PUBLIC CITIZEN Health Letter

SIDNEY M. WOLFE, M.D., EDITOR FEBRUARY 2013 – Vol. 29, No. 2

# Nondrug Therapies Help Dementia Patients And Their Caregivers

Dementia is a devastating disorder causing serious, progressive cognitive and behavioral disabilities. In addition to its impact on the patient, dementia adversely affects the mental and physical health of the patient's in-home caregiver — most frequently the patient's spouse or adult child.

It also is a disorder that is difficult to treat medically. Available drug therapies for the underlying diseases that cause dementia, such as Alzheimer's disease, offer little benefit and have potentially serious side effects. Moreover, patients suffering from the advanced stages of dementia are often prescribed dangerous medicines, such as powerful antipsychotic drugs, to control troublesome behaviors. This inappropriate prescribing has persisted despite explicit warnings on the labels of these drugs that they increase the risk of death in elderly patients with dementia.

Given the lack of safe, effective drug treatments, alternative interventions must be provided to dementia patients. A recent study suggests that a variety of nondrug, in-home therapies targeting caregivers can provide benefits to both dementia patients and their caregivers. The results offer hope for an improved quality of life with this terrible disorder.

**The [study] authors ... concluded that nondrug interventions targeting caregivers of dementia patients can significantly reduce the behavioral and psychological symptoms of those patients, as well as the caregivers' negative reactions to the symptoms.**

## Overview of dementia

Dementia is caused by progressive deterioration of the brain, which results in impaired cognition and memory loss. Dementia patients are unable to perform many normal daily activities, such as dressing, washing, cooking, eating and using the toilet.

Alzheimer's disease, the most common cause of dementia among the elderly, accounts for 60 to 80 percent of all cases. Approximately 4 million people in the U.S. currently suffer from Alzheimer's disease, and by 2050, an estimated 11 million to 16 million Americans will have it.

Other causes of dementia include vascular dementia (which is caused by multiple small strokes and is the underlying cause in 10 to 20 percent of dementia cases), frontotemporal dementia (associated with degeneration of the frontal and temporal lobes of the brain), Parkinson's disease, Huntington's disease and multiple sclerosis.

The signs of dementia are most often reported to a physician by a spouse or other close acquaintance of the patient. Typical signs of dementia include:

- difficulty remembering recent events;
- inability to perform complex tasks, such as balancing a checkbook;
- getting lost in familiar places;
- language problems, such as an inability to find the right word when speaking; and
- behavior changes that interfere with performance at work, daily activities and social relationships.

These symptoms have an insidious onset and progress gradually over many months to years.

In more advanced stages of dementia, patients exhibit troublesome behaviors and psychological problems, such as:

- screaming;
- physical aggression;
- personality clashes (arguments between patients and caregivers);
- repetitive questioning;
- wandering;
- depression;
- resistance to help with daily activities;
- paranoia; and
- not sleeping at night.

Most dementia patients in the U.S. live at home and are cared for by a

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PUBLIC CITIZEN
# Health Letter
FEBRUARY 2013
Vol. 29, No. 2

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The Health Research Group was co-founded in 1971 by Ralph Nader and Sidney Wolfe in Washington, D.C., to fight for the public's health and give consumers more control over decisions that affect their health.

Annual subscription rate is $18 (12 issues).



*Health Letter*
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family member living with them or nearby. The behaviors and problems associated with dementia place great stress on caregivers and are associated with depression, increased burdens, and large outlays of both time and money.

## Study overview

In a study published in September 2012 in the *American Journal of Psychiatry (AJP)*, researchers in Australia analyzed data from all randomized, controlled clinical trials (RCTs) testing nondrug therapies involving family caregivers of patients with dementia.

The researchers systematically searched computer databases of all English-language medical journals for relevant studies published from 1985 through July 2010. They found 23 RCTs, published between 1997 and 2010, meeting their search criteria. Using a study design known as a meta-analysis, the researchers pooled the results from the trials, which collectively included 3,279 dementia patients and their primary caregivers. (These RCTs all enrolled more than five dementia patients and their caregivers.)

The RCTs tested a wide range of interventions (see Figure 1), all of which were administered to caregivers with the goal of improving the health and well-being of the dementia patient, the caregiver or both. Many trials tested multiple interventions in combination.

The method of delivery of the interventions also varied significantly across trials and included:

- printed educational materials;
- telephone calls;
- individual sessions in the health care provider/office setting;
- group sessions in a classroom setting; and
- in-home sessions.

Many of the studies used a variety of such delivery methods, and the interventions lasted anywhere from six weeks to 24 months.

For dementia patients, the RCTs most commonly measured the frequency and severity of behavioral and psychological symptoms as rated by standardized questionnaires, typically based on the assessment of the caregiver. Four trials also measured how frequently the patients transitioned from the home care setting to an institutional care setting (e.g., assisted living facility or nursing home). For caregivers, the RCTs measured the psychological and emotional reactions (e.g., level of stress, anxiety and depression) to the dementia patients' behavioral and psychological symptoms and quality of life, again as rated on standardized questionnaires.

**Optimal care for patients with dementia clearly needs to involve nondrug interventions targeting the caregivers of dementia patients. Such treatment improves the health and well-being of both patient and caregiver.**

For the 17 RCTs that measured outcomes in dementia patients, analysis of the pooled data revealed a significant overall beneficial effect, as evidenced by reductions in the troublesome behavioral and psychological symptoms of dementia. For the few studies that looked at the rate at which dementia patients were institutionalized, no benefit was detected. However, the number of studies assessing this outcome was too small to reliably detect an effect.

