How Purdue Was Allowed to Push OxyContin

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Emergency Department, University Health Network

Conflicts of Interest

- In 2015-2017 I received funding for being a consultant on two projects – one looking at indication-based prescribing and a second examining which drugs should be provided free of charge by general practitioners. I was also paid for being on a panel discussing expanding drug insurance in Canada. I am on the Foundation Board of Health Action International.

Learning Objectives

1. Understand how promotion led to the widespread use of OxyContin
2. Examine the issue of conflict-of-interest in medical education about pain control
3. Explore how to control promotion related to any new drugs with the potential for abuse

Growth in OxyContin Use

- 2005 – not among the top 100 drugs by prescription numbers in Canada
- 2011 – over 1.64 million prescriptions — One of the top 60 most prescribed drugs (no. 54)

Drug Companies’ Dilemma

- Appropriate use & possibly lower sales
- Aggressive marketing, higher and possibly inappropriate use & larger sales

Promotional Spending on Opioids - US

Government Accountability Office: OxyContin Abuse and Diversion and Efforts to Address the Problem. Dec. 2003
Purdue Sales Force

Table 1: Sales Representative Positions Available for OxyContin Promotion, 1996 through 2002

<table>
<thead>
<tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Purdue Prescription Sales Division</td>
<td>318</td>
<td>319</td>
<td>377</td>
<td>471</td>
<td>562</td>
<td>641</td>
<td>641</td>
</tr>
<tr>
<td>Purdue Hospital Specialty Division</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>109</td>
<td>125</td>
<td>126</td>
</tr>
<tr>
<td>Subtotal—All Purdue sales representatives</td>
<td>318</td>
<td>319</td>
<td>377</td>
<td>471</td>
<td>671</td>
<td>765</td>
<td>767</td>
</tr>
<tr>
<td>Abbott Laboratories sales representatives</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
</tr>
<tr>
<td>Total</td>
<td>618</td>
<td>619</td>
<td>677</td>
<td>771</td>
<td>971</td>
<td>1,066</td>
<td>1,067</td>
</tr>
</tbody>
</table>

Government Accountability Office: OxyContin Abuse and Diversion and Efforts to Address the Problem, Dec. 2003

Key Messages

- Purdue aggressively marketed OxyContin
- Once OxyContin was listed on the Ontario Drug Benefit Formulary use of long acting oxycodone went up and so did deaths from opioids

In the United States

- Purdue acknowledged that its employees misled physicians about the risk of addiction
- Capitalized on the prevalent misconception that oxycodone is less potent than morphine when the converse is true
- Purdue
  - Targeted physicians who prescribed OxyContin frequently
  - Paid its sales representatives large bonuses as an incentive to increase OxyContin sales
  - Issued coupons entitling new patients to free samples at participating pharmacies

Information from Pharmaceutical Companies and the Quality, Quantity, and Cost of Physicians’ Prescribing: A Systematic Review

Geoffrey K. Spurting,1,2,3 Peter R. Mansfield1,2,3 Brett D. Montgomery4, Joel Leschin4, Jenny Douc4, Nooradin Othman5, Agnes S. Wirry6

PLoS Medicine 2010;7(10):e1000352

Review of 58 studies looking at frequency, cost and quality of prescribing after receiving information directly from the pharmaceutical industry:

- Only one study showed improvement in one aspect of prescribing
- All the rest showed either no change or prescribing got worse

Dhalla et al. CMAJ 2009;181:891-6
In the United States

• Purdue used very detailed information on physician prescribing practices to promote OxyContin since 1996

• Only in 2002 did Purdue begin to use this information “to identify patterns of prescribing that could point to possible improper sales representative promotion or physician abuse and diversion of OxyContin”

Canadian Regulation of Promotion

• Health Canada theoretically has the power to regulate promotion through the Food and Drugs Act

• In practice activities of sales representatives are regulated by the Code of Conduct of Rx&D
  – Self regulatory code
  – No active monitoring, just complaints based system

Willful Blindness

• When asked why companies fined for illegal promotion in the US had not been fined in Canada one Health Canada official said:
  – Health Canada “had not been made aware of any specific similar issue in Canada and has not received complaints concerning these companies”

Key Messages

• Purdue admitted in court that it engaged in illegal promotion in the US

• Health Canada never investigated whether this was true in Canada
Regulation of Journal Advertising in Canada

- Research-based companies have agreed to have all advertisements precleared by the Pharmaceutical Advertising Advisory Board
- PAAB governing body dominated by people from organizations that stand to gain financially from journal advertising
- Critics of PAAB have been threatened with legal action and called “a loose cannon” and “living in their own perfect world”

