

The following are pertinent excerpts from the report prepared by David B. Redwine, M.D. in a lupron product liability lawsuit. The entire report can be found on PACER or obtained from the court house.

Case 2:08-cv-00681-RLH-RJJ Document 99 Filed 08/25/2009

EXPERT REPORT OF DR. DAVID B. REDWINE

Expert Report of Dr. David B. Redwine, M.D.
Re: Karin Klein v. TAP Pharmaceuticals, Inc.
Lupron Depot 3.75 MG
Dated: March 19, 2009

Introduction:

In the products liability case of Karin Klein v. TAP Pharmaceutical Products, Inc., et al. U.S. District Court Case No. 2:08-CV-00681-RLH-RJJ, I was asked ... to offer my professional expert opinions concerning the use of Lupron and the condition of [plaintiff's] health.

Personal Qualifications:

... Within my own private practice that extends over 31 years ... [a]pproximately 750 of my patients had previously taken a GnRH agonist, usually Lupron Depot, often in the dose of 3.75 mg monthly. The cumulative duration of treatment of these patients has ranged from one month to over 2 years. I have personally observed these patients and their symptoms and the adverse consequences of taking Lupron Depot.

Examination of [plaintiff's] condition and her medical records:

The] medical record notes that [plaintiff] experiences pain in her neck, shoulders, middle back, lower back, and hips. [Plaintiff] also experiences joint pain. She also appears to suffer from fibromyalgia, myalgia, chronic fatigue syndrome ... insomnia, headaches, memory loss According to the DEXA scans and medical records, [plaintiff] has osteopenia and that her bone density has been severely decreased. ...

Lupron Depot:

... The state of menopause with Lupron is very unnatural, not only because it is artificially induced with medicines, but because FSH levels are not elevated as they are in normal menopause. Lupron temporarily stops menstruation, but does nothing to eradicate endometriosis from the woman's body. Lupron affects the autonomic nervous

system. Lupron not only affects the gonadal hormones, but is also a powerful modulator of autonomic neural function. The pituitary gland is the “master gland” and is below the brain in the skull. The pituitary gland affects every physiological process of the entire body. In addition to the pituitary gland’s endocrine functions, the pituitary gland may play a role in the immune response. Lupron suppresses the pituitary-gonadal system.

Lupron Depot was very aggressively marketed to gynecologists for endometriosis treatment. The marketing ploy was to give Lupron Depot free or at cut rate to physicians who then could charge the patient full price for the medicine. I was personally contacted by a TAP pharmaceutical rep about this sometime in the mid-1990’s, with the suggestion that I could earn over \$100,000 annually by treating all my patients with Lupron Depot. This aggressive marketing resulted in criminal prosecutions of TAP and fines in excess of \$850 million dollars.

I have personal experience that TAP pharmaceuticals has interfered in the continuing medical education of physicians in order to enhance the sales of Lupron Depot. In the late 1990’s, I was invited by Jim Perez, D.O., to speak in Columbus, Ohio to a meeting of Osteopathic physicians. I blocked out my office, did not schedule any surgery, and made my hotel and plane reservations, which were to be reimbursed by the conference organizers. I received a call from Dr. Perez only 2 days or so before my departure telling me that I couldn’t speak at the meeting. When I asked why, I was told that when TAP Pharmaceutical found out that I was speaking on endometriosis, they refused to pay for my expenses or honorarium because they were aware of my opposition to the use of Lupron Depot for endometriosis. I have since talked with a former TAP drug representative who told me that during her training with TAP, she was warned about my opposition to Lupron Depot and how it damaged the company’s bottom line.

TAP Pharmaceutical has financially supported medical studies which overstate the efficacy of Lupron Depot. These studies have typically involved very few patients followed for a short length of time, usually only during therapy or immediately thereafter. Typically there is a dropout rate of 5 – 10% due to side effects of the medication.

TAP has successfully pushed for a misguided form of clinical management of women with pelvic pain: empiric therapy with Lupron Depot for any woman with non-emergent undiagnosed pelvic pain. This violates the clinical dictum of arriving at a diagnosis before treatment. TAP has promoted in the gynecologic medical literature the fraudulent concept that if a woman’s pelvic pain is relieved by empiric injections of Lupron Depot then the pain should be considered due to endometriosis and treatment should be continued. This is fraudulent because there are several causes of pelvic pain besides endometriosis which can be aggravated by the normal function of ovarian production of estrogen and relieved by shutting the ovaries down. These other causes of pain which might respond to estrogen include uterine fibroids, adenomyosis of the uterus, primary dysmenorrhea (painful uterine cramps), and ovulation pain. TAP has a stable of physicians on its speaker’s panel who travel the world to spread the news of medical studies paid for by TAP. I was told by one prominent speaker that he made over \$100,000 in one year speaking on behalf of Lupron Depot. The results of this particular

medical fraud are immediately applicable to this case, because Lupron Depot was begun on [plaintiff] in August 2005, without a confirmed diagnosis of endometriosis. In fact, if the operative report from 2003 is to be believed, Lupron Depot was started in the face of the documented absence of endometriosis. The treating physician did not just wake up that morning in August 2005 and decide to treat unconfirmed endometriosis with Lupron Depot, but was reacting to the years of advertisements and weak clinical studies sponsored by TAP money. It is common knowledge that pharmaceutical companies control the practice of medicine by paying for studies with favorable results. Marcia Angell, the former editor of The New England Journal of Medicine has said that one cannot believe any study funded by a drug company. In my opinion, TAP Pharmaceutical's effect on two generations of gynecologists has been the most egregious example of Big Pharma controlling the practice of medicine.

