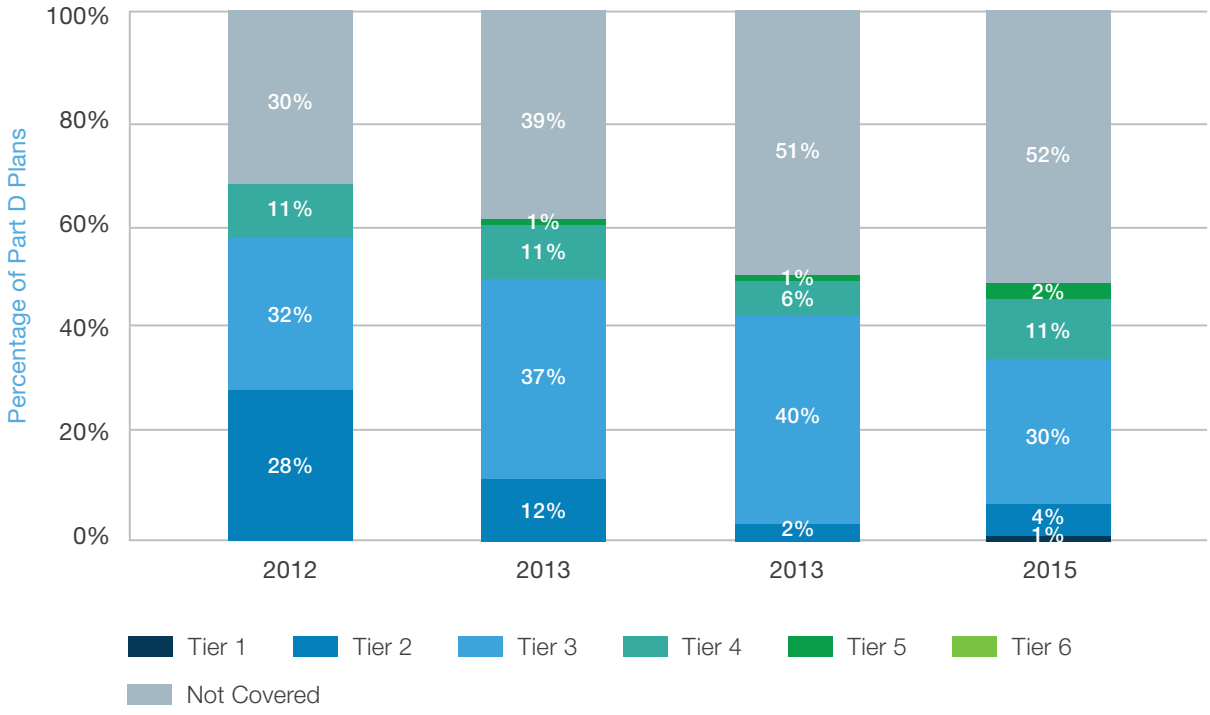
Source: Avalere Health Analysis, June 2015.

In addition, in 2015, 63 percent of Part D beneficiaries enrolled in a plan that covers Opana ER, versus 42 percent with OxyContin. In 2012, that rate was 70 percent for both drugs (**Figure 3**).

Part D plan coverage of Opana ER decreased by nearly a third between 2012 and 2015 (**Figure 2**). This equates to a 1.9 million reduction in the number of Part D beneficiaries enrolled in plans covering Opana ER—from 19.2 million patients in 2012 to 17.3 million in 2015.[ix] While only 30 percent of plans did not provide coverage for Opana in 2012, over half of all part D plans do not cover the drug in 2015.

As fewer plans have chosen to cover Opana ER, tier placement has similarly shifted. Fewer plans are placing Opana ER on their non-preferred generics tier 2 in 2015 compared to 2012, while slightly more plans are covering the drug on the specialty tiers 5 and 6 (**Figure 4**). Furthermore, an increasing percentage of plans also are placing quantity limits on Opana ER—95 percent in 2015 versus 74 percent in 2012.

