

## **BIOEQUIVALENCE TESTIMONY**

*Testimony presented by Dr. Becker to the New York Medicaid Pharmacy and Therapeutics Committee on Thursday, October 14, 2005*

My name is Dr. Carolyn Becker and I am an Associate Clinical Professor of Medicine in the Division of Endocrinology at Columbia University in Manhattan. I am representing the Endocrine Society, the largest organization of endocrinologists in the world with over 11,000 members including clinicians, researchers and educators. I serve as the Vice President for Physicians in Practice of the Endocrine Society and as such, am here to make the case that brand name levothyroxine sodium products should continue to be exempted from the requirements of the Mandatory Generic Program in New York State. If this exemption is reversed, there is potential for great harm to patients, confusion for doctors, and minimal if any savings for the State of New York. In the next few minutes, I would like to address all 3 of these points.

1. Levothyroxine is one of the most frequently prescribed medications in the U.S.: 13 million people take it every day and most take it chronically for many years.
2. Levothyroxine has a very narrow therapeutic window: in other words, small changes in dose that often result from product substitution can cause either excessive or inadequate hormone levels in the blood can have significant clinical consequences. These consequences include: recurrence of uncomfortable symptoms, atrial fibrillation, worsening of ischemic heart disease, bone loss and fractures, preterm delivery in pregnant women, hypercholesterolemia, and detrimental effects on the IQs of hypothyroid infants.
3. Levothyroxine is a drug with a long half-life of 7 days and requires 6-8 weeks to reach equilibrium in the blood. In clinical practice this means that it can take months and occasionally up to a year to find the right dose of levothyroxine for individual patients. Following any change in dose of levothyroxine, it is critical to recheck blood levels 6-8 weeks later to be sure the dose is correct.
4. The current FDA methods for determining bioequivalence of levothyroxine products are seriously flawed. They administer single large doses of levothyroxine to healthy, normal individuals and measure areas under the curve and maximal concentrations of the drug in the blood. But these techniques fail to measure the most important marker of biologic activity, TSH (thyroid stimulating hormone). The current FDA methods are also far too lax. They utilize pharmacokinetic methods that would allow two different preparations of levothyroxine that differed by 12.5% or more to be considered bioequivalent!! Such differences in bioactivity in products labeled as "bioequivalent" can have potent clinical effects, especially in susceptible patient populations such as the elderly, patients with heart disease, patients with thyroid cancer, pregnant women, and infants. In practice, we adjust levothyroxine doses by less than 12.5% (for example from 75 to 88 mcg, from 88 to 100 mcg, or from 100 to 112 mcg) which illustrates the fine tuning that is needed with this medication. The very narrow

toxic to therapeutic ratio of levothyroxine makes the FDA claims of “bioequivalence” in this setting not just meaningless but potentially quite dangerous.

5. If NY State removes levothyroxine sodium products from the list of drugs exempted from the Mandatory Generic program, this will cause great confusion and consternation for doctors and patients alike. Doctors will be asked to obtain telephone preauthorization prior to prescribing brand-name levothyroxine, prior to renewing brand-name levothyroxine, and prior to changing the dose of brand-name levothyroxine. In addition to taking up valuable physician or staff time that could be better spent caring for patients, this regulation will lead to inadvertent substitution of product formulations that are not equivalent—in this case, substitution of generic for brand-name levothyroxine—as many physicians may forget or lack the time to obtain preauthorization. In that case, proper testing of TSH levels in 6-8 weeks following the change in medication will not occur and patients will be placed at risk for adverse side effects from under- or overdosage. Moreover, since patients and physicians may not even be aware of the change in formulation, they may fail to recognize that symptoms that occur are due to the change in medication and not to some new disease state. This may lead to unnecessary testing, expensive work-ups, and in some cases, hospitalization. Physicians have these same concerns, whether a patient is switched from brand to generic or from one brand to another.
6. Finally, removing levothyroxine sodium from the exemption list will not save NY State money and in fact, may even be more costly. The cost of a single TSH blood test to monitor the effects of medication changes can cost \$75-100, depending on the lab, an expense that will negate any savings from switching from brand to generic. There is no compelling financial reason to advocate removing levothyroxine sodium from the Mandated Generic exemption.

In summary, on behalf of the Endocrine Society, other practicing physicians in the State of New York, and the thousands of patients who take levothyroxine, I would ask that you continue the current policy and keep levothyroxine sodium products exempted from the Mandated Generic drug program.

Thank you for giving me this opportunity to speak to you today about this important matter.