

Treatment Delayed is Treatment Denied— The Unintended Consequences of State Laws to Ban the Use of Physician Level Data

Executive Summary

Since 2006, more than twenty states have considered legislation to ban the commercial use of physician level data. Although three states (New Hampshire, Maine and Vermont) passed such laws with the intent to reduce costs of branded medications, none have done so since 2007. In contrast, opponents of these laws (as well as two federal judges) have proposed that restrictions on commercial use of data would not achieve the stated goals, would compromise patient care and health research, and that alternatives that do not have the potential to harm patients already exist.

The Massachusetts Biotechnology Council (MassBio), a not-for-profit organization founded in 1985, is committed to providing information to aid local, state and federal officials and the general public in making informed decisions about issues concerning biotechnology. Foremost among our objectives is to create an environment that recognizes and supports the development of science, technologies, and medicines that benefit people worldwide.

In line with these goals, we present a case study of unintended consequences of data restriction laws—“the canary in the coal mine.” Further, this report illuminates the process of care and dissemination of FDA-approved information supported by such data, and the dangerous ripple effects of selectively reducing access to information as a means to alter drug utilization.

MassBio member, Eisai Inc., which has a research facility in Andover, MA, is a U.S. pharmaceutical subsidiary of Tokyo-based Eisai Co., Ltd, a research based human healthcare company dedicated to developing and marketing specialty drugs that address unmet needs. In January 2009, after approval by the FDA, Eisai launched BANZEL® (rufinamide)—a prescription drug, approved for the adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome (LGS) in children 4 years and older and adults. LGS is a rare and catastrophic form of epilepsy.

Using physician level data, Eisai—after approval by the FDA—quickly delivered information regarding the clinical use of BANZEL to a specific, targeted physician population, and developed a rigorous, ongoing process for ensuring appropriate use of BANZEL by:

- Identifying the small population of physicians who treat patients with LGS
- Limiting promotion of the drug to child neurologists and epileptologists—neurologists who have completed specialized training in epilepsy and treat only epilepsy—with patients known to have LGS
- Working with physicians to manage risks related to specific concerns
- Providing professional services to enhance patient care
- Monitoring physician experience with BANZEL to quickly and effectively communicate new information to a broader physician community

The data restriction law in New Hampshire resulted in a lack of transparency about which neurologists in the state treat patients with LGS and created uncertainty for Eisai about which neurologists they should contact about BANZEL. Eisai's experience in New Hampshire points to how these laws reduce effectiveness and efficiency in the dissemination of information that impacts patient care and may increase the time it takes to get new drugs to patients—most importantly in this case, potentially delaying access to an effective product for a catastrophic illness.

As states and the federal government move toward healthcare reform, it will be critical for legislators to understand the system of care in order to assess how changes in policy will broadly impact health research and the public welfare.

Introduction

MassBio represents 630 biotechnology companies, universities and academic institutions. Three hundred and seventy (370) member companies are directly engaged in research, development and manufacture of innovative products that bring great benefit to people around the world. MassBio members are at the forefront of a trend in biomedical research that increasingly focuses on treatments for diseases that serve smaller populations.

Many states have leveraged private investment and public support for biotechnology research and development, e.g., Massachusetts' \$1 billion life sciences initiative.¹ Reasons for these investments include the advancement of clinical research and the development of new industry and employment in the respective state(s). Given the magnitude of these investments, it is important to consider any public policy initiative that effectively undermines the nurturing environment intended by political leadership.

Under the rubric of patient privacy and reducing healthcare costs, many states have considered restricting commercial use of HIPAA-compliant, physician level data. While the potential of such legislation to reduce costs is hypothetical at best, unintended consequences associated with loss of these data are quite clear.

These data have many uses impacting patient safety, physician education and commercial realization of innovative new therapies. In effect, these (patient-anonymous) data are essential to achieving clinical and commercial success.

