
Highlights

From January 2009 through December 2014, a total of 369,738 benzodiazepines were identified by State and local forensic laboratories and reported to the National Forensic Laboratory Information System (NFLIS). Alprazolam, clonazepam, and diazepam were the most commonly reported benzodiazepines from January 2009 through December 2014, with alprazolam accounting for 66% of all selected benzodiazepines. Alprazolam and clonazepam increased by 5% and 16%, respectively, from 2009 to 2014, while diazepam decreased by 30% during the same period.

Nationally, the number of prescriptions dispensed for benzodiazepines increased 226% between 2009 (40.9 million) and 2014 (133.4 million). The numbers of prescriptions dispensed for each of the selected benzodiazepines increased between 2009 and 2014, ranging from 73% for flurazepam to 339% for midazolam. The number of dispensed prescriptions (in millions) for alprazolam increased 224% from 2009 to 2014, clonazepam increased 258%, and lorazepam increased 227%.

The seizure-to-prescription ratio for alprazolam was 9.39 drug reports identified in NFLIS per 10,000 prescriptions dispensed between 2009 and 2014, representing an increase since 2001–2005, when the ratio was 5.96 drug reports per 10,000 prescriptions dispensed.

Introduction

The National Forensic Laboratory Information System (NFLIS) is a program of the Drug Enforcement Administration (DEA), Office of Diversion Control, which systematically collects drug identification results and associated information from drug cases submitted to and analyzed by Federal, State, and local forensic laboratories. This publication presents the results of selected benzodiazepines submitted to State and local laboratories from January 1, 2009, through December 31, 2014, and analyzed within three months of each calendar year. National annual estimates are presented, as are regional trends for alprazolam, clonazepam, and diazepam. Maps showing State-level reports of clonazepam, phenazepam, and etizolam are shown. NFLIS results for benzodiazepines that are not approved for therapeutic use in the United States are also included. In addition, Federal data from DEA and U.S. Customs and Border Protection (CBP) laboratories are presented, along with data from IMS Health's National Prescription Audit Plus Retail database.

Benzodiazepines are central nervous system depressants commonly prescribed to treat anxiety, insomnia, and seizures (see Appendix A for the most common benzodiazepines reported to NFLIS, including their trade names and year approved for use in the United States). Benzodiazepines are considered safer alternatives to barbiturates because they have fewer side effects and have a reduced risk of causing an overdose. However, benzodiazepine abuse is often associated with people taking benzodiazepines in combination with other controlled substances such as opiates, methadone, and cocaine. Benzodiazepines are taken in combination with opiates in particular because they enhance the euphoric effects of opiates; for other drugs, such as stimulants, benzodiazepines may temper the negative side effects (e.g., restlessness, agitation). Given that benzodiazepines and opiates can cause respiratory depression, overdose death data illuminate the risks associated with combining benzodiazepines with opiates. In 2011, there were 41,340 deaths related to drug poisonings, of which 13%, or 5,188 deaths, involved benzodiazepines and opioid analgesics. Many compounds within the benzodiazepine drug class are within Schedule IV of the Controlled Substances Act and require a prescription for legitimate use. Although flunitrazepam is in Schedule IV, it has Schedule I penalties. Some of the newly reported benzodiazepines have not been approved for use in the United States. Phenazepam and etizolam have legitimate use as prescription drugs in countries other than the United States. Abuse of phenazepam has been observed in several countries, including the United States, Scotland, and Finland. A death due to phenazepam in combination with opiates has been reported in the United States. Diclazepam has also been observed as a new benzodiazepine.
**National Estimates**

Table 1 presents national annual estimates of selected benzodiazepines that were submitted to State and local laboratories from January 2009 through December 2014 and analyzed within three months of the calendar year reporting period. From 2009 to 2014, a total of 369,738 benzodiazepine reports were identified by State and local laboratories. Reports of benzodiazepines increased 2% from 2009 to 2014. Alprazolam, clonazepam, and diazepam were the most commonly reported compounds during this period, with alprazolam accounting for a total of 66% of all selected benzodiazepines. Alprazolam and clonazepam increased by 5% and 16%, respectively, from 2009 to 2014, while diazepam decreased by 30% during the same period.

There were 439 phenazepam reports submitted to NFLIS during this period. Phenazepam increased from 8 reports in 2009 to 89 reports in 2014. Reports of etizolam increased from 3 reports in 2012 to 174 reports in 2014. Nimetazepam increased from 1 report in 2009 to 27 reports in 2014. Temazepam, triazolam, clorazepate, flurazepam, and oxazepam decreased in the number of reports to NFLIS from 2009 to 2014. Of those compounds, flurazepam had the greatest decrease during this period: 72%.