Likewise, for the 13 RCTs that measured outcomes in the caregivers, there was a significant overall improvement in measures of stress, anxiety, depression and quality of life.

## Implications of the study

The authors of the meta-analysis concluded that nondrug interventions targeting caregivers of dementia patients can significantly reduce the

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behavioral and psychological symptoms of those patients, as well as the caregivers' negative reactions to the symptoms. They also noted that these beneficial effects are at least comparable to those achieved with antipsychotic drugs administered to dementia patients. Most importantly, unlike antipsychotics (and other drugs), the interventions used in the 23 RCTs included in their review had no adverse effects on the dementia patients or the caregivers.

In an editorial in the September 2012 *AJP* commenting on the meta-analysis study, Dr. Laura Gitlin, a research sociologist at the Johns Hopkins University Schools of Nursing and Medicine and an internationally recognized expert on nonpharmacologic approaches in dementia care, noted the following:

> [T]he meta-analysis provides the strongest evidence to date that caregiver interventions have a twofold advantage: they reduce distress in caregivers, and they reduce behavioral symptoms in individuals with dementia. This quantitative synthesis of high-quality studies provides confirmation that helping families is an important vehicle for helping patients. As such, these interventions should be central to the clinical management of behavioral symptoms. The primary challenge remains how to widely implement and financially sustain delivery of these interventions to address the urgent need of families.

Quoting another editorial published in the *Annals of Internal Medicine* in 2006 that discussed the findings of one RCT funded by the National Institutes of Health and included in the *AJP* meta-analysis, Gitlin also stated the following:

> 'If these interventions [for dementia] were drugs, it is hard to believe that they would not be on the fast track to approval. The magnitude of benefit and quality of evidence supporting these interventions considerably exceed those of currently approved pharmacologic therapies (for dementia).' If not now, then when will these proven programs be made available to families who continue to receive suboptimal care or no treatment at all for behavioral symptoms? [The *AJP*] meta-analysis provides strong evidence that helping families is good news for dementia care.

Public Citizen's Health Research Group strongly agrees with Gitlin's viewpoint. Optimal care for patients with dementia clearly needs to involve nondrug interventions targeting the caregivers of dementia patients. Such treatment improves the health and well-being of both patient and caregiver. ✦

**Figure 1: Categories and Elements of Interventions Included in the Review**

| |
|---|
| **1. Skills training for caregivers** |
| Managing behavioral and psychological symptoms of dementia |
| Communicating better with care recipient |
| Using role play, videos modeling behavior management strategies, cognitive-behavioral interventions, vignettes, live interviews |
| Enhancing care recipients quality of life, e.g., improving daily activities, increasing pleasant events |
| **2. Education for caregivers** |
| Psychoeducation |
| Improving home care |
| Tailored advice and recommendations |
| Problem-solving methods |
| Improving support network |
| Computer-mediated automated interactive voice response |
| Planning: emergencies, legal, financial |
| **3. Activity planning and environmental redesign** |
| Planning activities with caregiver for care recipient |
| Modifying care recipient's physical and social environment |
| **4. Enhancing support for caregivers** |
| Social support |
| Web or telephone support |
| Strategies on how to access support |
| Family counseling |
| **5. Self-care techniques for caregivers** |
| Health management |
| Stress management |
| Coping with change as a result of caregiving |
| Music therapy |
| Counseling |
| **6. Miscellaneous** |
| Collaborative care with a health professional or care manager |
| Exercise for care recipient |

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# Early Testing for Alzheimer's Disease

New tests have become available in recent years claiming the ability to discover and diagnose Alzheimer's disease in its early stages, possibly even before the first mild symptoms of mental impairment begin to show. If you or a loved one are older and have experienced unusual memory loss or other signs of mental impairment, it may be tempting to try one of these tests to see if you might be experiencing the early stages of Alzheimer's disease.

Yet these early tests leave unanswered many important questions about how the disease will progress, and no effective treatment has been identified to prevent or delay the decline in mental function caused by Alzheimer's disease. This means that for many people, early testing will likely end up causing more problems than it solves and should thus be avoided in most cases.

## Alzheimer's disease and mild cognitive impairment

Alzheimer's disease is one of the most common causes of dementia, particularly in people over the age of 65. The disease causes a slow, progressive decline in memory and mental (cognitive) function that eventually leads to dementia, a state of mental impairment serious enough to interfere with day-to-day life.

Alzheimer's disease is definitively diagnosed and distinguished from other causes of dementia by the presence of a large number of abnormal formations in the brain known as amyloid plaques. The clearest way to diagnose a case of Alzheimer's disease is after death, when the brain can be examined directly through an autopsy.

Currently there is no treatment that can prevent, cure or stop the decline in mental function in people with Alzheimer's disease. Several drug therapies are currently marketed to treat later-stage Alzheimer's disease symptoms, but Public Citizen's WorstPills.org website has categorized each of these drugs as DO NOT USE, because none produce meaningful improvements in cognitive function and all have harmful side effects.

Alzheimer's disease often progresses very slowly, with people in its early stages often experiencing some level of mild mental (cognitive) impairment but still living life as normal. Not all people with mild cognitive impairment will progress into Alzheimer's-related dementia; in fact, they have a 12 percent chance of that happening each year. Some will never develop dementia or will develop it from causes other than Alzheimer's disease.