Uses bridge private, public and government sectors and include:

- Identifying clinicians who specialize in specific illnesses (physician specialty alone is not adequate in today's environment of sub-specialization)
- Accelerating recruitment of clinical investigators and research processes
- Enhancing communication among clinicians, researchers and the FDA/CDC in their efforts to track communicable disease

- Disseminating appropriate guidelines for safety and effectiveness once the FDA approves a drug
- Collaborating with the FDA and clinicians in risk management and risk minimization programs*

In the vast majority of states, data restrictions laws have not advanced. While the reasons differ by state, concern for patient care has been the prevailing consideration.

Within this context, the following case is a fact-based review of how Eisai judiciously and responsibly used physician level data to quickly deliver their new drug to patients and examines the potential impact of data restriction legislation on patient care.

Treatment Delayed Is Treatment Denied: A Case Study

Background

In November 2008, the FDA approved BANZEL®, a drug developed by Eisai Inc., for adjunctive use in the treatment of seizures associated with Lennox-Gastaut Syndrome (LGS) in children 4 years and older and adults. LGS is a rare and catastrophic form of epilepsy. In a pivotal clinical trial, BANZEL was shown to significantly reduce total seizures in patients with LGS and received approval under the Orphan Drug Act (which defines an orphan disease as one that affects less than 200,000 people).^{2,4}

Lennox-Gastaut Syndrome

Lennox-Gastaut Syndrome is a devastating form of childhood-onset epilepsy characterized by multiple types of seizures occurring many times a day (100 or more in some cases) and delayed intellectual development (Table 1).⁵ Seizures are often resistant to therapy, which results in high

*Of note, the 110th Congress passed the FDA Reauthorization Act. In the legislation there are increased demands for pharmaceutical and biotechnology companies to expand the scope of drug safety monitoring and post-market surveillance, in addition to rigorous standards already in place that require companies to contact providers about everything from product recall to labeling changes. New and existing safety provisions will be difficult to pursue and perhaps might even be unworkable without access to HIPAA-compliant provider level data.

rates of injuries due to tonic and/or atonic seizures, also known as “drop attacks” or “drop seizures.” Patients with LGS often wear protective helmets with face guards (Figure 1).⁴

Table 1. Most Common Seizure Types in Patients with LGS

Seizure Type	Description
Tonic	Stiffening of the muscles lasting a few seconds to minutes
Atypical Absences	Interruption of consciousness where person appears vacant and unresponsive
Sudden Tonic or Atonic Falls (“Drop Attacks”)	Brief loss of muscle tone and consciousness causing falls
Non-convulsive Status Epilepticus	Atypical absences with varying degrees of altered consciousness and periodic recurring brief tonic seizures
Myoclonic	Rapid contraction of the muscles causing jerking movements. Can also cause falls.
Other	Focal seizures, tonic-clonic generalized seizures, and unilateral clonic seizures are also common

Source: Excerpted from Arzimanoglu A, French J, Blume T, et al. Lennox-Gastaut syndrome: a consensus approach on diagnosis, assessment, management, and trial methodology. Vol 8, January 2009. www.thelancet.com/neurology Accessed on 9/25/09.

Incidence and Mortality: A Child Dies Every Day

Of approximately 300,000 children under the age of 14 who have epilepsy in the U.S., up to 4% have LGS. Long-term prognosis is poor. Eighty percent of patients will continue to have seizures into adulthood. Although types of seizures may change or lessen with age, behavioral issues and impaired functioning remain a challenge. Deaths of patients are often due to accidents and occur at the rate of 3% (360 children per year).^{2,4} That means that a child dies every day from the disease.

Figure 1. Patient with LGS wearing a protective helmet with face guard to protect against injury from “drop attacks.”



Source: Glauser, TA, Morita, DA. Lennox-Gastaut Syndrome. Emedicine from WebMD. <http://emedicine.medscape.com/article/1176735-overview> Updated: 1/05/10. Accessed on 1/18/10.

Treatment Options

Because of the complexity of the disorder and the high rate of complications, management of LGS requires a multidisciplinary team of medical specialists and psychosocial support.

