

Life Extension Magazine July 2009

AS WE
SEE IT**FDA Seeks to Ban Pyridoxamine**

By William Faloon

In this month's issue, you'll read about scientific studies that confirm how glycation accelerates age-related disease. The faster our body's proteins succumb to glycation reactions, the sooner we die.

Fortunately, several proven methods exist to slow toxic glycation processes. Nothing, however, completely stops glycation. The best we can do is to incorporate a wide range of anti-glycation strategies into our daily program as most members now do.

Glycation is the pathologic binding of glucose to proteins in our body. Proteins are the body's primary structural component. Glycation causes our proteins to crosslink and become non-functional. These non-functional proteins are referred to as advanced glycation end products.¹

Scientists have developed a method to break glycated protein crosslinks, thereby reversing this mechanism of aging. FDA regulatory barriers have impeded research into these crosslink breakers, also known as glycation-reversing agents.

Glycation also damages our body's lipids. The outer membrane of our cells is made up of phospholipids, cholesterol, and proteins. Glycation damages tissues throughout the body by degrading the structure and function of our cell membranes.^{2,3} Since a membrane is the interface between the cell's interior components (such as DNA and mitochondria) and the fluid surrounding the cell, maintaining these structures is critical to sustaining life.

The FDA wants to deny Americans access to one of the most effective ways to slow pathological glycation reactions in our aging bodies! Unless the FDA's insidious ban of this natural vitamin B6 compound is stopped, Americans will age faster and suffer increased incidences of degenerative diseases.

WHAT MAKES PYRIDOXAMINE SO SPECIAL?

Research supports the ability of pyridoxamine vitamin B6 to prevent chronic disease and inhibit disease progression. Pyridoxamine is particularly effective in inhibiting the formation of advanced glycation end products. Some of the age-related problems pyridoxamine may be effective against are:

- Skin wrinkling⁴
- Atherosclerosis⁵⁻⁷
- Chronic inflammations⁸
- Cataract formation⁹
- Kidney failure^{7,10-12}
- Diabetic complications^{3,5,7,9,11,13-15}
- Alzheimer's disease.^{16,17}

Unlike pyridoxine (the standard form of B6), high doses of pyridoxamine can be taken without concern for peripheral neuropathy.¹⁸⁻²⁰ Some have argued that pyridoxamine should be the only form of vitamin B6 used in supplements. That's unlikely to occur as the FDA has said it will now ban pyridoxamine in response to a petition filed by pharmaceutical interests to make it available only as a prescription drug!²¹

THE FDA'S POSITION

Kidney disease causes almost 500,000 Americans to require dialysis or a transplant.²² Diabetes is the leading cause of end-

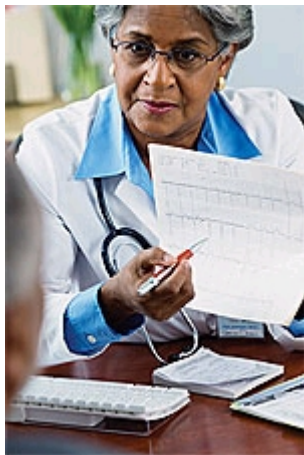


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The cell membrane is the outer barrier that contains and protects vital cellular structures such as DNA and mitochondria. Phospholipids and proteins in the cell membrane are highly vulnerable to toxic glycation reactions.

stage kidney disease.²³ With today's epidemic of type 2 diabetes, the market for a drug that protects against diabetic complications is huge.



Based on scientific data documenting its remarkable biologic effects, a drug company paid for studies to prove the efficacy of pyridoxamine in protecting against diabetic complications.

One of these studies showed that pyridoxamine slowed the rate of rise of a marker of kidney failure (creatinine) by 68% and improved certain parameters of kidney function in humans.²⁴ This company spent about \$100 million funding various pyridoxamine studies before it ran out of money.²⁵ The FDA wants to protect pharmaceutical financial interests, even if pyridoxamine is never approved as a new drug. According to the FDA, pyridoxamine cannot be marketed as a dietary supplement because:

“pyridoxamine is authorized for investigation as a new drug for which substantial clinical investigations have been conducted and their existence made public... ²”

The FDA's twisted position is that if vitamin companies can offer low-cost pyridoxamine supplements, then there is no incentive for a drug company to invest hundreds of millions of dollars getting it approved as a prescription drug. Said differently, to protect the financial interests of a pharmaceutical company, the FDA is willing to deny every health-conscious American access to the life-saving benefits of pyridoxamine, which include preventing the very disease the drug company is seeking to have pyridoxamine approved to treat!