It is difficult to predict whether a person with mild cognitive impairment will progress to Alzheimer's-related dementia. Identifying Alzheimer's patients early has historically been difficult, as doctors cannot usually examine a living person's brain directly or take a biopsy (piece of tissue) to look for amyloid plaques. Furthermore, even if Alzheimer's disease can be diagnosed at this stage, there is variation between individuals in terms of how a given number or type of abnormalities will affect symptoms of mental impairment.

Researchers have found that people with certain risk factors or conditions may be more likely to develop symptoms of dementia. For example, people with lower levels of education seem more likely to experience cognitive decline than people with higher education levels. Other risk factors include smoking, having hypertension or diabetes, or having a history of blood vessel problems (including stroke). There is limited evidence that people can actually reduce their risk of dementia by quitting smoking, living a heart-healthy lifestyle, and treating diabetes or hypertension.

## Early testing for Alzheimer's disease

Scientists have begun to experiment with tests to attempt to predict whether a person with mild (or even absent) symptoms may one day progress to Alzheimer's-related dementia. These tests come in various forms. One widely publicized, expensive test involves using a positron emission tomography (PET) scan to search for the amyloid plaques in the brain that may begin to appear even before symptoms manifest. Researchers have found that healthy people with these plaques in their brains are more likely to develop Alzheimer's-related dementia later in life. Other tests employ a series of different brain images combined with analysis of brain fluid to detect potential signs of early Alzheimer's disease before symptoms begin to appear.

These tests help researchers learn more about the disease, and they may lead to accurate, early diagnosis in some cases. However, they also create stress, cost money and leave many questions unanswered for patients and their families.

Some people may gain satisfaction from knowing an Alzheimer's disease diagnosis early, feeling it may allow them more time to prepare for the future by assessing care options and making important legal or financial arrangements. But learning a diagnosis also can be profoundly troubling and can create depression, anxiety and stress, both for the diagnosed individual and his or her family. Moreover, none of the current tests can help determine whether a person with early signs of Alzheimer's disease will progress quickly to dementia or continue to live normally for years.

A diagnosis may help encourage a person to give up smoking, treat hypertension or diabetes, and live a healthier lifestyle. But these actions are generally recommended in the first place and may also help prevent other conditions, such as stroke, heart attack and organ damage.

Finally, these tests are costly, and an Alzheimer's disease diagnosis may affect a person's ability to obtain health insurance coverage. With all the pitfalls

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and costs of early testing, many — if not most — people are probably better off avoiding testing and focusing their energy on staying healthy.

## Testing that may help

There are some tests for people with mild cognitive impairment that can be useful in identifying or excluding other conditions that may lead to reduced mental function. These conditions include nutritional deficiencies, sleep disorders, undiagnosed diabetes, autoimmune disorders, infections (such as Lyme disease), undetected cerebrovascular disease (such as stroke) or side effects from medications.

Testing also might be useful in helping to diagnose and manage symptoms. For example, PET scans are sometimes used to distinguish between Alzheimer's disease and frontotemporal dementia, a disease that affects behavior and personality and is more likely to be found in younger people with dementia. There is no treatment that can cure or slow the progress of frontotemporal dementia, but the symptoms of this disease may be managed differently than the symptoms of Alzheimer's disease.

## Emerging research

Some doctors who engaged in Alzheimer's research may encourage early testing and then offer enrollment in clinical trials to study new treatments for early Alzheimer's disease. One current research strategy is to take the treatments that have failed to delay or reverse the decline in cognitive function for patients with later-stage Alzheimer's disease and test them on patients with a less-advanced disease, in hopes that the timing of treatment will make a difference in effectiveness.

Patients should be cautious about enrolling in clinical trials for Alzheimer's disease and recognize that any potential benefits from proposed treatments are still hypothetical at best. All of the drugs that have previously been tested for treatment of mild cognitive impairment have proven disappointing. While it is still possible that an effective treatment may be found to delay or prevent Alzheimer's disease, patients should be wary of clinical tests or trials promising to diagnose and cure the disease, because it is still too early for researchers to know whether these products are actually effective.

**Ask yourself what health steps you would take if you received an early Alzheimer's diagnosis, and consider whether you could benefit from taking the same steps regardless of testing.**

## Recommendations

It is normal for memory and other mental processes to decline with age, and mild cognitive impairment does not mean a person will develop dementia. If you notice that you or a loved one are beginning to have difficulties with memory loss or confusion, you should consult a doctor to see if the impairment may be due to a treatable condition.

Tell your doctor if you are taking sleeping pills or tranquilizers, as these drugs can cause side effects such as confusion and memory loss that may be reversed by stopping the medication. Other drugs, including certain antidepressants, also have been associated with impaired mental function. Your doctor should run tests for hypertension, diabetes, or an infection that affects the brain and nervous system, such as Lyme disease.

Think carefully before getting a PET scan or other test specifically designed to detect Alzheimer's disease. Ask yourself what health steps you would take if you received an early Alzheimer's diagnosis, and consider whether you could benefit from taking the same steps regardless of testing. One example would be scheduling an appointment with an attorney who specializes in elder law to discuss the legal issues that affect people as they age and begin to require greater assistance from family members and other caregivers.

Also, talk with your doctor about general steps you can take to stay mentally and physically healthy as you age, including quitting smoking, eating a heart-healthy diet, and controlling blood pressure and diabetes. A training program in problem-solving or other types of therapy could offer organizational strategies and other tools to cope with mild symptoms of confusion and memory loss. Counseling or medication may be necessary to help address depression, which is common in people with mild cognitive impairment and also may affect family members.