The effects of Lupron are not isolated to women. Lupron Depot was originally developed and marketed for the treatment of men with prostate cancer. Of note, a JAMA study from July 9, 2008, found that therapy with Lupron is not associated with improved survival when compared with conservative management. This study also noted significant adverse events associated with administration of this drug including "approximately 10% to 50% increases in the risks of fracture, diabetes, coronary heart disease, myocardial infarction, and sudden cardiac death, in addition to adverse effects on fat mass, cholesterol and quality of life."

[Plaintiff] and Lupron Depot:

As a treating physician for over 31 years, I have observed over 750 patients who have been treated with GnRh agonists, most commonly Lupron Depot. I have personally observed my patients discuss and manifest adverse effects and symptoms similar to [plaintiff's] list of conditions ...

Many patients have continued to complain about symptoms lingering for up to 2 years following discontinuation of Lupron Depot. The most common lingering symptoms in my experience are joint aches and pains, muscle aches, memory disturbances, and weight gain. ...

It is my opinion, to a reasonable degree of medical probability that altering [plaintiff's] pituitary gland at the age of 17 with six injections of Lupron Depot 3.75 likely did produce her current condition and her significant bone density loss. Her current condition is entirely in context with the known short and long-term effects of Lupron Depot.

Lupron's Adverse Events:

In a review of a portion of the adverse events provided by TAP to the FDA, the adverse events and symptoms of [plaintiff] are seen again and again in the reports. This supports [plaintiff's] contentions and the symptoms that have been diagnosed and treated by other physicians.

I have reviewed a Clinical Summary written by Abbott entitled Study No. M86-039, comparing Lupron Depot and danazol in women with endometriosis which found that in measuring Spinal BMD by QCT the Lupron Depot group showed a mean BMD decrease of 7.0% (range -27.8 to +53.7%) compared to a 6.2% mean increase for the danazol patients (range -4.5% and +13.7%). However, one Lupron Depot patient (No. 577/DA) had an unexpected post-treatment increase of 53.7% which is considered to be a measurement error. If this patient is excluded, the mean change for Lupron Depot patients becomes a decrease of 15.7% which differs significantly from the 6.2% increase seen in danazol patients. Lupron Depot package insert and patient information only warns of a mean bone density loss of 3.2%.

I also reviewed an Endometriosis Safety Update No. 43818, which discussed the follow up on the bone density issue to the M86-039 Clinical Summary discussed above. This study notes that bone density measurements were performed on 32 patients in the follow up study. Only 11 of the 32 patients experienced a complete recovery. Thus 21 patients did not have a complete recovery and many showed further decreases. ...

Conclusions:

... 2. [Plaintiff's] complaints about Lupron are similar to the patient complaints that I have received in my practice and are similar in nature to the MedWatch Reports reviewed. Her complaints are also similar to side effects reported in the medical literature.

3. Based on my extensive experience in studying, diagnosis and treating endometriosis, it is my opinion, to a reasonable degree of medical probability and professional certainty that Lupron is ineffective in eradicating endometriosis. It treats symptoms, but not the disease. Further, the risks, expense and adverse effects of the drug do not outweigh the symptomatic benefits, but usually replace one set of bothersome symptoms with another set of bothersome symptoms. Based upon the evidence in my own practice and the research and evidence provided I believe the drug is also unsafe and harmful in addition to being ineffective.

4. It is my opinion, to a reasonable degree of medical probability that Lupron Depot was brought to market on the basis of small studies with little clinical or side-effect follow-up. Subsequent studies have portrayed it as the only medicine needed to manage pelvic pain, and TAP's goal to position Lupron Depot as the Cadillac treatment for endometriosis has unfortunately been very successful due to their financial support for favorable studies and their intrusion into the medical education process.

...

6. Ms Klein seems to be an earnest, intelligent woman who has been understandably upset by her condition and wants to get well. She states that these symptoms began only after being treated with Lupron Depot. Since many of her complaints are contextual with symptoms of Lupron Depot long reported in the literature, symptoms catalogued by TAP, and symptoms which I hear about from my own patients, it is my opinion, to a reasonable degree of medical probability highly likely that Lupron Depot was the cause of most, if not all, of these symptoms.

7. It is my opinion to a reasonable degree of medical probability that much more likely than not that Lupron Depot is the cause of Ms. Klein's bone density loss.

8. It is my opinion, to a reasonable degree of medical probability that Ms. Klein was physically damaged as a result injections of Lupron Depot given on the basis of fraudulent claims made in the scientific literature by agents of TAP Pharmaceutical: that undiagnosed causes of pelvic pain should be first treated with Lupron Depot and that if pain relief occurs, that this means that endometriosis is the most likely cause of the pain so therapy should be continued.

DATED this 19th day of March, 2009.

David B. Redwine, M.D.
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