WHEN MIGHT PYRIDOXAMINE BE AVAILABLE AS A PRESCRIPTION DRUG?

Even under the FDA's fast track program, obtaining new drug approval can take decades.

In the case of pyridoxamine, which has been around since life evolved on earth, there are numerous hurdles that have to be cleared before it becomes an official “drug.”

Assuming successful completion of a Phase IIb trial—this assumes an end-of-Phase II meeting and formal vetting of Phase III (pivotal, registrational) trial design(s) and associated study endpoints—and assuming at least two Phase III trials involving 1,500 patients studied for at least six months (and at least 500 patients studied for at least one year, and at least 200 studied for two years), with estimates for Phase III trial recruiting of 12 months and a nine-month turnaround time from the FDA following NDA (new drug application) submission, an estimated timeline would suggest that pyridoxamine might be available around 2014.

Until these clinical trials are completed, an outside FDA review committee recommends approval, and FDA bureaucrats grant approval, pyridoxamine will never be available to American citizens. The death toll from heart attack, kidney failure, and a host of other diseases preventable with pyridoxamine may then reach into the millions.²⁷



The FDA pretends to “protect the public health.” This cruel hoax is once again exposed by this bureaucratic edict that seeks to deny Americans access to a critically important disease-fighting nutrient.

PYRIDOXAMINE IS FOUND NATURALLY IN OUR FOOD!

Pyridoxamine occurs naturally in fish, chicken, walnuts, carrots, eggs, and other foods. People ingest small quantities each day. The FDA apparently feels so empowered that it thinks it can by proclamation ban an ingredient people obtain in their normal diet.

By defining the safest form of vitamin B6 (pyridoxamine) to be a “new drug,” the FDA has once again capitulated to pharmaceutical financial interests at the expense of the public's health.

WHAT IF PYRIDOXAMINE IS APPROVED AS A DRUG?

On March 25, 2008, the company seeking to have pyridoxamine approved as a “drug” stated that it will be conducting a Phase IIb study on diabetic patients with kidney disease. The estimated study completion date is August 2010.²⁶

If this study demonstrates a successful clinical outcome, it will then be submitted to the FDA for so-called “fast track” approval. It could take several years, if ever, before FDA approval is granted for pyridoxamine. In the meantime, according to the FDA’s Byzantine logic, no American is “allowed” to have pyridoxamine, effectively condemn-ing millions to needless suffering and death.

If pyridoxamine is ever approved, it will only be for very limited indications, such as end-stage kidney failure and diabetic neuropathies. Unless you happen to suffer from these diseases, you will find it difficult to obtain a “pyridoxamine prescription.” Then again, the cost of “prescription pyridoxamine” will be so astronomical that few will be able to afford it anyway.

If pyridoxamine becomes a new drug, the federal government will spend millions of tax dollars paying full retail price for it via the corrupt Medicare Prescription Drug Act, which adds another absurdity to the FDA’s proposed ban.



THE SILENT KIDNEY DISEASE EPIDEMIC

More than 26 million Americans over age 20 suffer chronic kidney disease, which represents 13% of the adult population!²²

Diabetes and poorly controlled blood pressure are the leading causes of kidney failure, meaning this epidemic is largely preventable with early detection.²⁸ Annual blood chemistry tests and regular blood pressure checks can identify deteriorating kidney function early and enable one to initiate corrective actions. Fortunately, most Life Extension members have their blood tested to monitor kidney filtration levels and glucose control.

Unfortunately, millions of Americans do not have regular blood tests (or blood pressure checks), resulting in the silent development of end-stage renal disease. For too many victims, they don’t find out their kidneys have failed until admitted to a hospital emergency room with severe symptoms.