While it may be tempting to seek certainty from testing, remember that with or without an Alzheimer's diagnosis, there always will be uncertainty about how symptoms of cognitive impairment will progress. Given the limited benefits of early testing, it is probably better to focus on the concrete, general steps one can take to stay healthy and plan for the future rather than putting effort and resources into obtaining an early diagnosis with no clear benefits. ✦

# Novel Tactics Impede Generic Competition to Suboxone Tablets

When a brand-name drug's patent or exclusivity period expires, opening the door to competition by generic drugmakers, sales of the brand-name drug often dramatically and quickly dwindle, typically declining around 80 percent or more within six months. To avoid this outcome, pharmaceutical companies faced with a drug's patent expiration or with new generic competition have employed an assortment of unethical if not illegal tactics to extend their profits long after legal monopoly has faded. Such strategies have traditionally included frivolous lawsuits against would-be generic competitors; new patent applications for almost identical drug formulations; and so-called "pay for delay" deals with potential competitors, in which the manufacturer of a branded drug pays off one or more generic drug companies to delay the introduction of generic formulations. (The legality of this particular anticompetitive practice will be addressed by the U.S. Supreme Court later this year.)

But few, if any, companies have gone as far as to pre-emptively withdraw an off-patent drug from the market to make way for a newly patented successor in the way that British-based Reckitt Benckiser Pharmaceuticals did in September 2012. Claiming a concern for children's safety, the company abruptly announced that it was discontinuing the widely used buprenorphine/naloxone (Suboxone) tablets, which treat addiction to heroin and opioid painkillers, in favor of a new format: a film that, like the tablet, dissolves under the tongue. The move raised concerns regarding both the company's true motives and the resulting difficulties presented for patients needing access to the life-saving medication.

## Dubious motives

Reckitt recently commissioned the Rocky Mountain Poison and Drug Center (RMPDC) to investigate the risk of pediatric exposure from Suboxone tablets relative to its newly patented Suboxone film formulation. In its decision to withdraw the tablets from the market, Reckitt cited the RMPDC study's results, which showed that children could be accidentally harmed by easy access to Suboxone tablets marketed in bottles. The company focused on the study's finding that its film version, sold as individual units wrapped in blister packaging, was eight times less likely to be ingested by children than the tablet version packaged in bottles containing up to 30 tablets. The RMPDC's director, Dr. Richard Dart, explained that this was most likely because the film's blister packaging was more difficult for children to open, with fewer doses accessed each time, than the tablets' bottle packaging.

"Reckitt Benckiser Pharmaceuticals has a moral obligation to act as quickly as possible on safety data relating to its products," a company spokesman told *Forbes*. The spokesman noted that a risk-management strategy including patient education had been in place since 2003 to minimize accidental exposure to children.

Some critics asked why the company had waited so long to take such a drastic measure, when the rate of pediatric exposure to Suboxone tablets had been increasing for years prior to the September 2012 announcement from Reckitt. Others asked why, given the study's findings that unit-dose packaging could mitigate much or possibly all of the risk of the tablet version, Reckitt didn't simply change the tablets' packaging.

Reckitt offers unit-dose, child-resistant blister packaging for Suboxone in non-U.S. markets, including Canada and the United Kingdom. However, the company claimed that the Food and Drug Administration (FDA) approval process necessary to introduce the same packaging in the U.S. would have taken too long. It also cited "technical issues involving the integrity of the tablet when attempting to remove it from the packaging," an issue apparently overcome in other markets. Although Reckitt admitted that "later studies revealed that unit-dose packaging of Suboxone may be feasible [in the U.S.]," the company instead "focused its resources on the development of Suboxone Film."

In October 2009, Reckitt lost its exclusive marketing rights for the Suboxone tablet. The company's 2011 annual report stated that "… up to 80 percent of the revenue and profit of the Suboxone tablet business in the U.S. might be lost in the year following the launch of generic competitors, with the possibility of further erosion thereafter." Its September 2012 announcement to withdraw Suboxone tablets from the market came one year before, observers say, the company widely expected generic competitors to enter the market, in 2013. (No generics have yet been introduced.)

"They are (removing the tablets) because generics are expected in 2013 on the tablet," Sanford Bernstein analyst Ronny Gal told Ed Silverman, a reporter on the pharmaceutical industry, in *Forbes*. "The critical question is whether their argument that film is always safer for children will convince [the FDA] not to approve any oral solid generic."

The company formally denied any link between the possibility of generic competition and its decision to abruptly phase out the tablets.

## Transitioning patients: traditional and novel tactics

A year before the withdrawal of the tablets, Reckitt stated in its 2011 report that its goal was to "support

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conversion" of as many tablet users as possible to the film formulation. To this end, the company initiated a marketing campaign to persuade physicians to switch patients from the tablet to film form. It also employed more direct tactics to complement the marketing push, raising the price of the tablets to levels higher than the film versions. As a result of these efforts, tablet sales fell 19 percent between August 2011 and August 2012, while sales of Suboxone film doubled during the same period. By September 2012, the film version had captured 70 percent of the Suboxone market, clearing the way for the announcement of the withdrawal of the tablets that month.