![Table 1](image)

1 Includes drug reports submitted to laboratories from January 1, 2009, through December 31, 2014, that were analyzed within three months of the calendar year reporting period.

2 Numbers and percentages may not sum to totals because of rounding.

* Estimate suppressed because of low precision.

Regional Alprazolam, Clonazepam, and Diazepam Trends

This section presents NFLIS data for annual regional trends for alprazolam, clonazepam, and diazepam per 100,000 persons aged 15 or older. By region, the highest rates of alprazolam continued to be reported in the South from 2009 to 2014 (Figure 1). The estimated number of alprazolam reports in the South peaked in 2010 at a rate of 29.90 reports per 100,000 persons (27,443 reports), then gradually decreased to a rate of 22.13 reports per 100,000 persons (21,040 reports) in 2013, followed by a slight increase. The Midwest and Northeast fluctuated between slight increases and decreases in alprazolam during this period. By region, the lowest rates for alprazolam continued to be reported in the West.

During 2009, the Northeast and the South had similar rates for clonazepam at 5.03 and 5.02 reports per 100,000 persons (2,266 and 4,549 reports), respectively. The rates for clonazepam in the South continually increased, surpassing the Northeast in 2012. The estimated number of clonazepam reports in the Midwest increased from a rate of 3.95 reports per 100,000 persons (2,112 reports) in 2009 to a rate of 4.53 reports per 100,000 persons (2,477 reports) in 2014. Clonazepam reports were also the lowest in the West.

Unlike alprazolam and clonazepam, the lowest rates for diazepam were in the Northeast, whereas the rates in the West were only slightly higher. All regions generally had decreasing numbers of diazepam reports from 2009 to 2014. The greatest decreases in diazepam reports from 2009 to 2014 were in the West and South with rates of 2.32 to 1.24 reports per 100,000 persons (1,310 to 746 reports) and 4.33 to 3.00 reports per 100,000 persons (3,923 to 2,870 reports), respectively.

Note: U.S. Census 2014 population data by age were not available for this publication. Population data for 2014 were imputed.
NFLIS collects the results of drug evidence from DEA and CBP laboratories. The data reflect the results of evidence from drug seizures, undercover drug buys, targeted operations, and other evidence analyzed at DEA and CBP laboratories across the country. Although DEA data capture both domestic and international drug cases, the results presented in this section describe only those drugs obtained within the United States. Similarly, the CBP data represent seizures at U.S. points of entry and domestic drug cases.

A total of 37,936 drug reports were submitted to the DEA and CBP during 2014 and analyzed within three months of the calendar year reporting period. The most commonly identified benzodiazepine was alprazolam, which accounted for less than 1% (274 reports), followed by diazepam (41 reports), clonazepam (26 reports), and lorazepam (8 reports). In addition, midazolam (3 reports), etizolam (2 reports), phenazepam (2 reports), temazepam (2 reports), and bromazepam (1 report) were also submitted to DEA and CBP laboratories during 2014 and analyzed within 90 days.

Selected Benzodiazepines of Interest

Although phenazepam, etizolam, and diclazepam are not approved for therapeutic use in the United States, they have received attention in recent years for their abuse or involvement in drug-related deaths. Raw counts within the NFLIS data show that between January 2009 and December 2014, phenazepam and etizolam were more common than diclazepam. Phenazepam was first reported to NFLIS in 2005 and had a total count of 302 reports between January 2009 and December 2014, and etizolam was first reported in 2012 and had a total count of 254 reports during that same period. Diclazepam was first reported in 2014 and by the year’s end had a total count of 2 reports.

Counts of Alprazolam Reported with Other Drugs

This section examines State and local laboratory counts of alprazolam identified with other drugs within the same item. The NFLIS data presented in this section are actual reported data rather than national estimates. In addition, this section does not present counts of true combinations (e.g., powders mixed together) but instead provides counts of separate drugs reported together in the same item. For example, a laboratory may consider a bag of pills containing alprazolam and oxycodone to be one item. As a result, both drugs would be reported as substances within that single item. Policies for determining what an item is vary by laboratory.

During 2014, 325 reports of alprazolam and other drugs were identified within the same item. As shown in Figure 4, of the 325 reports of alprazolam with other drugs within the same item, 30% of the reports involved alprazolam and illicit drugs (98 reports), including methamphetamine (11%), cocaine (7%), heroin (6%), and cannabis/THC (6%). In addition, 27% were reports of alprazolam and narcotic analgesics (88 reports), the most common being oxycodone (5%, data not shown). Finally, 19% of the reports of alprazolam involved alprazolam and other benzodiazepines (62 reports), including etizolam (6%), clonazepam (3%), and nimetazepam (3%).