**PAAB Board**

- Association of Faculties of Medicine of Canada (AFMC)
- Association of Medical Advertising Agencies
- Best Medicines Coalition (BMC)
- BIOTECanada
- Canada’s Research-Based Pharmaceutical Companies (Rx&D)
- Canadian Association of Medical Publishers (CAMP)
- Canadian Generic Pharmaceutical Association (CGPA)
- Canadian Medical Association (CMA)
- Canadian Pharmacists Association (CPhA)
- Consumers Council of Canada
- Canadian Association of Retired Persons (CARP)
- Consumer Health Products Canada
- Fédération des Médecins du Québec (FMQ)

**Specific types of harm mentioned (n=1692)**

- Non-serious AE
- Contra-indications
- Serious AE
- Drug Interactions

**Information on health effects provided**

≥ 1 benefit or ≥ 1 harm

- Vancouver [n=438]: 79% benefit, 12% harm, 1% both
- Montreal [n=420]: 68% benefit, 18% harm, 6% both
- Sacramento [n=468]: 77% benefit, 9% harm, 4% both
- Toulouse [n=488]: 65% benefit, 16% harm, 8% both
- Total [n=1692]: 75% benefit, 81% harm, 8% both

**Known by Purdue to be false**

Canadian Family Physician 2000

**Basis for the statement was a single letter in the New England Journal of Medicine**

**Doesn’t mention that WHO pain ladder developed for cancer pain**

**To the Editor:** Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well-documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients, Peridural in one, and hydrocodone in one. We conclude that despite widespread use of narcotic drugs in hospital, the development of addiction is rare in medical patients with no history of addiction.

Jane Porter
Hermine Jick, M.D.
Boston Collaborative Drug Surveillance Program

Waltham, MA 02154

Boston University Medical Center

Original Product Monograph (Prescribing Information)

• OxyContin approved in Canada in 1996
  – Long-acting formulation would impart a lower risk for abuse compared with other opioid analgesics
• Product Monograph not modified until 2006

WHO Pain Relief Ladder vs. “Modified” WHO Analgesic Ladder

<table>
<thead>
<tr>
<th>Step</th>
<th>WHO Pain Relief Ladder</th>
<th>Modified WHO Analgesic Ladder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1</td>
<td>Non-opioids ± adjuvants</td>
<td>Aspirin, paracetamol (acetaminophen)</td>
</tr>
<tr>
<td>Step 2</td>
<td>Mild or weak opioids ± non-opioids ± adjuvants</td>
<td>Codeine</td>
</tr>
<tr>
<td>Step 3</td>
<td>Strong opioids ± non-opioids ± adjuvants</td>
<td>Morphine</td>
</tr>
</tbody>
</table>

Bayer Admits Violating Industry Code

Industry Sales Reps

• To a Montreal doctor after rosiglitazone (Avandia) had been linked to congestive heart failure and cardiac problems
  – “Avandia is safe even in patients with heart disease as long as they don’t suffer from heart failure”

Entrees run from about $40 to $75 per person
Most Money is Spent Promoting Drugs of Little Therapeutic Value

<table>
<thead>
<tr>
<th>Category</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major therapeutic gain</td>
<td>0 (0.0)</td>
<td>3711 (2.3)</td>
<td>3369 (1.6)</td>
</tr>
<tr>
<td>Moderate therapeutic gain</td>
<td>5816 (3.5)</td>
<td>9050 (5.7)</td>
<td>9268 (4.5)</td>
</tr>
<tr>
<td>Little to no therapeutic gain</td>
<td>159 399 (96.5)</td>
<td>149 941 (92.0)</td>
<td>192 644 (95.8)</td>
</tr>
<tr>
<td>Overall</td>
<td>165 615 (100.0)</td>
<td>163 902 (100.0)</td>
<td>205 271 (100.0)</td>
</tr>
</tbody>
</table>

Key Messages

- There is poor control over drug promotion in Canada
- The CMA's guidelines are good but the CMA does little to publicize them
- Promotion doesn’t provide information about therapeutically important drugs

Key Opinion Leaders

- Doctors paid to speak for drug companies
- Purdue pays about 100 doctors per year to speak on its behalf
  - Up to $2000 per talk
- Dr. Brian Goldman (CBC: White Coat, Black Art)
  - Began working for an unnamed pharmaceutical company in the late 1990s, doing talks and educational videos funded by "unrestricted" company grants.
  - "If I travelled to another city to give the talk, it was on the company’s dime," he wrote. "I was put up in five-star hotels and taken to nice restaurants. When I travelled across the continent, I was invariably given a ticket in business class.”