Goals of treatment are to achieve the fewest seizures and the fewest adverse events with the least number and severity of medical interventions, so that patients can have the best quality of care possible. Antiepileptic drugs that have a broad spectrum of activity against multiple seizures types are first-line treatment. However, since no one drug alone has been shown to be effective in managing LGS, multiple drug therapy and other approaches are often necessary—including catastrophic and costly surgery in which half the brain is removed or disabled (Table 2).⁵⁻⁷

Burden of Illness

Patients often endure years of treatment trials and complications with varying effects on seizure reduction. Kim SanInocencio, the mother of an adult son with LGS and co-founder with her daughter Christina of the LGS Foundation, says, “Every family experiences LGS differently, but we all share one thing in common, and that is living with the unexpected. Because day to day, the seizures—and the consequences—are different, we all live in great anticipation of new treatment options that could make a difference.”⁶

Table 2. Treatment Options for LGS

Type	Description
Combination therapy with multiple antiepileptic drugs (AEDs) and other classes of drugs	<p>Few clinical studies exist on comparative efficacy of medications; response rates vary</p> <p>Side effects may include irritability, mood disorders, depression, sedation, cognitive issues and behavioral problems; class labeling for AEDs includes increased risk for suicide</p>
Ketogenic diet	<p>High fat diet with low carbohydrates and protein (4:1 ratio); requires strict supervision and even the slightest departure may cause the diet to lose its effect. Results vary; may decrease seizures by 50% in some patients; 10%-15% become seizure free</p> <p>Side effects: dehydration, constipation, kidney stones, bone fractures, vomiting, high cholesterol levels, slower growth rates in children</p>
Vagus nerve stimulation	<p>A device that is implanted surgically under the patient’s arm or near the chest and emits electrical impulses to help control seizures. Side effects include infection, pain, chest spasm, voice alteration, increased coughing</p> <p>Estimated cost: \$15,000 to \$20,000</p>
Brain surgery including resection, corpus callosotomy, functional hemispherectomy, and multiple sub-pial transection	<p>May be recommended to patients who do not respond to antiseizure medications; degree of improvement and side effects are variable</p> <p>Estimated cost: \$50,000 to \$200,000 based on type of procedure</p>

Sources:

LGS Foundation Website. www.lgsfoundation.org Accessed on 9/25/09.

Arzimanoglou A, French J, Blume T, et al. Lennox-Gastaut syndrome: a consensus approach on diagnosis, assessment, management, and trial methodology. Vol 8, January 2009. www.thelancet.com/neurology Accessed on 9/25/09.

Epilepsy Foundation of American website. www.efa.org Accessed on 9/25/09.

For patients with LGS, many of whom are wheelchair bound, common everyday activities are severely limited by uncontrolled seizures and behavior problems. According to a recent study conducted by the LGS Foundation, almost 50% of children no longer attend school while 21% miss school 50% or more of the time.

Lennox-Gastaut Syndrome affects the entire family, testing emotional, physical, social and financial resources. Because children with LGS need constant care and vigilance, parents often give up employment to become full time

caregivers and advocates and/or struggle with decisions about placing their child in an institution or group home. Siblings, too, are often involved as caregivers and their lives are affected as the family’s attention and resources are focused on the needs of the child with LGS.

The stress of having a child with uncontrolled seizures is compounded by the stress of reduced income, social isolation, and the demands of interacting with a complex support system consisting, in part, of healthcare providers, insurance companies, and school officials. And

yet, these families are remarkable in their ability to advocate for their children and sustain hope that effective treatments will be found.

For Kim SanInocencio’s son, Michael, that hope was realized when BANZEL was added to his antiepileptic drug treatment. After living with LGS for 18 years, enduring many injuries and complications, treatment failures with almost all antiepileptic drugs as well as implantation and removal of a vagus nerve stimulation device, Michael has had a good response to BANZEL. Michael and his family report a reduction in the number of seizures he experiences and less worry about his having seizures on a daily basis.^{6,8}