With its own tablets removed from the market, the company also moved to prevent any other tablet formulation from competing with its new film version. On the day of its announcement of the withdrawal of Suboxone tablets from the market, Reckitt filed a Citizen's Petition with the FDA requesting that the agency not approve any other tablet formulation of Suboxone unless the generic manufacturer implemented "national public health safeguards involving pediatric exposure educational campaigns and child-resistant, unit-dosed packaging to reduce the risk of pediatric exposure." While few disagreed that these precautions would be desirable, critics quickly noted that generic manufacturers had, in fact, been trying to implement these measures for months, with Reckitt stifling their efforts.

In 2011, the FDA had already mandated that, as a condition of approval, interested generic manufacturers must devise a risk evaluation and mitigation strategy (REMS), with some of the components referred to in Reckitt's petition, to mitigate pediatric risks. However, the agency required the creation of a single, industry-wide REMS and mandated that all potential generic makers must work through Reckitt, as the manufacturer of the brand-name drug, to devise the program. This ensured that generic manufacturers would depend on Reckitt's cooperation in devising the REMS.

Generic manufacturers complained that Reckitt subsequently dragged its feet, with little to no progress made on the unified REMS necessary to bring a new generic Suboxone tablet to market. "There are many components in their REMS, and these can be very stringent, but Reckitt won't tell us what they are. They've seized upon this and used the situation to their advantage. And no progress has been made," one industry source told *Forbes*. Reckitt denied obstruction of the process, claiming that it was "actively engaged in these multiparty discussions."

That the FDA preferred a single, standardized REMS, and that it relied on Reckitt, the only manufacturer of Suboxone at the time, to devise such a program, was reasonable. However, there is no indication that the FDA has either criticized or pressured Reckitt since that time regarding the company's apparent refusal to cooperate with the generic makers. The FDA has 180 days from the petition's submission to respond to Reckitt's petition (as of Jan. 16, 2013, there has been no response), and it remains to be seen whether the agency will grant the company's request in light of the lack of any progress by the company on a REMS.

## Profits over patients

For all the talk of its concern for public health, Reckitt is apparently less concerned with how its decision to effectively extend its monopoly on Suboxone for another 10 years will affect access to its medication.

The replacement of the tablet with a film version that will remain under patent until 2022 creates a major financial barrier for Suboxone patients who may be unable to continue paying monopoly prices for the new formulation. (According to a Reckitt spokesperson, the wholesale average cost for a bottle of 30 Suboxone tablets as of October 2012 ranged from $161.70 for the 2-milligram (mg) dose to $289.80 for the 8-mg dose, and a 30-day supply of Suboxone film runs from $117.85 for the 2-mg dose to $211.15 for the 8-mg dose. Generic versions of drugs typically cost around 75 percent less than brand-name drugs.)

Patients who cannot currently afford the Suboxone tablet to treat addiction to heroin and opioid painkillers but could potentially afford generic versions will continue to face the same financial barriers with the new film version. The move will similarly cost Medicaid, which covers many poor patients on Suboxone for opioid addiction, at a time when the public health insurance program faces the prospect of increasing cuts by financially strapped state governments.

Furthermore, continued access to Suboxone is more critical than ever. The epidemic of addiction to opioid pharmaceuticals is now at an all-time high, with the number of deaths due to opioid overdoses tripling from 2000 to 2009. More than 15,000 people died from accidental opioid overdoses in 2011, now dwarfing deaths from heroin abuse, which have held steady.

It remains to be seen how long Reckitt can continue to shrewdly fend off generic competition. Whatever the outcome, the tenacity of the company makes strikingly clear the lengths to which brand-name drug manufacturers will go to preserve their monopoly profits on life-saving medicines. As the number of truly innovative drugs continues to decline, some of the most innovative output emerging from the modern-day drug industry seem to be an ever-evolving arsenal of tactics wielded to stifle generic competition. ✦

## HRG Works for You!

### Our latest work involves a dangerous tuberculosis drug and our continued response to the fungal meningitis outbreak

The work of Public Citizen's Health Research Group (HRG) doesn't end with our *Health Letter* and *Worst Pills, Best Pills News* publications. HRG uses current academic research, government data and information from whistleblowers to advocate for consumers by:

- petitioning the government to remove unsafe drugs or medical devices from the market, and to require warnings of dangerous side effects on other drugs;
- testifying before government committees and arguing against approval of unsafe or ineffective drugs and medical devices;
- writing letters to government agencies about the adverse effects of drugs and medical devices; and
- lobbying Congress to strengthen the regulatory oversight of drugs and medical devices.

Our latest consumer advocacy includes:

- **Letter to Food and Drug Administration (FDA) Opposing Approval of Bedaquiline — 12/21/2012 —** Public Citizen strongly opposes the accelerated approval of bedaquiline, used to help patients with multiple drug-resistant tuberculosis, because patients taking the drug in addition to standard tuberculosis treatment during a phase 2 clinical trial were five times more likely to die than those who took a placebo.

- **Letter to Department of Health and Human Services (HHS) Secretary Regarding the FDA Commissioner's Congressional Testimony on Compounded Drugs — 12/18/2012 —** Public Citizen criticizes FDA Commissioner Margaret Hamburg for undermining her agency's authority in congressional testimony in November 2012 regarding the oversight of compounding pharmacies, as well as offering a plan that would effectively weaken the agency's oversight of drug manufacturing.

- **Comments to Senate Committee on Health, Education, Labor, and Pensions on the FDA's Flawed Proposal for Oversight of Compounding Pharmacies — 11/30/2012 —** In response to the recent fungal meningitis outbreak, the FDA proposed a new regulatory framework for compounding pharmacies that would weaken, rather than strengthen, existing laws governing drug manufacturing. Public Citizen believes it wiser to strengthen existing laws by clarifying the line between traditional pharmacy compounding and drug manufacturing and clearing up the federal standards governing traditional compounding. All drug manufacturers must be held to the same rigorous safety and quality standards.