End-stage renal disease is the name for kidney failure so advanced that it cannot be reversed. End-stage renal disease means that kidney function is so poor that the patient cannot be kept alive without aggressive and often only partially effective treatment.

There are 336,000 Americans receiving chronic dialysis treatment right now.²² Another 136,000 Americans are surviving with a kidney transplant.²² These treatments can induce serious side effects that shorten the patient’s life span. The annual cost of dialysis alone is about \$70,000, most of which is borne by Medicare (which is facing near-term insolvency).²⁹

The National Kidney Foundation estimates that more than 67,000 Americans die of kidney failure each year,²² but this is an understated statistic. That’s because kidney failure often causes death from heart attack,³⁰ stroke,³⁰ or osteoporosis.^{31,32} Doctors signing death certificates often omit kidney disease as an underlying cause of fatal disease in their patients.³³

Kidney failure is so devastating to aging individuals because it causes startlingly high levels of homocysteine³¹ and C-reactive protein,³⁴ greater incidences of anemia,^{35,36} and a host of other complications.

The FDA is seeking to ban pyridoxamine, which has been demonstrated to significantly delay the progression of kidney disease.¹¹⁻¹³

Pyridoxamine has been shown to slow the elevation of creatinine, a blood marker of kidney function by 68%.²⁴ These data indicate that many of those destined to perish from kidney disease will be dying prematurely because of the FDA’s draconian actions to keep pyridoxamine away from the public.

AS WE SEE IT

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SCOUNDRELS!

I yearn for the day when the public recognizes pharmaceutical companies as the morally bankrupt institutions they really are.

Perhaps the most misleading television commercial of all time was a pharmaceutical industry scientist (or actor pretending to be a scientist) claiming that drug companies sincerely care about the public's health. While some well-meaning people work for drug companies, the actions of management reveal their only objective is to make money.

Drug company financial projections are based on aging Americans contracting lots of age-related diseases like kidney failure. Diabetes inflicts damage to tissues throughout the body by accelerating toxic glycation reactions.^{37,38} If too many diabetics find out about supplemental pyridoxamine, the need for prescription pyridoxamine could plummet as many incidences of diabetic-induced kidney disease could be prevented.

Drug companies have a strong economic bias for denying you access to pyridoxamine. The more glycation damage that occurs in your body, the greater your need will be for their expensive drugs.

DRUG COMPANIES MAKE TONS OF MONEY SELLING SUPPLEMENTS AS DRUGS

The FDA believes that allowing a drug that is being clinically tested to also be sold as a dietary supplement will prevent pharmaceutical companies from funding research. This is a false assumption.

Each year, more than \$400 million of an expensive drug called Niaspan® is sold for the purpose of increasing beneficial HDL and reducing artery-clogging triglycerides (and LDL). Niaspan® is nothing more than extended-release niacin that one can purchase as a low-cost dietary supplement.³⁹

While extended-release niacin* has long been available as a supplement, the most money is being made by pharmaceutical interests by virtue of mainstream doctors prescribing Niaspan® to their cardiac patients and Medicare/ insurance companies paying its inflated price.

Another dietary supplement that went through pharmaceutical-funded clinical trials to prove its efficacy is the prescription fish oil drug called Lovaza® (previously named Omacor®).⁴⁰ Even though Lovaza® costs about seven times more than the same amount of EPA/DHA obtainable from dietary supplements, sales are exploding because many doctors are prescribing this fish oil drug to their cardiac patients. In 2007, pharmaceutical-giant GlaxoSmithKline bought the maker of Lovaza® for an astounding \$1.65 billion. Glaxo paid this astronomical amount of money for the ownership of this prescription fish oil knowing full well that dietary supplement fish oil could be obtained at a fraction of the price.

FDA's contention that pyridoxamine sales must be banned in order for clinical research to be funded is a farce designed to enrich pharmaceutical interests even more than they are now.

*Caution: Life Extension's concern with extended-release niacin is that it can potentially cause liver damage that would not occur in response to regular niacin. The reason is that niacin interferes with healthy methylation patterns in the liver. The exposure to the liver of extended-release niacin may induce chronic methylation deficits that result in chronic liver damage.⁴¹ These methylation deficits may be prevented by taking folic acid, vitamin B12, and other methylation-enhancing nutrients.⁴²⁻⁴⁴

WHAT YOU CAN DO TO FIGHT BACK!

