

Statement of Principles concerning HYPERTHYROIDISM AND THYROTOXICOSIS (Reasonable Hypothesis)

(No. 5 of 2022)

The Repatriation Medical Authority determines the following Statement of Principles under subsection 196B(2) of the *Veterans' Entitlements Act 1986*.

Dated 24 December 2021

The Common Seal of the Repatriation Medical Authority was affixed to this instrument at the direction of:

Professor Terence Campbell AM Chairperson

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1 Name

This is the Statement of Principles concerning *hyperthyroidism and thyrotoxicosis (Reasonable Hypothesis)* (No. 5 of 2022).

2 Commencement

This instrument commences on 31 January 2022.

3 Authority

This instrument is made under subsection 196B(2) of the *Veterans' Entitlements Act 1986*.

4 Repeal

The Statement of Principles concerning hyperthyroidism and thyrotoxicosis No. 27 of 2013 (Federal Register of Legislation No. F2013L00723) made under subsection 196B(2) of the VEA is repealed.

5 Application

This instrument applies to a claim to which section 120A of the VEA or section 338 of the *Military Rehabilitation and Compensation Act 2004* applies.

6 Definitions

The terms defined in the Schedule 1 - Dictionary have the meaning given when used in this instrument.

7 Kind of injury, disease or death to which this Statement of Principles relates

(1) This Statement of Principles is about hyperthyroidism and thyrotoxicosis and death from hyperthyroidism and thyrotoxicosis.

Meaning of hyperthyroidism

- (2) For the purposes of this Statement of Principles, hyperthyroidism:
 - (a) means a functional endocrine disorder in which the thyroid gland synthesises and secretes excessive amounts of thyroid hormone sufficient to produce clinical symptoms and signs of thyroid hyperfunction or to warrant medical treatment; and
 - (b) excludes:
 - (i) euthyroid hyperthyroxinaemia;
 - (ii) gestational transient thyrotoxicosis;
 - (iii) Graves disease:
 - (iv) sick euthyroid syndrome; and
 - (v) toxic multinodular goitre and toxic thyroid adenoma.

- Note 1: Hyperthyroidism typically presents with elevated serum concentrations of the thyroid hormones thyroxine (T4) and/or triiodothyronine (T3), and usually with a reduced concentration of thyroid-stimulating hormone.
- Note 2: Clinical symptoms and signs of thyroid hyperfunction are nonspecific and typically include anxiety, emotional lability, weakness, tremor, palpitations, heat intolerance, increased perspiration and weight loss.
- Note 3: Hyperthyroidism due to toxic multinodular goitre or toxic thyroid adenoma is covered by the Statements of Principles concerning goitre. In the circumstance where hyperthyroidism is due to Graves disease, it is covered by the Statements of Principles concerning Graves disease.
- Note 4: Hyperthyroidism may be acute or chronic. The acute form may present as a thyrotoxic crisis.
- Note 5: thyrotoxic crisis is defined in the Schedule 1 Dictionary.

Meaning of thyrotoxicosis

- (3) For the purposes of this Statement of Principles, thyrotoxicosis:
 - (a) means a functional endocrine disorder that results from the action of inappropriately high thyroid hormone levels in tissues sufficient to produce clinical symptoms and signs of thyroid hyperfunction or to warrant medical treatment; and
 - (b) excludes:
 - (i) euthyroid hyperthyroxinaemia;
 - (ii) gestational transient thyrotoxicosis;
 - (iii) Graves disease;
 - (iv) sick euthyroid syndrome; and
 - (v) toxic multinodular goitre and toxic thyroid adenoma.
 - Note 1: Inappropriately high thyroid hormone levels in thyrotoxicosis can arise from endogenous or exogenous sources.
 - Note 2: Thyrotoxicosis typically presents with elevated serum concentrations of the thyroid hormones thyroxine (T4) and/or triiodothyronine (T3), and usually with a reduced concentration of thyroid-stimulating hormone.
 - Note 3: Clinical symptoms and signs of thyroid hyperfunction are nonspecific and typically include anxiety, emotional lability, weakness, tremor, palpitations, heat intolerance, increased perspiration and weight loss.
 - Note 4: Thyrotoxicosis due to toxic multinodular goitre or toxic thyroid adenoma is covered by the Statements of Principles concerning goitre. In the circumstance where thyrotoxicosis is a clinical manifestation of Graves disease, it is covered by the Statements of Principles concerning Graves disease.
 - Note 5: Thyrotoxicosis may be acute or chronic. The acute form may present as a thyrotoxic crisis.
 - Note 6: thyrotoxic crisis is defined in the Schedule 1 Dictionary.