Even fewer reports of benzodiazepines other than alprazolam were reported with other drugs within the same item. Overall, only 172 reports of clonazepam and other drugs were identified within the same item, as were 115 reports of diazepam and other drugs, 37 reports of lorazepam and other drugs, and 3 reports of temazepam and other drugs (data not shown).
This section presents NFLIS data at the State level for the number of drug reports identified as clonazepam, phenazepam, and etizolam during 2009 and 2014. The geographic data presented here are based on information provided to the forensic laboratories by the submitting law enforcement agencies in the county of origin associated with the drug seizure incident. It is important to note that these data represent only those items that were submitted to and analyzed by forensic laboratories. In addition, a small number of laboratories within a few States were not reporting data to NFLIS, and their absence may affect the relative distribution of drugs seized and analyzed.

As shown in Figure 5, a total of 46 States reported clonazepam during 2009. During that time, 21 States had between 1 and 99 reports, 13 States had between 100 and 299 reports, and 9 States had between 300 and 499 reports. Three States had 500 or more reports of clonazepam during 2009. By 2014, the number of States reporting 500 or more clonazepam reports increased to seven (Figure 6). The States with the highest numbers of clonazepam reports during 2014 were mainly in the Northeast, South, and Midwest. Most States in these three regions had 100 or more reports. In comparison, only three States in the West had 100 or more reports of clonazepam during the same period.

As shown in Figure 7, only one State reported phenazepam during 2009. By 2014, nine States had reported phenazepam. Of these, two States had 20 or more reports, one had between 10 and 19 reports, and six had between 1 and 5 reports (Figure 8). The Midwest, Northeast, and South had at least one State with phenazepam reports during 2014. No States in the West had any phenazepam reports during that time. States showing the highest number of phenazepam reports were in the South, specifically Texas, Georgia, and Louisiana.
No States reported etizolam during 2009 (Figure 9). By 2014, 22 States had reported etizolam, including one that had 50 or more reports and one that had between 10 and 29 reports (Figure 10). The remaining 20 States reporting etizolam had between 1 and 9 reports.

Selected Benzodiazepine Prescriptions Dispensed

IMS Health's National Prescription Audit Plus Retail database provides data on the number of prescriptions that have been dispensed for legitimate use. Nationally, the number of prescriptions for benzodiazepines increased 226% overall between 2009 (40.9 million) and 2014 (133.4 million) (Table 2).

The numbers of prescriptions dispensed for each of the selected benzodiazepines increased between 2009 and 2014, ranging from 73% for flurazepam to 339% for midazolam. The number of dispensed prescriptions (in millions) for alprazolam—the most commonly prescribed benzodiazepine across all years—increased 224% from 2009 to 2014. Clonazepam, the second most dispensed benzodiazepine in 2014, increased 258% from 2009 to 2014. Lorazepam increased 227% with 8.9 million prescriptions in 2009 and 29.0 million prescriptions in 2014.

Table 2

<table>
<thead>
<tr>
<th></th>
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<th></th>
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<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Alprazolam</td>
<td>15.2</td>
<td>47.2</td>
<td>48.7</td>
<td>49.2</td>
<td>49.5</td>
<td>49.2</td>
<td>223.5</td>
<td>36.9</td>
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<td>Clonazepam</td>
<td>8.3</td>
<td>25.8</td>
<td>26.9</td>
<td>28.1</td>
<td>29.2</td>
<td>29.8</td>
<td>258.2</td>
<td>22.3</td>
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<td>Lorazepam</td>
<td>8.9</td>
<td>27.0</td>
<td>27.5</td>
<td>28.0</td>
<td>28.8</td>
<td>29.0</td>
<td>227.3</td>
<td>21.7</td>
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<tr>
<td>Diazepam</td>
<td>4.6</td>
<td>14.3</td>
<td>14.7</td>
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<td>14.8</td>
<td>14.6</td>
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<td>Temazepam</td>
<td>2.8</td>
<td>8.5</td>
<td>8.5</td>
<td>8.3</td>
<td>8.3</td>
<td>8.3</td>
<td>196.9</td>
<td>6.2</td>
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<td>Triazolam</td>
<td>0.4</td>
<td>1.2</td>
<td>1.2</td>
<td>1.2</td>
<td>1.2</td>
<td>1.1</td>
<td>181.7</td>
<td>0.9</td>
</tr>
<tr>
<td>Clorazepate</td>
<td>0.4</td>
<td>0.9</td>
<td>0.9</td>
<td>0.8</td>
<td>0.8</td>
<td>0.8</td>
<td>115.8</td>
<td>0.6</td>
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<tr>
<td>Oxazepam</td>
<td>0.2</td>
<td>0.5</td>
<td>0.4</td>
<td>0.4</td>
<td>0.3</td>
<td>0.3</td>
<td>78.5</td>
<td>0.2</td>
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<tr>
<td>Flurazepam</td>
<td>0.2</td>
<td>0.4</td>
<td>0.4</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>73.0</td>
<td>0.2</td>
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<tr>
<td>Estazolam</td>
<td>0.05</td>
<td>0.2</td>
<td>0.2</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>127.2</td>
<td>0.1</td>
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<tr>
<td>Midazolam</td>
<td>0.006</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>0.03</td>
<td>339.2</td>
<td>0.0</td>
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<tr>
<td>Total</td>
<td>40.9</td>
<td>126.0</td>
<td>129.3</td>
<td>131.3</td>
<td>133.2</td>
<td>133.4</td>
<td>226.1</td>
<td>100.0</td>
</tr>
</tbody>
</table>