- **Letter to the FDA Urging Re-Inspection of Compounding Pharmacies With Serious Safety Violations — 11/29/2012 —** The dangers of unregulated compounding pharmacies have been made tragically clear in the wake of the recent fungal meningitis outbreak. Public Citizen urges the FDA to promptly re-inspect each of the 16 compounding pharmacy facilities where serious safety concerns were uncovered in earlier inspections and initiate a systematic program to determine whether other compounding pharmacies are engaged in illegal practices.

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*Visit www.citizen.org/hrgpublications to read full reports and testimonies as HRG fights for government accountability in the interest of the public's health.*

# Product Recalls

## December 5, 2012 – January 1, 2013

This section includes recalls from the Food and Drug Administration (FDA) Enforcement Report for drugs and dietary supplements (www.fda.gov/Safety/Recalls/EnforcementReports/default.htm), and Consumer Product Safety Commission (CPSC) recalls of consumer products.

## DRUGS AND DIETARY SUPPLEMENTS

### Recalls and Field Corrections: Drugs – Class I

Indicates a problem that may cause serious injury or death

**Reumofan Plus Tablets**, 30-count bottle per box. Volume of product in commerce: 25,888 boxes. Marketed without an approved NDA/ANDA: contains undeclared drug ingredients, making it an unapproved drug. Lot #s: all lots within expiry through 2016. Samantha Lynn, Inc.

### Recalls and Field Corrections: Drugs – Class II

Indicates a problem that may cause temporary or reversible health effects; unlikely to cause serious injury or death

**Atorvastatin Calcium Tablets**, 10 mg, 90 tablets per bottle. Volume of product in commerce: 120,201 bottles. Presence of particulate matter: Certain batches of atorvastatin tablets 10 mg, 20 mg and 40 mg may contain small glass particulates. Lot #s: 2436144, 2436582, 2441567 and 2441568, expiration date 08/31/2014. Ranbaxy Inc.

**Atorvastatin Calcium Tablets**, 20 mg, 90 tablets per bottle. Volume of product in commerce: 203,198 bottles. Presence of particulate matter: Certain batches of atorvastatin tablets 10 mg, 20 mg and 40 mg may contain small glass particulates. Lot #s: multiple lots affected, expiration date 8/31/2014. Ranbaxy Inc.

**Atorvastatin Calcium Tablets**, 40 mg, 90 tablets per bottle. Volume of product in commerce: unknown. Presence of particulate matter: Certain batches of atorvastatin tablets 10 mg, 20 mg and 40 mg may contain small glass particulates. Lot #s: multiple lots affected, multiple expiration dates. Ranbaxy Inc.

**Atorvastatin Calcium Tablets**, 40 mg, 500 tablets per bottle. Volume of product in commerce: unknown. Presence of particulate matter: Certain batches of atorvastatin tablets 10 mg, 20 mg and 40 mg may contain small glass particulates. Lot #s: multiple lots affected, expiration date 8/31/2014. Ranbaxy Inc.

**Levothroid (Levothyroxine Sodium Tablets)**, USP 50 mcg, 100-count bottles. Volume of product in commerce: 13,692 100-tablet bottles. cGMP Deviations: Does not meet in-process specification requirements. Lot #: 1097830, expiration date 1/31/2013. Lloyd Inc. of Iowa.

**Levothroid (Levothyroxine Sodium Tablets)**, USP 88 mcg, 100-count bottles. Volume of product in commerce: 31,252 100-tablet bottles. cGMP Deviations: Does not meet in-process specification requirements. Lot #s: 1096369, expiration date 11/30/2012 and 1092046, expiration date 7/31/2012. Lloyd Inc. of Iowa.

**Levothroid (Levothyroxine Sodium Tablets)**, USP 112 mcg, 100-count bottles. Volume of product in commerce: 37,827 100-tablet bottles. cGMP Deviations: Does not meet in-process specification requirements. Lot #s: 1096371, expiration date 5/31/2013, and 1092299, expiration date 1/31/2013. Lloyd Inc. of Iowa.

**Levothroid (Levothyroxine Sodium Tablets)**, USP 125 mcg, 100-count bottles. Volume of product in commerce: 19,162 100-tablet bottles. cGMP Deviations: Does not meet in-process specification requirements. Lot #: 1095210, expiration date 4/30/2013. Lloyd Inc. of Iowa.

**Levothroid (Levothyroxine Sodium Tablets)**, USP 137 mcg, 100-count bottles. Volume of product in commerce: 36,978 100-tablet bottles. cGMP Deviations: Does not meet in-process specification requirements. Lot #s: 1095212, expiration date 4/30/2013; and #1088877, expiration date 11/30/2012. Lloyd Inc. of Iowa.

**Levothroid (Levothyroxine Sodium Tablets)**, USP 300 mcg, 100-count bottles. Volume of product in commerce: 1,443 100-tablet bottles. cGMP Deviations: Does not meet in-process specification requirements. Lot #: 1097178, expiration date 7/31/2013. Lloyd Inc. of Iowa.

**Pradaxa (Dabigatran Etexilate)**, 75 mg capsules, 60-count bottles. Volume of product in commerce: 8,381 bottles. Defective container: Damaged bottles could allow moisture to get into the bottle and may thus impair the quality of the product. Lot #: 201900, expiration date 01/2015. Boehringer Ingelheim Roxane Inc.