Death from hyperthyroidism or thyrotoxicosis

(4) For the purposes of this Statement of Principles, hyperthyroidism or thyrotoxicosis, in relation to a person, includes death from a terminal event or condition that was contributed to by the person's hyperthyroidism or thyrotoxicosis.

Note: terminal event is defined in the Schedule 1 - Dictionary.

8 Basis for determining the factors

The Repatriation Medical Authority is of the view that there is sound medical-scientific evidence that indicates that hyperthyroidism or thyrotoxicosis and death from hyperthyroidism or thyrotoxicosis can be related to relevant service rendered by veterans, members of Peacekeeping Forces, or members of the Forces under the VEA, or members under the MRCA.

Note: MRCA, relevant service and VEA are defined in the Schedule 1 - Dictionary.

9 Factors that must exist

At least one of the following factors must as a minimum exist before it can be said that a reasonable hypothesis has been raised connecting hyperthyroidism or thyrotoxicosis or death from hyperthyroidism or thyrotoxicosis with the circumstances of a person's relevant service:

- (1) having iodine excess within the 6 months before the clinical onset of hyperthyroidism or thyrotoxicosis;
 - Note 1: Iodine excess may be due to consuming foods, dietary supplements or medications with a high content of iodine.
 - Note 2: *iodine excess* is defined in the Schedule 1 Dictionary.
- (2) being administered an iodine-containing radiographic contrast agent within the 6 months before the clinical onset of hyperthyroidism or thyrotoxicosis;
- (3) taking amiodarone for a continuous period of at least 2 weeks, within the 1 year before the clinical onset of hyperthyroidism or thyrotoxicosis;
- (4) taking a drug from the specified list of drugs within the 6 months before the clinical onset of hyperthyroidism or thyrotoxicosis;

 Note: *specified list of drugs* is defined in the Schedule 1 Dictionary.
- (5) taking minocycline for at least the 6 months before the clinical onset of hyperthyroidism or thyrotoxicosis;
- (6) taking a drug containing at least 10 milligrams of iodine daily for a continuous period of at least 4 weeks, within the 6 months before the clinical onset of hyperthyroidism or thyrotoxicosis;
- (7) having a thyroid-stimulating, hormone-secreting pituitary adenoma at the time of the clinical onset of hyperthyroidism or thyrotoxicosis;
- (8) having a chorionic gonadotrophin-secreting neoplasm at the time of the clinical onset of hyperthyroidism or thyrotoxicosis;
 - Note: chorionic gonadotrophin-secreting neoplasm is defined in the Schedule 1 Dictionary.

- (9) having a primary or metastatic neoplasm involving the thyroid gland at the time of the clinical onset of hyperthyroidism or thyrotoxicosis;
- (10) for hyperthyroidism or thyrotoxicosis first presenting as thyrotoxic crisis only, having an acute precipitating event within the 48 hours before the clinical onset of hyperthyroidism or thyrotoxicosis;

Note: *acute precipitating event* and *thyrotoxic crisis* are defined in the Schedule 1 - Dictionary.

- (11) for thyrotoxicosis only:
 - (a) having struma ovarii at the time of the clinical onset of thyrotoxicosis;

Note: struma ovarii is defined in the Schedule 1 - Dictionary.

- (b) having metastatic thyroid carcinoma containing functional thyroid tissue at the time of the clinical onset of thyrotoxicosis;
- (c) having a form of thyroiditis from the specified list of forms of thyroiditis at the time of the clinical onset of thyrotoxicosis;

Note: specified list of forms of thyroiditis is defined in the Schedule 1 - Dictionary.

- (d) having trauma involving the thyroid gland within the 14 days before the clinical onset of thyrotoxicosis;
 - Note: trauma involving the thyroid gland is defined in the Schedule 1 Dictionary.
- (e) ingesting excess thyroid hormone in medication, dietary supplements or in food containing thyroid extracts within the 3 months before the clinical onset of thyrotoxicosis;
- (12) having iodine excess within the 6 months before the clinical worsening of hyperthyroidism or thyrotoxicosis;
 - Note 1: Iodine excess may be due to consuming foods, dietary supplements or medications with a high content of iodine.

Note 2: *iodine excess* is defined in the Schedule 1 - Dictionary.