The Challenge: Finding the Right Physicians with the Right Patients

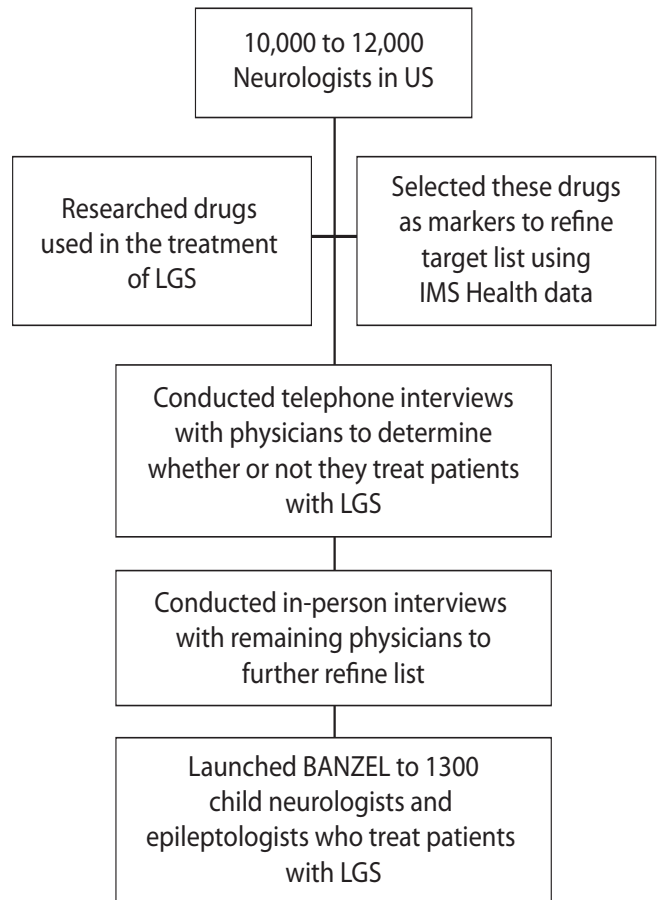
The potential for inappropriate use of BANZEL and its impact on patient safety, created an imperative for Eisai to refine the target audience for launch. Essential to this process was the use of physician level data, which Eisai licensed from IMS Health, the nation’s largest health information organization.

The steps used for identifying the appropriate target audience for BANZEL are outlined in Figure 2. By this process, Eisai identified a list of 1300 child neurologists and epileptologists—from a universe of 10,000 to 12,000 general neurologists—and was able to target messaging to those physicians most knowledgeable about how to use and evaluate BANZEL in clinical practice.

Clearly, the value of physician level data lies in the ability to identify clinicians among all neurologists who are actually treating patients with LGS. The objective was to ensure that the product was made available as quickly and responsibly as possible to appropriate physicians. The ability to use physician level data was essential in achieving that goal, not only in terms of communicating appropriate use and patient safety information but it also allowed the most effective and efficient use of resources. Without this ability, the cost of identifying and communicating with the right physicians would have been exorbitant.

The experience in New Hampshire did not serve

Figure 2. How Eisai Identified the Right Physicians with the Right Patients to Ensure Appropriate Use of BANZEL



patient care well as there were delays at the physician-interaction level—an example of how data restriction laws there made identifying the right physicians very difficult and prevented immediate and direct communication with physicians about the benefits and risks of BANZEL.

Managing Risk

In all other states, physician level data facilitated early communication with targeted physicians by sales representatives about possible adverse events, e.g., in patients with familial short QT syndrome and drug-drug interactions, especially the synergistic interaction with valproate which increases BANZEL blood levels by 16% to 70%.⁹

Eisai believed it was critical for initial use of BANZEL to be carefully assessed by experts in LGS since inappropriate utilization may result in negative patient outcomes and, as a consequence,

lead to other patients being denied effective treatment.

Communicating Safety and Efficacy Information

Clinical study results and insights from researchers experienced with the adjunctive use of BANZEL were rapidly disseminated through interaction with healthcare providers, supported by the use of physician level data. Representatives also provided physicians with information about visiting faculty, on-line programs, and materials for caregivers including printed brochures.