**Tramadol Hydrochloride Tablets,** USP 50 mg, 1,000-count tablets per bottle. Volume of product in commerce: 2,264 bottles. Adulterated presence of foreign tablets: A customer complaint was received that a bottle of tramadol hydrochloride tablets USP 50 mg contained some tablets of metoprolol tartrate tablets USP, 50 mg. Lot #: GKK1373, expiration date 09/2013. Caraco Pharmaceutical Laboratories, Ltd.

# CONSUMER PRODUCTS

Contact the Consumer Product Safety Commission (CPSC) for specific instructions or return the item to the place of purchase for a refund. For additional information from the CPSC, call its hotline at (800) 638-2772. The CPSC website is www.cpsc.gov. Visit www.recalls.gov for information about FDA recalls and recalls issued by other government agencies.

**Name of Product; Problem; Recall Information**

**2011 Havoc Bicycles.** The bicycle frame can crack at the joint where the top tube meets the down tube. A cracked tube can separate and cause the rider to lose control, posing a risk of injury or death. Norco Bicycles, at (800) 227-5579 or www.norco.com.

**2012 PAPYRUS Holiday Signature Ornaments.** The presence of Aspergillus mold spores were discovered on the products, posing a risk of respiratory or other infections in individuals with chronic health problems or who have impaired immune systems. Schurman Retail Group, at (855) 730-7998 or www.papyrusonline.com.

**2012 PAPYRUS Signature Collection Picture Frames.** The presence of Aspergillus mold spores were discovered on the products, posing a risk of respiratory or other infections in individuals with chronic health problems or who have impaired immune systems. Schurman Retail Group, at (855) 730-7998 or www.papyrusonline.com.

**2012 PAPYRUS Signature Collection Tree.** The presence of Aspergillus mold spores were discovered on the products, posing a risk of respiratory or other infections in individuals with chronic health problems or who have impaired immune systems. Schurman Retail Group, at (855) 730-7998 or www.papyrusonline.com.

**All-Terrain Vehicle (ATV).** A weld on the ATV's front right and left upper suspension arms can separate, causing the driver to lose control of the vehicle, posing a crash hazard. American Honda, at (866) 784-1870 or http://powersports.honda.com.

**Arctic Cat Snowmobiles.** The fuel tank can leak, posing a fire hazard. Arctic Cat, at (800) 279-6851, or www.arcticcat.com.

**Artificially Lit Christmas Trees.** The Christmas tree base can overheat, posing a fire hazard. GKI Bethlehem Lights, at (800) 248-1434 or www.gkilights.com.

**Baby Jogger City Versa™ Strollers.** The stroller frame can fail to lock in place and collapse while in use, posing a fall hazard to children in the stroller. Baby Jogger, at (877) 506-2213 or www.babyjogger.com.

**Catalina Outdoor Fireplace.** The glass components of the Catalina Outdoor Fireplace can break when a fire is lit, posing a burn and laceration hazard. Christmas Tree Shops, at (888) 287-3232 or www.christmastreeshops.com.

**Classic by Easy-Rest Foam Core Mattresses.** The mattresses fail to meet the mandatory federal open flame standard for mattresses, posing a fire hazard to consumers. Easy-Rest Inc., at (602) 442-6609 or www.easyrestinc.com.

**Dream On Me Bath Seats.** The bath seats fail to meet federal safety standards, including the requirements for stability. Specifically, the bath seats can tip over, posing a risk of drowning to babies. Dream On Me, at (877) 201-4317 or online at www.dreamonme.com.

**Dream On Me Bed Rails.** The bed rail can separate from the mattress allowing a child's body to become entrapped if it slips between the rail and the mattress. This poses suffocation and strangulation hazards to children. Dream On Me, at (877) 201-4317 or online at www.dreamonme.com.

**Falls Creek Kids Infant and Toddler Denim Jeans.** The snap on the front of the infant and toddler denim jeans may come loose and separate from the fabric, posing a choking hazard to young children. Meijer, at (800) 927-8699 or www.meijer.com.

**High-Powered Magnet Desk Toy.** When two or more magnets are swallowed, they can link together inside a child's intestines and clamp onto body tissues, causing intestinal obstructions, perforations, sepsis and death. Internal injury from magnets can pose serious, lifelong health effects. Reiss Innovations, at (866) 212-8314 or www.DynoCube.com.

**Home Depot Mug.** The silver-colored simulated bucket handle below the rim can spark when used in a microwave oven, posing a fire hazard. Home Depot, at (877) 527-0313 or www.homedepot.com.

**Izoard XP Bicycles.** The bicycle fork's steerer tube can break while in use, posing a fall hazard. Wilier USA, at (888) 849-7779 or www.wilier-usa.com.

**Jotul and Scan Gas Fireplace Inserts.** The fireplace insert's electrical wiring can come into contact with the metal rating plate on the insert, posing electrical shock and burn hazards to consumers. Jotul North America, at (800) 797-5912 or www.jotul.com.

**Leg Press.** The weight platform locking mechanism can fail and the backrest can disengage during normal use, posing a risk of injury to the consumer. Cybex International, at (888) 678-3846 or www.cybexintl.com.

**Low Lead Ball Valve/Shut-Off Gas Valves.** The valves can crack and cause gas to leak. This poses fire and explosion hazards. Danville Sales Office for Fu San Machinery, at (855) 779-9200 or www.fsvalve.com.tw.

