

## **ESA Position Statement on Desiccated Thyroid or Thyroid Extract**

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### **Introduction**

Desiccated thyroid or thyroid extract refers to either porcine (or mixed bovine and porcine) thyroid glands, dried and powdered for therapeutic use. All brands contain a mixture of thyroid hormones: T4 (thyroxine), T3 (triiodothyronine) in the proportions usually present in the thyroid gland (approximately 80% T4 and 20% T3). The following strengths are available: 1/8, 1/4, 1/2, 1, 2, and 3 grain tablets as well as 4 and 5 grain tablets. One grain (about 60 mg) of desiccated thyroid contains about 38 mcg of T4 and 9 mcg of T3. Because the preparation is whole thyroid gland, each 60 mg tablet also contains over 59 mg of all of the other constituents of thyroid glands, a small component of which may be biologically active.

As most doctors prescribe thyroxine rather than thyroid extract, the use of thyroid extract has become associated with alternative and complementary medicine practitioners (1,2). Desiccated thyroid or thyroid extract is not a pure product, not approved by the TGA, not available on the PBS, not produced by a pharmaceutical company, not subject to existing TGA regulations, has limited quality control, and is marketed as a “bioidentical hormone”, while “bioidentical” has been determined by the FDA in the USA as a marketing term.

Desiccated thyroid or thyroid extract is preferred by a minority of patients and doctors who claim better relief of some symptoms, such as fatigue and depression.

A number of specific claims are commonly made about thyroid extract:

1. Thyroid extract is better than thyroxine because it contains both T4 and T3.
2. Doses should be increased until symptoms are relieved regardless of laboratory tests, even if the TSH is decreased below the normal range, which can lead to adverse effects such as irregularity of the heart beat (atrial fibrillation) or thin bones (osteoporosis).
3. Other constituents of the dried thyroid glands besides the T4 and T3 (e.g. unmeasured amounts of diiodothyronine (T2), monoiodothyronine (T1), calcitonin, other protein-bound iodine) may contribute to a perceived greater effectiveness or confer additional benefits.
4. Thyroid extract is "natural" and therefore preferable to synthesized thyroxine molecules.

The following areas of uncertainty do exist:

1. Is the reason some people fail to have complete relief of symptoms when tests show normal levels simply because there are other causes

of fatigue, depression, and weight gain that are mistakenly attributed to the thyroid? Could a placebo effect explain the better relief of these symptoms from thyroid extract?

2. Does a combination of T4 and T3 provide more effective symptom relief for some people than T4 alone? Multiple controlled trials have shown inconsistent benefits of various ratios of T4 and T3. However, there may be a subgroup who require T3 in addition to T4, because they cannot generate normal amounts from T4. However, if such a group exists the means to detect it have not.
3. Could the perceived benefit simply result from overtreatment? This is potentially deleterious to the patient in the long term, increasing the risk of both osteoporosis and atrial fibrillation.

Despite claims of proponents that desiccated thyroid or thyroid extract are superior to thyroxine or combinations of T4 and T3 for most people with hypothyroidism, no controlled clinical trials have been published, and most endocrinologists are concerned that superiority is due to a placebo effect or an effect of overtreatment.

### Considerations

	<b>Thyroxine</b>	<b>Thyroid Extract</b>
<b>Molecular structure</b>	Identical to human thyroxine	Porcine or bovine thyroxine and triiodothyronine; other components
<b>TGA oversight</b>	Yes	No
<b>Dosage</b>	Monitored; accurate and consistent	Monitored; may be inaccurate or inconsistent
<b>Purity</b>	Monitored; pure	Not monitored; impure
<b>Safety</b>	Tested; risks known	Not tested in trials; risks unknown
<b>Efficacy</b>	Tested and proven	Not tested; unproven
<b>Scientific evidence</b>	Existent; conclusive	Insufficient

The controversies surrounding the safety and efficacy of “bioidentical hormones” such as desiccated thyroid or thyroid extract illustrate the need for further scientific and medical scrutiny of these substances. Until such studies are completed, physicians should exercise caution when prescribing “bioidentical hormones” and counsel their patients about the controversy over the use of these preparations. Additionally, patients should educate themselves about hormone therapies and engage in candid discussions with their doctors. Much consideration should be given to the decision to undergo any hormone therapy, and “bioidentical hormones” present unique and additional concerns because of the process by which many of them are made and the lack of quality controls. In particular, purity and dose equivalence with thyroxine and between different preparations are not regulated.

### **ESA Position**

In general, desiccated thyroid hormone or thyroid extract, combinations of thyroid hormones, or triiodothyronine should **not** be used as thyroid replacement therapy.

ESA advocates the use of a high-quality brand preparation of levothyroxine. Bioequivalence of levothyroxine preparations is based on total T4 measurement and not TSH levels; therefore, bioequivalence is not the same as therapeutic equivalence. However, the only two brands of levothyroxine (Oroxine, Eutroxig) available in Australia are identical.

Importantly, therapy should be titrated after an interval of at least 6 weeks following any change in levothyroxine dose. The serum TSH level is most important, and a free T4 estimate may also be included in the assessment.

There is a resurgence of interest in the possible benefits of treatment of hypothyroidism with combinations of T4 and T3 or with thyroid extract. The small-scale study that seems to have sparked this interest treated patients for only 5 weeks, focused on mood changes, used a T4 plus T3 combination that differs substantially from that found in natural thyroid products, may have found benefit in only a subset of patients, and has not been replicated (3,4). Insufficient evidence is available to know which patients with hypothyroidism, if any, would be better treated with a combination of T4 plus T3, rather than with T4 alone.

The ESA strongly recommends that all hormonal preparations that are intended to provide replacement therapy, whether prepared and classified according to standard pharmaceutical guidelines, or as compounded, natural or nutritional products, should be subject to similar quality assurance and potency criteria, including clear analytical definition of their composition.

The ESA is concerned that patients are receiving potentially misleading or false information about the benefits and risks of “bioidentical hormones” such as desiccated thyroid or thyroid extract. Therefore, ESA supports TGA regulation and oversight of all hormones—“bioidentical” and traditional—regardless of chemical structure or method of manufacture.

This should include, but not be limited to, the following:

- Surveys for purity and dosage accuracy of desiccated thyroid or thyroid extract.
- Mandatory reporting of adverse events.
- A registry of adverse events related to the use of bioidentical hormone preparations, including desiccated thyroid or thyroid extract, should be supported by the TGA and could be managed by an external organization, as the TGA does not regulate or monitor these compounds.
- Inclusion of uniform information for patients, such as warnings and precautions, in packaging of bioidentical hormone products, including desiccated thyroid or thyroid extract

## **References:**

1. American Association Of Clinical Endocrinologists Medical Guidelines For Clinical Practice For The Evaluation And Treatment of Hyperthyroidism And Hypothyroidism. Updated version 2006.
2. The Endocrine Society (USA). Bioidentical Hormones Position Statement. October 2006.
3. Bunevicius R, Kazanavicius G, Zalinkevicius R, Prange AJ Jr. Effects of thyroxine as compared with thyroxine plus triiodothyronine in patients with hypothyroidism. *N Engl J Med.* 1999; 340:424-429.
4. Bunevicius R, Prange AJ. Mental improvement after replacement therapy with thyroxine plus triiodothyronine: relationship to cause of hypothyroidism. *Int J Neuropsychopharmacol.* 2000; 3:167-174.