We know that pyridoxamine was used as a dietary supplement in the early 1990s. If we can prove that pyridoxamine was sold in the United States prior to October 1994, the FDA will not be allowed to ban it. The Dietary Supplement Health and Education Act



protects supplements marketed prior to October 1994.

If you used pyridoxamine prior to October 1994, please let us know so we can add your name to an affidavit and use any evidence you have to overturn the FDA's proposed ban on pyridoxamine.

The FDA is controlled by the Executive branch of government. Writing to members of Congress may not work since they do not directly control arbitrary FDA decisions, such as the banning of pyridoxamine at the bureaucratic level. The White House, on the other hand, can with one phone call, demand that the FDA reverse its position and allow the free sale of pyridoxamine as a dietary supplement.

We therefore urge Life Extension members to mail the form letter that appears on page 3 to the health administrative affairs officer at The White House and demand that the FDA lift its proposed ban on pyridoxamine.

Whether you suffer from diabetes or just normal aging, your proteins are undergoing glycation every second of the day. Pyridoxamine is an effective method to inhibit these lethal glycation reactions.^{45,46}

It takes just a few minutes to mail the White House your concerns about the hideous effects that will occur if pyridoxamine is denied to Americans. The encouraging news is that initiatives are already in place to stop this kind of financial fleecing on the part of pharmaceutical companies, so The White House may be receptive to your letters.

DRUG COMPANIES WANT TO ALSO BAN PYRIDOXAL-5'-PHOSPHATE

For decades, the FDA has used all kinds of pathetic excuses to try to classify dietary supplements as prescription drugs. Interestingly, conventional medicine often attacks the value of dietary supplements, while simultaneously seeking to have the FDA approve the same supplement as highly effective prescription drugs.

You have just read about the potential health benefits of pyridoxal-5'-phosphate. If a drug company has its way with the FDA, however, this form of vitamin B6 might also be banned. A drug company has recently filed a petition with the FDA to classify pyridoxal-5'-phosphate as a drug.

The basis for this petition are favorable clinical studies showing that when cardiac bypass patients are given the monohydrate form of pyridoxal-5'-phosphate prior to surgery, there is a significant reduction in postsurgical complications, including reduction in heart attack incidence.⁴⁹⁻⁵¹ Pyridoxal-5'-phosphate monohydrate prevents cellular calcium overload in preclinical and clinical studies of cardiac ischemia-reperfusion injury.⁵¹

Once again, a dietary supplement that can benefit all aging humans (pyridoxal-5'-phosphate) may soon only be allowed in patients undergoing heart surgery—and may never get approved unless the drug company can fund more clinical studies.

The encouraging news is that there appears to be adequate documentation to prove that pyridoxal-5'-phosphate was indeed sold as a dietary supplement prior to October 15, 1994. This simple fact should preclude the FDA from banning this form of vitamin B6 that has demonstrated potent anti-glycation properties.

ENGINEERING AROUND THIS LETHAL DILEMMA

The FDA's arbitrary decision to deny Americans free access to pyridoxamine has galvanized health freedom activists throughout the United States. This may become the FDA's "Waterloo" from the standpoint of antagonizing such a broad spectrum of the American public that the agency's powers may be eroded through legislative action.

In the meantime, regrettably, vitamin manufacturers have been intimidated in such a way that they will no longer make supplements containing pyridoxamine. Since pyridoxamine is such a crucial anti-glycation agent, we at Life Extension have worked overtime to devise a stop-gap measure to protect our members' vital structures from glycation-induced degradation.

The encouraging news is that there is a form of vitamin B6 that may have comparable and possibly superior benefits to pyridoxamine. When different forms of vitamin B6 (B6 "vitamers") are ingested, the ultimate active form of B6 is pyridoxal-5'-phosphate. In laboratory studies, this form of vitamin B6 inhibits protein glycation^{47,48} and demonstrates more potent lipid anti-glycation³ effects compared with pyridoxamine. The chart on this page shows how much more effective pyridoxal-5'-phosphate is to any other form of B6 in inhibiting lipid glycation.