Prior to development of these programs, the Eisai marketing, medical services, and sales team underwent comprehensive training that addressed disease state, the full range of treatment modalities as well as the patient/family experience of living with LGS.

Creating Ongoing Dialogue

Using physician level data, Eisai was also able to monitor experience with BANZEL and to create ongoing dialogue with physicians about benefits and risks. These data are fundamental to the role of representatives as clinical liaisons providing additional service and support to ensure that patients are receiving the highest quality of care. For example, they provide:

- Efficient distribution of valuable samples (which are limited due to BANZEL's orphan status) to targeted physicians who can assess treatment effects in individual patients without having to prescribe a full course of therapy thereby delaying patient co-pay until efficacy and safety have been established
- Timely access to drugs at the pharmacy level to ensure that patients will not have to delay treatment. Representatives coordinate with physicians to make sure that the pharmacies used by their patients are informed about and stock BANZEL
- Quick and effective diffusion of clinical experience with BANZEL, including serving as intermediaries to link physicians who share information and consult on patient cases

Unintended Consequences of Data Restriction Laws

Delaying the dissemination of new products and information to patients is an unintended consequence of data restriction legislation. At the patient level, treatment delayed is treatment denied. And for patients with critical conditions like LGS, denial of care could result in tragic consequences.

During the 2009-2010 legislative session, physician level data restriction bills have been filed in over twenty states around the country with most states deciding against banning use. In the three states that have enacted laws to prohibit commercial use of data—New Hampshire, Maine and Vermont—proponents argue that the legislation will improve patient privacy, reduce inappropriate marketing practices, protect physician privacy, and reduce healthcare costs. Opponents argue that privacy is not an issue and that other ways to manage cost are working in the system, for instance, tiered formularies.

Those who support the ban further argue that physicians learn about treatment innovations from medical journals and their peers, and that there is no need for sales representatives to provide education. Yet, these methods may be insufficient for rapid dissemination of information, especially to the specific subgroup of physicians whose patient populations can benefit from it the most. This may cause a delay in treatment for those patients with the greatest need for help—such as those with LGS.

New Hampshire is the “canary in the coal mine,” proving the real world consequences of passing this legislation. As predicted by opponents, and confirmed by Eisai's experience of trying to market BANZEL in New Hampshire, the benefits of this legislation are unknown, while the harm is clear: these laws create inefficiencies in the dissemination of information and may result in delayed access for patients to new products like BANZEL.

At a time when Americans are worried about healthcare rationing, this legislation amounts to arbitrary rationing rather than a system of care based on clinical facts, benefits, and risks.

Summary

In conclusion, this case presents one example of how MassBio member companies are engaged in and dedicated to improving patient care through the discovery, development and responsible marketing of innovative treatments. State support of the life sciences, as demonstrated by Massachusetts' \$1 billion life sciences initiative, creates a nurturing and open environment that is vital to the development of new science, technology, and safe and effective medicines that benefit people worldwide. It is important to consider carefully any public policy initiative that jeopardizes that environment.

Moreover, as advocates of physician level data predicted, and experience in New Hampshire bears out, restricting the use of physician data has the potential to hinder quality of care. In effect, at the patient level, treatment delayed is treatment denied. In addition, the inability for company representatives to target communications to the appropriate physicians could make the cost to educate them about drugs so prohibitive as to limit research and development of orphan drugs for rare and devastating diseases like LGS.

With Eisai's experience in New Hampshire as an early warning, legislators need to give careful consideration to the consequences of legislation restricting the use of physician level data. Of paramount concern: how widespread delays in the dissemination of information about new medications will delay patient care and impair the overall quality of healthcare in their respective states.

Eisai's judicious and responsible use of data to launch BANZEL supports the role of physician level data as essential to the safe and appropriate use of pharmaceuticals and to bringing new, life-saving and life-enhancing drugs to patients in the most effective and efficient way possible.

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A Product of



One Cambridge Center Cambridge, MA 02142
Phone: 617.674.5100 Fax: 617.674.5101

Contact: Sarah MacDonald, Director of Communications
Phone: 617.674.5115 Email: sarah.macdonald@massbio.org

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