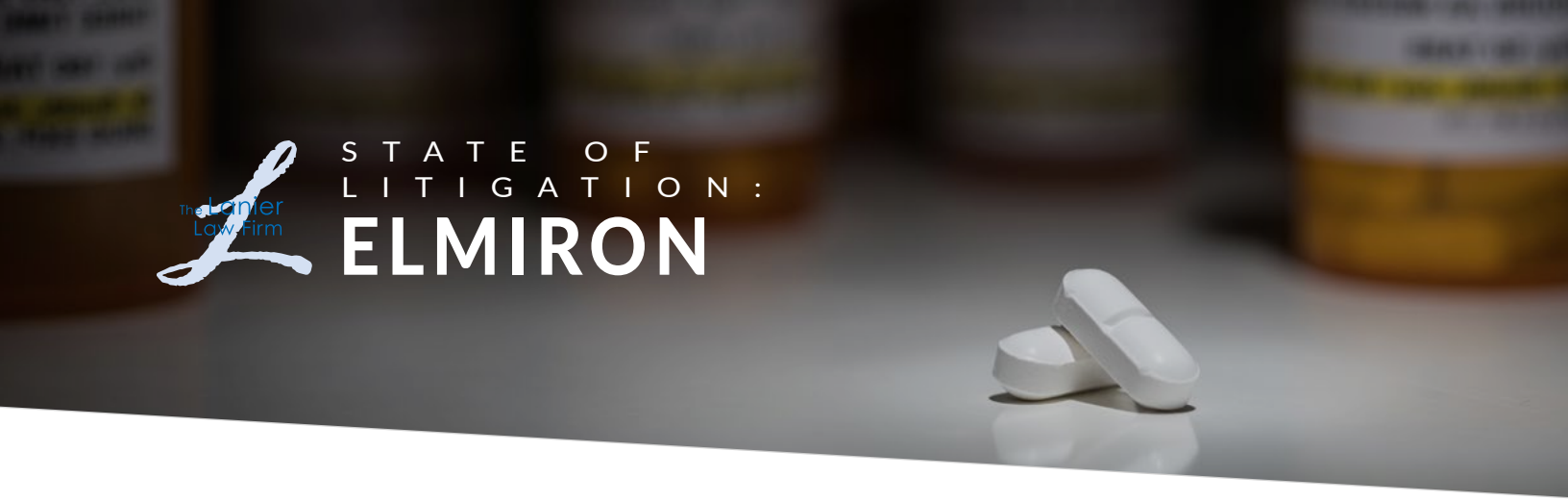

STATE OF LITIGATION: ELMIRON

BIG PHARMA IS AT IT AGAIN

Big pharma is at it again: A drug is marketed to suppress one ailment, while the company fails to warn and actually conceals the negative effects the drug has elsewhere on the human body.

This time, a drug named Elmiron is damaging people's ability to see, damaging their eyes and, according to independent studies, causing vision loss. Elmiron has been sold since the mid-1990s to hundreds of thousands of people who suffer from a particular urinary disorder, called interstitial cystitis. Victims of vision loss linked to Elmiron began filing lawsuits against the manufacturer in May 2020.

Elmiron is the leading drug to treat interstitial cystitis, or painful bladder syndrome, which affects more than 12 million Americans, most of whom are women.

WHAT IS ELMIRON?

Elmiron is the brand name of pentosan polysulfate sodium (PPS). PPS is part of a family of anticoagulant drugs, or blood thinners. However, Elmiron is used to treat urinary disorders linked to interstitial cystitis (IC). IC, or painful bladder syndrome, is a condition that causes chronic pain and discomfort in the abdomen, pelvic and genital regions, as well as increasing the urgency and frequency of bladder functions. Elmiron relieves the symptoms of IC by preventing irritation and swelling of the bladder walls and is believed to protect the bladder by creating a synthetic mucus layer that guards against irritants in the urine. Elmiron is not a cure for IC, but it does aid in relieving its symptoms.

The drug was developed and marketed by Janssen Pharmaceuticals, Inc. (Janssen), a corporate subsidiary of Johnson & Johnson (J&J), beginning in 1996 when it was first approved by the Food and Drug Administration (FDA). Elmiron is one of only two drugs worldwide that are marketed and approved to treat discomfort caused by IC, a disorder affecting more than 12 million people in America. Most Elmiorn users are women and many have taken the drug for more than 10 years. Since its introduction, Elmiron has become standard treatment for IC.

As a result, Janssen has profited substantially from the sale of the drug. One hundred oral capsules of 100 milligrams each costs almost $1,000 with a recommended dose of three capsules per day, the equivalent of approximately a one-month supply. Sales of Elmiron are estimated to garner at least $150 million in revenue per year in the United States alone. There is no generic option to reduce Janssen's market share and lower prices.