**Mattresses and Mattresses with Foundations.** The mattresses fail to meet the mandatory federal open flame standard for mattresses, posing a fire hazard to consumers. American Mattress Manufacturing, at (855) 628-6344 or www.americanmattressmfg.com.

## CONSUMER PRODUCTS (CONTINUED)

**Metal Chairs.** The chairs' back legs can bend when a seated person leans back. This poses fall and injury hazards to consumers. Grandin Road, at (888) 298-4651 or www.grandinroad.com.

**Muddy Outdoors Tree Climbing Sticks.** The climbing sticks can break, posing risk of serious injury or death to users. Muddy Outdoors, at (877) 366-8339 or www.gomuddy.com.

**RIDGID Coil Roofing Nailer and RIDGID Clipped Head Framing Nailer.** The trigger assembly on the nailers can malfunction and involuntarily discharge a fastener, posing a laceration or injury hazard to consumers. One World Technologies, at (800) 597-9624 or www.ridgid.com.

**Sassy®-branded Hug N' Tug Puppy and Monkey and Carter's®-branded Hug N' Tug Monkey Toys.** The beads inside the clear plastic sphere at the center of the toys can be released and pose a choking hazard to young children. Sassy, at (800) 323-6336 or www.sassybaby.com.

**Shelly's Diner® Collectible Ceramic.** The diner's power adapter can overheat and melt the adapter's plastic housing, posing a fire hazard. Enesco, LLC, at (800) 436-3726 or www.department56.com/recall.

**Snowmobiles.** The bolt attaching the front, lower left shock can fail and cause the operator to lose control of the vehicle. This poses a serious hazard of injury or death. Polaris, at (888) 704-5290 or www.polaris.com.

**Stepladder and Stepstool Combination.** When extended, the inner side rails can separate from the outer side rails, causing the user to fall. Wing Enterprises Inc., at (855) 595-3378 or www.littlegiantladders.com/switch-it-recall.

**Top-Loading Washing Machines.** An unbalanced load can cause the washing machine to shake excessively and the drum to come loose during use, posing a risk of injury to consumers and property damage to the surrounding area. LG, at (855) 400-4639 or www.lg.com/us.

**Water Balz, Growing Skulls, H2O Orbs "Despicable Me" and Fabulous Flowers Toys.** When the marble-sized toy is ingested, it expands inside the body and causes a blockage in the small intestine, resulting in severe discomfort, vomiting and dehydration, which could be life threatening. The toys do not show up on an X-ray and require surgery to be removed from the body. Dunecraft Inc., at (800) 306-4168, or www.dunecraft.com.

**WFT-E7A Wireless File Transmitter.** A chemical used in the rubber part on the top cover of the product can result in a reaction that changes the rubber from black to white and poses a risk of skin irritation to the consumer. Canon, at (855) 902-3277 or www.usa.canon.com.

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increasingly sensitive about the need to obey the law.

The seemingly never-ending, record-breaking succession of billion-dollar fines against this industry argues instead, in my view, that industry *does* see these penalties as merely "the cost of doing business." This is yet another reason for the quite out-of-control prices of prescription drugs.

*Information for this article was derived, with permission, from a summary of the conference by FDAWebView, www.fdaweb.com.* ✦

PUBLICCITIZEN Health Letter

# Outrage of the Month!

## More About Drug Industry Lawlessness

During a December panel discussion at the Washington, D.C.-based Food and Drug Law Institute, a nonprofit organization providing an ongoing forum for discussing legal issues involving the Food and Drug Administration (FDA) and the drug industry, the growing epidemic of criminal and civil legal violations by the pharmaceutical industry was a hot topic. (For more information on the topic, see our reports on the past two decades of such violations, "Rapidly Increasing Criminal and Civil Monetary Penalties Against the Pharmaceutical Industry: 1991 to 2010," at www.citizen.org/hrg1924, and "Pharmaceutical Industry Criminal and Civil Penalties: An Update," at www.citizen.org/hrg2073.)

Eric Blumberg, deputy chief counsel for litigation at the FDA, pulled no punches. Commenting on the growing, billions-per-year monetary fraud settlements by the drug industry, he stated: "Money is clearly not doing the job; *qui tam* (whistleblower) complaints are still falling across my desk like snowflakes! We need to employ a 'bigger hammer,' to send people to jail." He advocated, as he has previously, greater use of the so-called Park Doctrine, which allows prosecutors to hold corporate executives personally responsible for regulatory infractions *without need to prove prior knowledge or intent to defraud*. Blumberg pointed out that under the Park Doctrine, corporate executives and managers not only have a positive duty to seek out and take steps to eliminate fraud, but also a duty to put into place policies and procedures to prevent violations. This duty, he stated, cannot be delegated to lower-level executives or employees.

A frequent complaint of industry officials and lawyers is that the Park Doctrine is too harsh: in part, they say, because executives in large multinational operations cannot know everything that goes on everywhere in their organization, thus requiring them to delegate and rely on others for compliance. Blumberg rejected this notion: "I'd say to them, 'You took the job, with its seven- or eight-figure compensation package, with full knowledge of the consequences. You can't have your cake and eat it too!'"

A lawyer for a large Washington, D.C., law firm that frequently represents the drug industry acknowledged that some (other) people believe that expensive sanctions for health fraud are just "the cost of doing business." He countered that corporations are

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Health Letter, Public Citizen Health Research Group
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