TO: State Boards of Pharmacy

FROM: Scott Brunner, CAE
Chief Executive Officer

Savannah Cunningham, PharmD
Director of Public Policy

DATE: December 2, 2022

SUBJECT: *Update on compounded desiccated thyroid extract (DTE)*

The FDA has recently sent identical letters, attached here, to the National Association of Boards of Pharmacy and the Federation of State Medical Boards as follow-up to its September 16 letter to NABP stating that desiccated thyroid extract – and thus Thyroid USP – has been classified as a biologic drug and is therefore ineligible for compounding. The September 16 letter also stated that DTE "can put patients at harm" and that "therapies containing DTE are biological products subject to licensure under Section 351(i) of the PHS Act."

The new letters are what we believe to be an attempt to provide better guidance to state boards of pharmacy regarding state enforcement of FDA's previous letter to NABP, which may have been perceived by some boards of pharmacy as an FDA directive to enforce a ban on DTE compounding by 503A pharmacies.

In the November 16 letters, FDA states that "DTE products continue to be available, and FDA intends to make any additional information regarding DTE products available to the public. While the Agency continues to address any complaints related to DTE products prepared by state-licensed pharmacists, we have not to date taken steps more generally to remove products prepared by drug compounders containing DTE or limit compounder access to DTE." The letters also states that "FDA expects to employ a risk-based enforcement approach with respect to violative compounded drugs, giving the highest enforcement priority to compounded drugs and violations of the Federal Food, Drug, and Cosmetic Act and FDA regulations that pose the greatest public health risks, such as serious adverse events or serious product quality or adulteration issues."

Based on our conversations with FDA officials, we interpret those statements to mean that FDA intends, at least for the foreseeable future, to take no action against compounders of DTE unless they receive a complaint about adverse events or product quality—in which case, the agency would commence an investigation of the pharmacy that prepared the DTE drug that is the source of the complaint.

We urge state boards of pharmacy to adopt that same position and take no enforcement action against compounders who prepare compounded DTE, at least until FDA changes its position.

We must note that FDA's most recent letter fails to address the process by which FDA has reclassified DTE/Thyroid USP as a biologic in the first place. Our concerns are outlined below:

- In its letter to NABP, FDA states that it considers thyroid USP to be a biologic based on a component in the product, thyroglobulin, that is not an active ingredient of the medication. The letter states the agency is making that judgment based on the number of amino acids in thyroglobulin under the definition of a protein under the definition of a biologic. (As further noted below, this is the only instance we're aware of of a drug being designated a biologic based on a component that is not the active ingredient.)
- Currently, multiple manufactured thyroid USP drug products (NP Thyroid, Armour Thyroid, etc.) marketed and distributed by pharmaceutical companies. These products are not listed in FDA's Purple Book, which tells us they are not the subject of a Biologics License Application (BLA) and are thus not biologic products. (We note that thyroglobulin is not listed in the Purple Book either.) If FDA's newly stated position on DTE also applies to those commercially available drugs – and we see no reason for differentiation between and compounded DTE – will they be required to have a biologics license to continue to manufacture them?
- FDA's letter claims that levels of the hormone can vary from batch to batch—and yet the manufactured products make no mention of the thyroglobulin content in the package inserts of those products. Nor do those product labels provide any mention of thyroglobulin content. If the agency has such concerns about the hormone quantity, why is the presence of thyroglobulin absent in those products' insert and label?
- The package inserts and labeling of the manufactured thyroid USP products clearly describe levothyroxine and liothyronine as the active ingredients. Products that are deemed biologics are typically deemed so based on the active ingredient being the biologic agent, as opposed to a substance that is not described in any of the labeling, including the package insert.
- In addition to thyroglobulin not being the active ingredient, Section 503A of the FDCA allows for chemicals to be used as the API of a human drug compound if the chemical has an applicable USP monograph. FDA has indicated that applicable USP monographs are the "drug" monographs in USP. Thyroid USP has an applicable drug monograph, and thyroglobulin content is not a specification to be tested for in the monograph.

In coming days, APC will be submitting formal comments to FDA outlining our concerns. We first raised those concerns with them verbally in a special meeting on November 9. We'll restate them in another listening session with FDA on December 13.

Despite our ongoing concerns, we're grateful for FDA's willingness to respond to our request for more clarity on whether compounders may continue, at least for the time being, to prepare DTE for patients. We now know how FDA says it will approach that situation. We encourage your state board of pharmacy to adopt a stance identical to FDA's so that patients in your state who rely on compounded DTE to live normal lives can continue to be served.

If APC may be helpful to you on this or any other matter related to pharmacy compounding, please contact us at scott@a4pc.org