1Numbers and percentages may not sum to totals because of rounding.

Source: IMS Health's National Prescription Audit Plus Retail database.
**Diversion of Selected Benzodiazepines**

Through the years, NFLIS has been able to provide an approximation of the extent to which prescription drugs are diverted by comparing IMS Health’s National Prescription Audit Plus Retail data with forensic laboratory data on drugs seized by law enforcement. In 2006, the DEA published a report on prescription drugs reported in NFLIS between 2001 and 2005 that showed drugs with the highest seizure-to-prescription ratios. The list of drugs with high seizure-to-prescription ratios included the following benzodiazepines: alprazolam, diazepam, clonazepam, and lorazepam.

Table 3 compares the 2001–2005 ratios from that report with the results from 2009 to 2014 using NFLIS and IMS Health’s prescription data. As shown, across the selected four drugs, alprazolam had the largest seizure-to-prescription ratio in 2009–2014 (9.39 drug reports identified in NFLIS per 10,000 prescriptions dispensed), which points to a higher level of diversion given the availability of the drug. Moreover, alprazolam had the largest ratio change between 2001–2005 and 2009–2014. During this time, clonazepam and lorazepam both showed modest increases for their respective seizure-to-prescription ratios, while the ratio for diazepam between those two periods decreased. Notably, across all four drugs, the numbers of reports in NFLIS and the numbers of prescriptions increased between the 2001–2005 and 2009–2014 periods.

<table>
<thead>
<tr>
<th>Selected Benzodiazepine</th>
<th>Drug Reports Identified in NFLIS</th>
<th>Prescriptions Dispensed</th>
<th>Drug Reports Identified in NFLIS per 10,000 Prescriptions Dispensed</th>
<th>Drug Reports Identified in NFLIS</th>
<th>Prescriptions Dispensed</th>
<th>Drug Reports Identified in NFLIS per 10,000 Prescriptions Dispensed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam</td>
<td>101,135</td>
<td>169,691,000</td>
<td>5.96</td>
<td>243,138</td>
<td>258,944,000</td>
<td>9.39</td>
</tr>
<tr>
<td>Diazepam</td>
<td>39,565</td>
<td>65,299,000</td>
<td>6.06</td>
<td>39,747</td>
<td>77,789,000</td>
<td>5.11</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>29,340</td>
<td>82,534,000</td>
<td>3.55</td>
<td>67,215</td>
<td>148,003,000</td>
<td>4.54</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>8,038</td>
<td>112,318,000</td>
<td>0.72</td>
<td>14,649</td>
<td>149,078,000</td>
<td>0.98</td>
</tr>
</tbody>
</table>


**Appendix A: Selected Properties of the Most Commonly Reported Benzodiazepines in NFLIS**

<table>
<thead>
<tr>
<th>Benzodiazepine</th>
<th>Examples of Common Drug Trade Names</th>
<th>Approved for Use in the United States</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam</td>
<td>Xanax*</td>
<td>1981</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>Klonopin*</td>
<td>1974</td>
</tr>
<tr>
<td>Diazepam</td>
<td>Valium*</td>
<td>1963</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>Ativan*</td>
<td>1977</td>
</tr>
</tbody>
</table>

Note: The U.S. Government does not endorse or favor any specific commercial product or company. Trade, proprietary, or company names appearing in this publication are used only because they provided some context for the drugs reported herein.
Special Report:
Benzodiazepines Reported in NFLIS, 2009–2014

U.S. Drug Enforcement Administration
Office of Diversion Control
8701 Morrissette Drive
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January 2016

References


Methodology: A summary of the NFLIS estimation methodology can be found in the NFLIS Statistical Methodology publication at https://www.nflis.deadiversion.usdoj.gov/Reports.aspx.

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