For more than a decade, Janssen marketed Elmiron as a safe and effective treatment for IC. When first introduced, and in the ensuing years, the label and prescribing information accompanying the drug contained no warnings. In fact, the packaging expressly provided: "Warnings: None." Elmiron was viewed as relatively safe with few significant side effects.

With no generic option available and most patients taking three capsules per day for more than 10 years, Elmiron's estimated revenue is $150 million per year in the United States alone.

WHAT IS ELMIRON? (*Continued*)

Side effects include unusual bleeding or bruising, mood changes and heartburn, as well as causing negative interactions with aspirin, ibuprofen and other blood-thinning medications. Other common side effects include hair loss, diarrhea, nausea, bloody stool, headache, rash, abnormal liver function tests, dizziness and bruising.

Eventually, Janssen attributed the following vision-related side effects to Elmiron that were designated as affecting less than 1% of users: conjunctivitis, optic neuritis, amblyopia and retinal hemorrhage. No mention of permanent vision loss or maculopathy was present on Elmiron's official website, prescription guide or patient-facing materials.

Maculopathy is any pathological condition of the macula, an area at the center of the retina associated with highly sensitive and accurate vision and responsible for the ability to read, recognize faces and colors, and see fine detail. The macula is located behind the retina. The retina senses light and sends a signal to the brain that produces the ability to see. Accordingly, damage to the retinal portion of the eye can diminish the ability to see. Retina damage associated with maculopathy is the most common cause of blindness in the Western world. This year, studies linking vision loss to Elmiron forced Janssen to include maculopathy warnings on its label this year but not until after thousands had been adversely affected.

THE STUDIES

The line of studies identifying Elmiron's toxicity began between 2015 and 2017 when doctors from the Emory Eye Center in Atlanta, noticed a trend among six patients with abnormal damage to the macula region of their eyes. They were all diagnosed with pigmentary maculopathy, a condition causing severe vision impairment, including blurred vision, extreme sensitivity to light and dark, and difficulty transitioning from natural light to indoors. Blindness may also occur as the disease progresses. All six patients were similarly found to be long-term users of Elmiron. As a result, the Emory Eye Center published a preliminary report in 2018 suggesting that Elmiron was toxic to the retinal tissue of the human eye, specifically, causing injury to the retinal pigment epithelium, a layer of cells that nourishes the retina.

In April 2019, physicians at the Emory Eye Center published an expanded case study of 10 patients who developed pigmentary maculopathy after taking Elmiron for IC. Appearing in *The Journal of Urology*, the case study provided details of the Elmiron dosage and duration for the 10 patients. The authors noted there were 156 other patients being treated at Emory who suffered from IC but did not use Elmiron, and none of those patients showed any signs of pigmentary maculopathy. The doctors recommended that patients with signs of vision deterioration stop taking Elmiron and those without symptoms undergo an eye exam with retinal imaging.

Additional studies published in October and November 2019 found similar results. Researchers at Kaiser Permanente found greater toxicity in patients who took the drug for longer periods of time. A cohort study in the *British Journal of Ophthalmology* found that users taking the drug for seven years significantly increased their odds for macular disease compared with those taking it for five years. Similarly, a report by Dr. Rachel M. Huckfeldt and Dr. Demetrios G. Vavvas presented a case study showing that a patient's pentosan-associated maculopathy continued to worsen six years after ceasing the medication.

These warnings prompted a more detailed study into the risks of taking Elmiron and its toxicity to the eyes by the American Academy of Ophthalmology (AAO). Its research, presented in 2019, by Dr. Robin A. Vora, Dr. Amar P. Patel and Dr. Ronald Melles revealed that patients taking Elmiron showed clear signs of toxicity. About 25% of patients who used Elmiron long-term displayed signs of maculopathy or significant eye damage. The study revealed that the rate of toxicity was compounded by the amount of the drug consumed:

> *"It's unfortunate," Dr. Vora said in an American Academy of Ophthalmology news release. "You have a patient with a chronic condition like interstitial cystitis, for which there is no cure and no effective treatment. They get put on these medications because it's thought to have few side effects and few risks, and no one thinks about it again. And year after year, the number of pills they're taking goes up and up."*

THE STUDIES *(continued)*

The AAO study team suggested that the rate of toxicity rose with the amount of the drug consumed, from 11% of those taking 500 to 1,000 grams to 42% of those taking 1,500 grams or more. The study also noted that the damage could masquerade as other macular degeneration-related diseases.