Figure 4: Coverage and Tier Placement for Opana ER/CR, 2012-2015



Tier 1: Preferred Generics
Tier 2: Non-Preferred Generics
Tier 3: Preferred Brands
Tier 4: Non-Preferred Brands
Tier 5: Specialty / Injectable Tier
Tier 6: Specialty / Injectable Tier

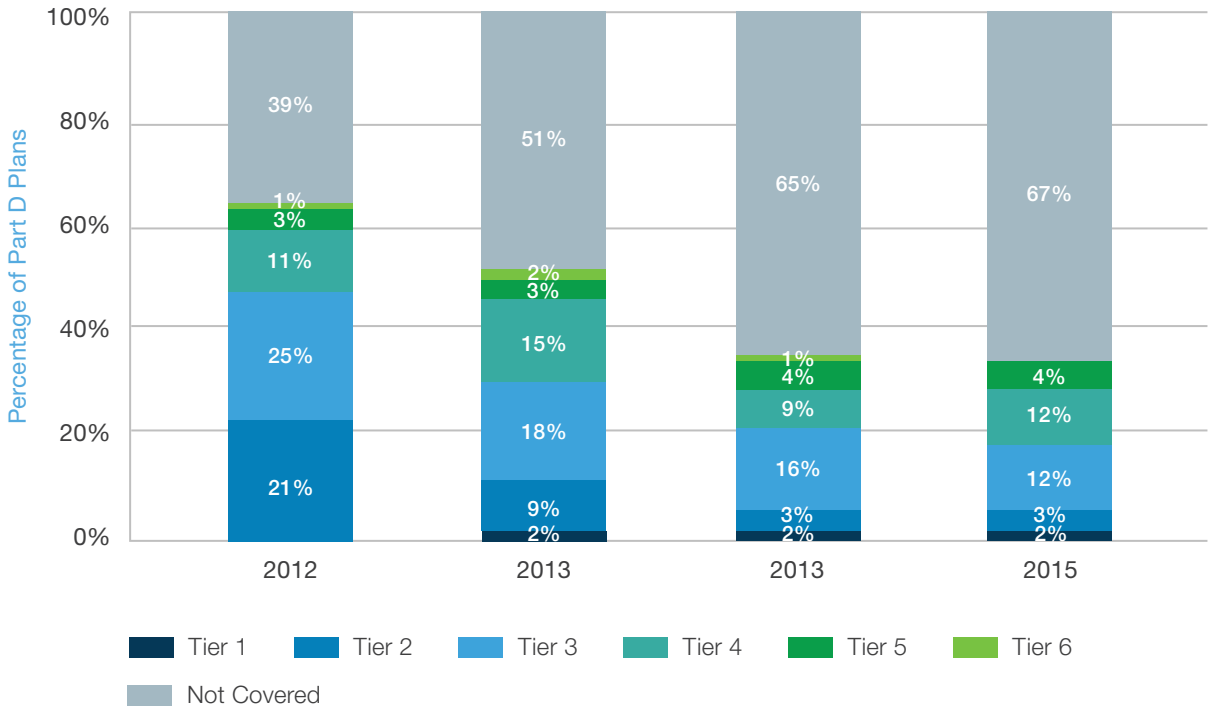
Source: Avalere Health Analysis, June 2015.

ix This figure increased between 2014 and 2015, a possible result of plan consolidation between those two years.

Surprisingly, Part D plan coverage of OxyContin follows a more negative trend than that experienced by Opana ER between 2012 and 2015. Despite its abuse-deterrent labeling, OxyContin is covered by fewer plans in 2015 than 2012 and is less likely to be placed on lower cost-sharing tiers.