University of Toronto & Pain Week

- Since 2000, the University of Toronto has given a one-week course on pain management to all of its health science students
- Between 2002 and 2006, the course was funded by unrestricted educational grants from four pharmaceutical companies, including Purdue
- Up until 2010, students were given a book on pain management that was Purdue produced
  - One of the co-authors of the book, and an unpaid guest lecturer for the course, was on the speakers’ bureau for Purdue

Textbook Produced by Purdue

- Contained the ‘modified WHO analgesic ladder’ that listed oxycodone among weak opioids
- Earlier edition said that long-acting opioid formulations had a ‘lower abuse potential’ than short-acting formulations
- In some instances, bookmarks displaying trade names of the Purdue’s products were tethered to the books

Inquiry into U of T Pain Week

- Curriculum should not be "directly funded (in whole or in part) by industry donors who have, or may have, or be perceived to have financial interests in the assessment or management of pain."
- Only University of Toronto faculty members should teach the course
Key Messages

- Doctors were complicit in the promotion of OxyContin
- OxyNeo approved in US April 5/2010
- OxyNeo approved in Canada Aug. 22/2011
- OxyContin not discontinued in Canada until March 2012
- Canadian patent on OxyContin expired Nov. 2012
- Purdue says that it did not discontinue OxyContin because it needed to get OxyNeo onto provincial formularies
  - Purdue was keeping a drug on formularies that was known to have a high abuse potential

Provincial Formulary Coverage for OxyNeo

<table>
<thead>
<tr>
<th>Province</th>
<th>Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alberta</td>
<td>General coverage</td>
</tr>
<tr>
<td>British Columbia</td>
<td>Restricted access</td>
</tr>
<tr>
<td>Manitoba</td>
<td>Restricted access</td>
</tr>
<tr>
<td>New Brunswick</td>
<td>Not covered but reimbursed for patients using OxyContin when it was discontinued</td>
</tr>
<tr>
<td>Newfoundland &amp; Labrador</td>
<td>Not covered but reimbursed for patients using OxyContin when it was discontinued</td>
</tr>
<tr>
<td>Northwest Territories</td>
<td>Not covered</td>
</tr>
<tr>
<td>Nova Scotia</td>
<td>Not covered but reimbursed for patients using OxyContin when it was discontinued</td>
</tr>
<tr>
<td>Nunavut</td>
<td>Not covered</td>
</tr>
<tr>
<td>Ontario</td>
<td>Restricted access</td>
</tr>
<tr>
<td>PEI</td>
<td>Not covered but reimbursed for patients using OxyContin when it was discontinued</td>
</tr>
<tr>
<td>Quebec</td>
<td>Restricted access</td>
</tr>
<tr>
<td>Saskatchewan</td>
<td>Restricted access</td>
</tr>
<tr>
<td>Yukon</td>
<td>Not covered</td>
</tr>
</tbody>
</table>

OxyNeo Sales ($)

<table>
<thead>
<tr>
<th>Year</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sales</td>
<td>122,443</td>
<td>111,975</td>
<td>106,520</td>
</tr>
</tbody>
</table>

OxyNEO Promotion in Canada, 2013

<table>
<thead>
<tr>
<th>Amount spent on sales reps &amp; journal ads ($)</th>
<th>Number of pages of medical journal ads</th>
<th>Number of visits by sales reps</th>
</tr>
</thead>
<tbody>
<tr>
<td>3,014,000</td>
<td>143</td>
<td>17,000</td>
</tr>
</tbody>
</table>

IMS Health|Brogan: Canadian Pharmaceutical Annual Report 2013

Hippocrates Hypocrisy

Key Messages

- The switch from OxyContin to OxyNeo was for marketing reasons
- Purdue hasn’t changed how it promotes its products

What Can Be Done?

1. Prior to the approval of any product that has a high potential for abuse the company marketing the product needs to develop a plan to deal with misprescribing;
2. For the first two years, or until the potential for abuse can be evaluated, promotion of the product needs to be strictly overseen by Health Canada;
3. There should not be any distribution of samples;
4. A panel of doctors who see sales representatives should be recruited to provide Health Canada with information about the messages that the sales representatives are delivering;
5. Regulatory authorities should set up a prescription event monitoring program;
6. Drugs felt to have a high abuse potential should have a special mark on all prescriptions to alert doctors and patients of this danger;
7. Physician groups represented on the PAAB should push for a more rigorous code.
8. The CMA should vigorously promote its guidelines