One could still argue that pyridoxamine is the preferable form. Some of the unique benefits of pyridoxamine probably derive from the pyridoxamine molecule itself. There are very few published studies that compare pyridoxamine and pyridoxal-5'-phosphate

side-by-side.

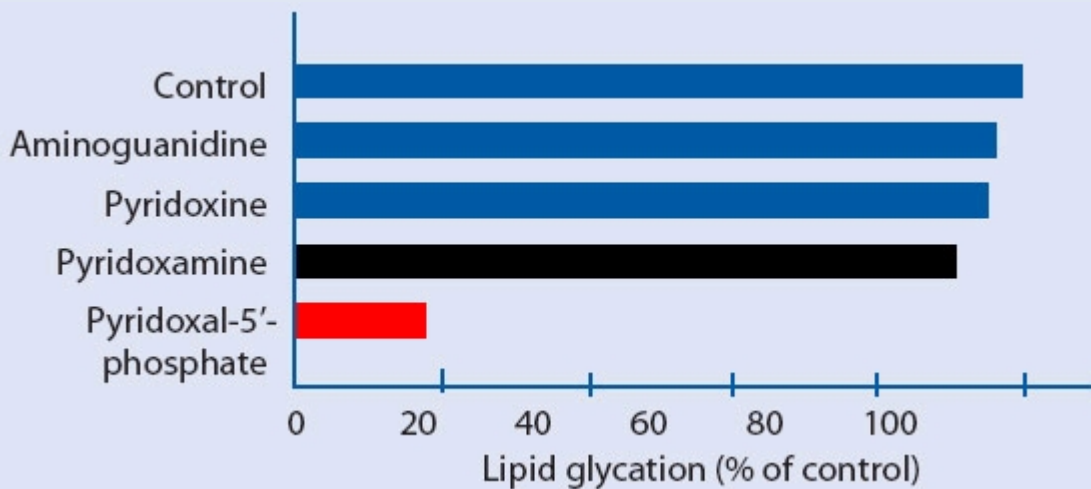
For many years, it was thought that orally ingested pyridoxal-5'-phosphate is degraded in the digestive tract and does not provide systemic benefits. Published studies reveal that the pyridoxal-5'-phosphate, when swallowed, is orally bioavailable and demonstrates systemic benefits, including protecting vital kidney structures analogous to the way pyridoxamine does.¹¹

Relying on the published scientific literature, we at Life Extension are replacing pyridoxamine in all of our products with a double-dose of pyridoxal-5'-phosphate. While the cost to us is very high, we are not about to let the FDA's insanely prejudiced actions deprive our members of this vital vitamin B6 metabolite.

At this time, we have a limited supply of pyridoxamine-containing supplements available.

Pyridoxamine is included in Life Extension Mix, Mito-chondrial Energy Optimizer, and as a stand-alone 50 mg supplement. Once this supply is sold out, we will substitute a double-dose of pyridoxal-5'-phosphate in all these supplements, but will not increase the price.

EFFICACY OF AMINO GUANIDINE AND B6 VITAMERS IN INHIBITING LIPID GLYCATION³



This chart was prepared using data from the Journal of Lipid Research (Volume 47, 2006) in which differing compounds were screened for their ability to inhibit lipid glycation. As can be clearly seen, the RED bar shows far less lipid glycation in the presence of pyridoxal-5'-phosphate than any other form of vitamin B6, including pyridoxamine (black bar).

The fact that we have engineered around the FDA embargo should not diminish the urgent need to contact The White House to demand that this scientifically absurd prohibition by the FDA be reversed. While Life Extension members may obtain the same benefits from pyridoxal-5'-phosphate, most of the public will not find out about this superior form of vitamin B6, and will succumb unnecessarily to a host of age-related diseases.

In this month's issue, we feature an in-depth article that describes the benefits of pyridoxal-5'-phosphate. I ask all members, to mail the letter on the next page to the White House to protest the inappropriate banning of pyridoxamine.

For longer life,

William Faloon

Letter to the White House

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