Unintentional Pediatric Exposures to Buprenorphine – Lessons Learned

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Disclosures

• RADARS® System is independently owned and operated by Denver Health & Hospital Authority, a political subdivision of the state of Colorado.

• Funding for the RADARS System comes from data subscriptions, including many manufacturers of prescription opioids and stimulants.

• Specific study discussed today was funded by Reckitt Benckiser Pharmaceuticals.
Root Causes, Clinical Effects, and Outcomes of Unintentional Exposures to Buprenorphine by Young Children

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Objective To characterize the rates, root causes, and clinical effects of unintentional exposures to buprenorphine sublingual formulations among young children and to determine whether exposure characteristics differ between formulations.

Retrospective Cross-Sectional Study Design

- Unintentional exposures to buprenorphine-containing products
  - RADARS® System Poison Center Program
  - Reckitt Benckiser pharmacovigilance system
- Children age 28 days to <6 years
- Negative binomial regression to estimate average exposure rates
- Root cause, expert panel evaluation of causality and severity of moderate to severe AEs
Table 1: Characteristics of Children Aged 28 Days to < 6 Years with Unintentional Exposures to Buprenorphine

*Key finding: no difference in age distribution between products*

<table>
<thead>
<tr>
<th>AGE</th>
<th>Total Bup* n=2380</th>
<th>Bup Tablets n=154</th>
<th>Bup/Naloxone Tablets n=2107</th>
<th>Bup/Naloxone Film n=118</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not Reported</td>
<td>24 (1.0%)</td>
<td>1 (0.6%)</td>
<td>18 (0.9%)</td>
<td>5 (4.2%)</td>
</tr>
<tr>
<td>28 To 364 Days</td>
<td>148 (6.2%)</td>
<td>15 (9.7%)</td>
<td>123 (5.8%)</td>
<td>10 (8.5%)</td>
</tr>
<tr>
<td>1 Year To &lt;2 Years</td>
<td>885 (37.2%)</td>
<td>58 (37.7%)</td>
<td>788 (37.4%)</td>
<td>39 (33.1%)</td>
</tr>
<tr>
<td>2 Years To &lt;3 Years</td>
<td>888 (37.3%)</td>
<td>61 (39.6%)</td>
<td>787 (37.4%)</td>
<td>40 (33.9%)</td>
</tr>
<tr>
<td>3 Years To &lt;4 Years</td>
<td>320 (13.4%)</td>
<td>18 (11.7%)</td>
<td>279 (13.2%)</td>
<td>22 (18.6%)</td>
</tr>
<tr>
<td>4 Years To &lt;5 Years</td>
<td>100 (4.2%)</td>
<td>2 (1.3%)</td>
<td>94 (4.5%)</td>
<td>4 (3.4%)</td>
</tr>
<tr>
<td>5 Years To &lt;6 Years</td>
<td>36 (1.5%)</td>
<td>0 (0.0%)</td>
<td>35 (1.7%)</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Exact Age Not Reported</td>
<td>3 (0.1%)</td>
<td>0 (0.0%)</td>
<td>1 (0.0%)</td>
<td>2 (1.7%)</td>
</tr>
</tbody>
</table>
Figure 2. Rates of unintentional exposure to buprenorphine among children aged 28 days to less than 6 years, adjusted for drug availability.
Key Findings of Root Cause Evaluation Pertinent to PROTECT:

- **Access/storage**
  - Taken out of original package – why?
  - Cutting/altering dose (prescribing behavior and/or patient-driven dosing?)
  - Stigma associated with medication?

- **Packaging**
  - Unit dose AND child resistant?
Buprenorphine Packaging

- **Tablets**: typically in bottle with child-resistant closure
Buprenorphine Packaging

- **Film**: unit dose packaging with child-resistant foil pouch
Buprenorphine Packaging
Buprenorphine Packaging

• NEW Tablet: unit dose packaging with child-resistant foil blister pack
Summary

• Toxicity of pediatric exposure is of concern with all opioids and measures to protect these children are imperative in new drug development.

• Access/storage of buprenorphine is the leading contributing factor to pediatric exposures, not a new problem.

• The role of self-management of dosing and alteration of original product, problem specific to patient population, therapeutic indication, drug or drug class?