The same doctors published a January 2020 follow-up study of 117 patients that solidified their conclusions that there is "strong support to the growing body of evidence that links long-term PPS [or, Elmiron,] use to the potential development of a toxic maculopathy." The AAO studies indicate that if caught in its early stages, the damage to the retina may cease after taking medication. In later stages, after prolonged use of the drug, the disease can lead to permanent vision loss.

This research found that symptoms associated with Elmiron damage to the eyes include:

- Areas of vision loss in the field of vision
- Difficulty adjusting to dim lighting or darkness
- Difficulty reading
- Difficulty seeing objects at close range
- Vision dimming

The June 2021 issue of The *Canadian Journal of Ophthalmology* published the latest clinical evidence linking Elmiron to a significantly increased risk of vision damage.

In the study, researchers gathered data on patients who had been treated with PPS at UCLA and then screened with retinal imaging to check for any damage to the macula. The results showed that 20 percent of those patients showed signs of PPS-associated maculopathy. According to the study's authors, the data "suggests a significant risk of macular toxicity for PPS-treated patients."

They added that exposure to more PPS (in higher doses or for longer periods) was associated with more severe damage and recommended that any patient taking PPS get an initial eye examination and annual retinal imaging thereafter.

THE LITIGATION

Beginning in May 2020, product liability lawsuits alleging failure to warn were filed against Janssen. So far the plaintiffs are mostly women between the ages of 37 to 79 years of age. The complaints allege that Elmiron was "designed, marketed, and distributed [...]while knowing significant risks that were never disclosed to the medical and healthcare community."

The claims state that Janssen "withheld material adverse events" and "failed to disclose the serious link between Elmiron use and significant visual damage, including pigmentary maculopathy."

According to the lawsuits, Janssen did not completely understand the negative impact the drug would have on patients When brought to market, they did not have a clear understanding of why Elmiron relieves the symptoms of IC, assuming that it coats the bladder, thus providing protection from irritants. Ultimately, Janssen admits that only a fraction of the drug resolves in the bladder, with the balance absorbed elsewhere, including epithelial cells that coat the retina.

Injuries in lawsuits include:

- *blurred vision*
- *degenerative maculopathy*
- *halo vision*
- *macular retinopathy*
- *macular/pattern dystrophy*
- *pigmentary maculopathy*
- *reduced night vision*
- *scotoma*
- *retinopathy*
- *retinal pigment epithelium atrophy*
- *metamorphopsia*
- *vision impairment*
- *unilateral or bilateral blindness*
- *vision loss*

TINA PISCO LITIGATION

Plaintiff Tina Pisco began taking Elmiron in 2012 after an IC diagnosis. Within six years, her vision rapidly deteriorated. She was first diagnosed with permanent retinal injury in both eyes in March 2019. Fourteen months later, on May 4, 2020, Pisco filed suit against Janssen and J&J in the United States District Court for the Eastern District of Pennsylvania, alleging that Elmiron caused her injuries. The complaint notes that the label and prescribing information that accompany Elmiron contained no warnings. The lawsuit asserts that misinformation makes the companies liable for her injuries.

NEW JERSEY LITIGATION

Plaintiff Valerie Hull was documented as "patient zero" in the Emory Eye Center's 2018 study, and she filed suit in the Superior Court of New Jersey, Middlesex County, naming Janssen and Teva Branded Pharmaceutical Products R&D as defendants. On August 12, 2020, two additional lawsuits were filed in the United States District Court for the District of New Jersey, alleging that plaintiffs Clara Johns and Shirley Ruth Levy suffered vision loss after taking Elmiron for years.

Plaintiffs cite retinal damage, distorted and blurred vision, and toxic maculopathy and accuse the manufacturer of having been aware of the dangers but failing to warn users of the risks. The federal complaints state, "Despite study after study providing clear evidence of the dangers of PPS, defendants failed to adequately investigate the threat that PPS poses to patients' eyes and vision or warn patients of the risk that they would suffer retinal injury and vision impairment."

Warning-label changes come too late

Health Canada announced in October 2019 that pigmentary maculopathy would be added to the warnings and precautions on the Elmiron label. Janssen updated the Elmiron label in other countries, but it was not until June 2020, after litigation had begun, that the company changed the label for Elmiron products sold in the U.S. to reflect the risk of vision loss.

Under pressure from a now mounting number of Elmiron lawsuits, the FDA approved Janssen's request to change the Elmiron warnings on the label to include the risk of retinal pigmentary "changes." Janssen now admits these permanent vision injuries can occur with both long-term and short-term use of the drug. The label changes are too late – the influx of lawsuits has begun, with anticipated class-action suits on the horizon.

The Lanier Law Firm is prepared to file complaints and assist other counsel in the prosecution of claims related to Elmiron.
Visit lanierlawfirm.com/referrals to tell us about your case.

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