Between 2012 and 2015, OxyContin's level of coverage among Part D plans declined by over 45 percent. By 2015, only a third of Part D plans covered OxyContin, a decline from 61 percent in 2012 (**Figure 1**). Accordingly, the proportion of Part D beneficiaries in a plan that covers OxyContin also decreased from 70 percent (19.2 million Part D enrollees) to 42 percent (11.7 million Part D enrollees). In addition, more Part D plans that cover the drug are placing it on higher cost-sharing tiers. In 2012, 21 percent of all Part D plans placed OxyContin on tier 2, compared to just 3 percent in 2015 (**Figure 5**).

Figure 5: Coverage and Tier Placement for OxyContin, 2012-2015

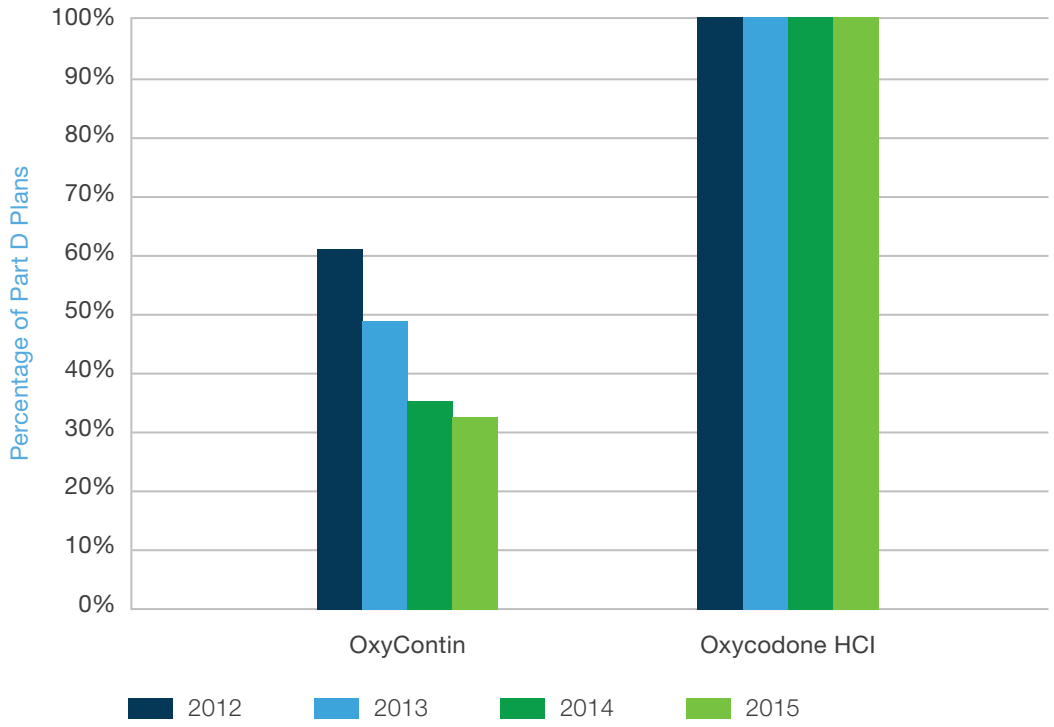


Tier 1: Preferred Generics
Tier 2: Non-Preferred Generics
Tier 3: Preferred Brands
Tier 4: Non-Preferred Brands
Tier 5: Specialty / Injectable Tier
Tier 6: Specialty / Injectable Tier

Source: Avalere Health Analysis, June 2015.

While there is no true generic equivalent version of OxyContin, Avalere analyzed the coverage rate of generic Oxycodone HCl IR, the active ingredient in OxyContin. Although coverage rates of OxyContin have decreased since 2012, nearly 100 percent of Part D plans analyzed cover Oxycodone HCl (**Figure 6**). Moreover, while a branded drug might be expected to have a higher rate of prior authorization, the safety and potential for abuse of these products makes it notable that Part D plans place prior authorization (PA) requirements on branded OxyContin at a higher rate than generic Oxycodone HCl, with 25 percent of Part D plans requiring PA on OxyContin in 2015 compared to only 0.3 percent of plans requiring PA for Oxycodone HCl (**Figure 7**).

