



## INDUSTRY EDUCATION

### Synthetic vs Porcine Thyroid Dosing



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Hypothyroidism, a condition in which the body does not produce adequate thyroid hormones, affects up to 5% of the general population with some estimating that a further 5% of cases go undiagnosed. Primary hypothyroidism, the failure of the thyroid to produce adequate thyroid hormone, accounts for more than 99% of all thyroid cases, with other pathogeneses such as underproduction of thyroid stimulating hormone (TSH) from the pituitary or deficiency of thyrotropin releasing hormone and other causes accounting for just a small number of cases.<sup>1</sup> Though iodine deficiency is the most common cause of primary hypothyroidism globally, in the United States autoimmune thyroid diseases such as Hashimoto thyroiditis is the most common cause.<sup>2</sup>

Standard of treatment for hypothyroidism is supplementation with levothyroxine sodium, though, liothyronine sodium and desiccated thyroid extract (DTE) products are also used for the management of hypothyroidism. One prospective, randomized, double-blind, crossover study of 75 patients compared three treatment groups: DTE, levothyroxine sodium, and a levothyroxine sodium/liothyronine sodium combination group. The patients spent 12 weeks in each arm of treatment and completed various tests such as questionnaires and weight measurements. The study found no statistically significant difference for preference of any of these treatments over another. Though the level of statistical significance was not reached, patients with Hashimoto hypothyroidism preferred DTE or combination levothyroxine sodium and liothyronine sodium over levothyroxine sodium treatment alone.<sup>3</sup> One review of 125 patients who switched from levothyroxine sodium treatment alone to DTE (specifically, Armour Thyroid in the case of this study) found patients complained less of weight gain and fatigue when in a euthyroid state on DTE as compared to levothyroxine sodium. However, this review also noted that patients in the Armour Thyroid group were more likely to report adverse effects such as palpitations as compared to those on levothyroxine sodium alone.<sup>4</sup> Another randomized, double-blind crossover study had patients take either DTE or levothyroxine sodium for 16 weeks, then switch to the other group for the same

duration. Overall, DTE didn't result in a significant improvement of quality of life, however, the study did find that 48.6% of patients noted they preferred DTE as compared to only 18.6% who preferred levothyroxine sodium alone, and 32.9% who had no preference. Of the subset of patients that preferred DTE, it was found that those patients noted a small amount (an average of 4lbs) of weight loss on DTE vs other treatments.<sup>5</sup>

## A Comparison of Concentrations

Though evidence does not suggest that DTE or combination levothyroxine/liothyronine products are superior for all patients, the evidence does suggest that some patients may find additional benefit or express a preference for such treatments, while others may prefer synthetic thyroid replacement alone, perhaps due to potentially increased adverse events that could be associated with DTE products.<sup>6</sup> Given these differences in preference, patients may switch back and forth between thyroid therapies trying to find the treatment that works best for them. Unfortunately, thyroid dose conversion is not an exact science. One review of survey results from a survey designed by the American Thyroid Association, the Endocrine Society, and the American Association of Endocrinologists found some providers had difficulty in dose adjustment with thyroid extract products and it was hypothesized that some adverse effects could be related to dosing issues associated with the use of DTE.<sup>7</sup>

One of the challenges of switching between these therapies is aiming for a similar initial dose. One randomized, double-blind, crossover study designed to investigate the effectiveness of DTE as compared with levothyroxine sodium also worked to develop a recommended levothyroxine sodium to DTE conversion chart based on their results. They found:

<b>Dose</b> (Note: levothyroxine doses are noted in mcg and DTE doses are noted in mg)									
Levothyroxine Sodium (mcg)	88	100	112	125	137	150	175	200	250
DTE (mg)	60	68	76	85	93	102	119	136	170

DTE = desiccated thyroid extract  
Approximate conversion is 1.47mcg levothyroxine to 1mg DTE  
Table adopted from Table 7 from Hoang T et al.<sup>8</sup>

A second study; a randomized, double-blind, crossover study designed to compare effectiveness of levothyroxine sodium, DTE, and levothyroxine/liothyronine combinations, used the below dosing conversions when switching patients between treatments.

<b>Dose</b> (Note: levothyroxine and liothyronine doses are noted in mcg and DTE doses are noted in mg)									
Levothyroxine Sodium (mcg)	88	100	112	125	137	150	175	200	250
Levothyroxine Sodium/Liothyronine (mcg)	63/7.5	75/7.5	82/7.5	88/10	100/10	112/10	125/12	150/15	175/20
DTE (mg)	60	67.5	75	82.5	90	105	120	135	165

DTE = desiccated thyroid extract  
Table adopted from Table 2 from Shakir M et al.<sup>9</sup>

Though these tables offer similar conversion rates, even between studies some variability does exist, further highlighting the challenges of switching between dosage forms. Furthermore, we cannot apply exact conversion math calculating the amount of mcg per grain of levothyroxine and liothyronine in thyroid products and assuming that would be the equivalent dose of the combination product from a therapeutic perspective.

One grain of thyroid (which can vary between 60mg to 65mg depending on the commercially available product and is typically approximately 65mg for bulk DTE) contains 38mcg of levothyroxine and 9mcg of liothyronine per the USP monograph for Thyroid Tablets.<sup>10</sup> Though the above tables are not exact matches for each other, in both cases it is clear that a higher dose of synthetic levothyroxine sodium or combination levothyroxine and liothyronine sodium is needed to match the therapeutic effect of similar doses from DTE. Further complicating the dosing comparison is that liothyronine sodium and levothyroxine sodium are not directly substitutable for each other. Though an exact dose conversion can be difficult to find, some studies suggest liothyronine sodium has a potency approximately 3-5x that of levothyroxine sodium, so when modifying ratios between these two thyroid hormones, this difference in potency must be considered to avoid suprathreshold thyroid hormone levels and subsequent adverse effects.<sup>11,12</sup> It is also important to note that liothyronine sodium has a more rapid onset of action than levothyroxine sodium, which can impact adverse event profile and impact dosing conversion as well given that switching from once daily levothyroxine to a combination once daily levothyroxine/liothyronine product, even if the dose conversion is correct for the patient, could result in adverse effects due to this different pharmacokinetic profile.<sup>13</sup>

## Assisting Patients through Dose Conversions

Dose conversion between various types of thyroid products is challenging. For patients who will be switching from synthetic thyroid products to DTE or the reverse, consider citing resources such as those listed in the tables above to assist with dose conversion rather than simply converting directly based on the listed mcg per grain of the DTE product. The American Thyroid Association recommends monitoring serum levothyroxine and liothyronine 2-6 weeks after initiation of therapy, so note that patients may need more frequent monitoring after conversions between DTE and synthetic thyroid products until they are euthyroid.<sup>14</sup>

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