Figure 6: Coverage Rate by Drug, Oxycodone HCl, 2012-2015



Source: Avalere Health Analysis, June 2015.

Figure 7: Rate of UM Tools by Drug, Oxycodone HCl, 2012-2015

OxyContin				Oxycodone HCl			
	PA	ST	QL		PA	ST	QL
2012	17%	12%	76%	**2012**	0%	0%	22%
2013	23%	11%	87%	**2013**	0%	0%	70%
2014	18%	19%	91%	**2014**	0%	0%	80%
2015	25%	8%	92%	**2015**	0.3%	1%	92%

PA = Prior Authorization
ST = Step Therapy
QL = Quantity Limits

Source: Avalere Health Analysis, June 2015.

Although these results are naturally limited by the fact that only one product that received abuse-deterrent labeling had Part D coverage data available for this analysis, our findings indicate that coverage of abuse-deterrent OxyContin has declined at a greater rate than the long-acting opioids class in general and non-abuse deterrent branded alternative (e.g., Opana ER). In addition, OxyContin is covered significantly less than generic, non–abuse deterrent formulations (e.g., Oxycodone HCl).

This analysis did not attempt to explain plan behavior and does not take into account other factors, including the cost of these products. Nonetheless, the results may suggest plans do not heavily weigh abuse-deterrent labeling in their coverage decisions and more favorably cover lower-cost generic alternatives.

It is also possible that, despite FDA labeling claims indicating abuse-deterrent opioids may result in reduction in abuse[34] and empirical evidence that shows the introduction of abuse-deterrent OxyContin can reduce opioid overdoses[35], plans may be waiting for more evidence that such products do in fact limit abuse before expanding coverage. It will be important to closely monitor these trends, including coverage of the recently approved abuse-deterrent opioids.

IMPLICATIONS FOR HEALTHCARE STAKEHOLDERS

The high rate of opioid abuse across the country has led to significant policymaker and public interest in abuse-deterrent opioids that may reduce the prevalence and impact of abuse. However, Avalere's analysis shows that Part D plans are favoring generic, non–abuse deterrent opioids on their formularies. Although it is not clear if this trend is tied to health plans reacting to the cost of abuse-deterrent opioids or a perceived lack of sufficient data to prove their effectiveness in reducing abuse, patients currently have greater access to generic opioids which are more susceptible to abuse.

As more abuse-deterrent products receive FDA approval, health plans will continue to have the difficult role of balancing the higher cost of these new formulations with their possible benefits. Furthermore, while abuse-deterrent opioids are an option for physicians to prescribe to their patients who may be at risk of opioid abuse, the ability of physicians to ensure their patients are receiving abuse-deterrent opioids is largely determined by health plan coverage, tiering, and UM.

It will be important for policymakers to monitor and consider the implications of these trends. There are a range of policy tools, from legislation to regulation and guidance to demonstration projects, which policymakers may consider as they weigh how to ensure sufficient incentives and policy tools to support the development of additional abuse-deterrent opioids. Lack of or disadvantaged market access to abuse-deterrent opioids compared with non–abuse deterrent options impacts incentives to invest in these new products. At the same time, the potential increase in costs due to new innovations may be a barrier to policies that increase the coverage of abuse-deterrent opioids, especially in public programs, despite potential long-term public health savings associated with lower levels of opioid abuse. While the greater number and quality of abuse-deterrent options—both brand and generic—can support competition, reduce cost, and increase plan coverage, the potential of abuse-deterrent technologies may not be fully realized as long as non–abuse deterrent alternatives have less restrictive insurance coverage.

CONCLUSION

When used as prescribed, opioid analgesics are safe and effective for their intended use, and are an important element in treating patients suffering from chronic pain. As policymakers continue to consider options to combat opioid abuse, it will be important for them to consider how to ensure patient access, including access to new innovations that might help limit potential abuse, while balancing this imperative with cost challenges.

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