- (13) being administered an iodine-containing radiographic contrast agent within the 6 months before the clinical worsening of hyperthyroidism or thyrotoxicosis;
- (14) taking amiodarone for a continuous period of at least 2 weeks, within the 1 year before the clinical worsening of hyperthyroidism or thyrotoxicosis;
- (15) taking a drug from the specified list of drugs within the 6 months before the clinical worsening of hyperthyroidism or thyrotoxicosis;

 Note: *specified list of drugs* is defined in the Schedule 1 Dictionary.
- (16) taking minocycline for at least the 6 months before the clinical worsening of hyperthyroidism or thyrotoxicosis;

- (17) taking a drug containing at least 10 milligrams of iodine daily for a continuous period of at least 4 weeks, within the 6 months before the clinical worsening of hyperthyroidism or thyrotoxicosis;
- (18) having a thyroid-stimulating, hormone-secreting pituitary adenoma at the time of the clinical worsening of hyperthyroidism or thyrotoxicosis;
- (19) having a chorionic gonadotrophin-secreting neoplasm at the time of the clinical worsening of hyperthyroidism or thyrotoxicosis;
 - Note: chorionic gonadotrophin-secreting neoplasm is defined in the Schedule 1 Dictionary.
- (20) having a primary or metastatic neoplasm involving the thyroid gland at the time of the clinical worsening of hyperthyroidism or thyrotoxicosis;
- (21) for thyrotoxic crisis only, having an acute precipitating event within the 48 hours before that clinical worsening of hyperthyroidism or thyrotoxicosis;

Note: *acute precipitating event* and *thyrotoxic crisis* are defined in the Schedule 1 - Dictionary.

- (22) for thyrotoxicosis only:
 - (a) having struma ovarii at the time of the clinical worsening of thyrotoxicosis;

Note: struma ovarii is defined in the Schedule 1 - Dictionary.

- (b) having metastatic thyroid carcinoma containing functional thyroid tissue at the time of the clinical worsening of thyrotoxicosis;
- (c) having a form of thyroiditis from the specified list of forms of thyroiditis at the time of the clinical worsening of thyrotoxicosis;
 - Note: *specified list of forms of thyroiditis* is defined in the Schedule 1 Dictionary.
- (d) having trauma involving the thyroid gland within the 14 days before the clinical worsening of thyrotoxicosis;
 - Note: trauma involving the thyroid gland is defined in the Schedule 1 Dictionary.
- (e) ingesting excess thyroid hormone in medication, dietary supplements or in food containing thyroid extracts within the 3 months before the clinical worsening of thyrotoxicosis;
- (23) inability to obtain appropriate clinical management for hyperthyroidism or thyrotoxicosis.

10 Relationship to service

- (1) The existence in a person of any factor referred to in section 9, must be related to the relevant service rendered by the person.
- (2) The factors set out in subsections 9(12) to 9(23) apply only to material contribution to, or aggravation of, hyperthyroidism or thyrotoxicosis

where the person's hyperthyroidism or thyrotoxicosis was suffered or contracted before or during (but did not arise out of) the person's relevant service.

11 Factors referring to an injury or disease covered by another Statement of Principles

In this Statement of Principles:

- (1) if a factor referred to in section 9 applies in relation to a person; and
- (2) that factor refers to an injury or disease in respect of which a Statement of Principles has been determined under subsection 196B(2) of the VEA;

then the factors in that Statement of Principles apply in accordance with the terms of that Statement of Principles as in force from time to time.

Schedule 1 - Dictionary

Note: See Section 6

1 Definitions

In this instrument:

acute precipitating event means a physical or psychological stimulus or event that causes a sudden, intense psychological or physical response.

Note: Examples of an acute precipitating event include:

- (a) abrupt cessation or lowering of anti-thyroid therapy;
- (b) acute illness such as acute myocardial infarction, stroke and congestive heart failure;
- (c) acute iodine load;
- (d) experiencing an acute, severe, emotional stressor;
- (e) infection:
- (f) parturition;
- (g) physical trauma or injury; and
- (h) surgery.

chorionic gonadotrophin-secreting neoplasm means a neoplasm that secretes the beta subunit of human chorionic gonadotrophin, and includes seminoma, choriocarcinoma, non-seminomatous germ cell tumour, hydatidiform mole, teratoma and islet cell tumour.

hyperthyroidism—see subsection 7(2).

iodine excess means:

- (a) an average intake of more than 1,100 micrograms of iodine per day for adults, or more than 900 micrograms per day for those aged 18 years and under, for a continuous period of at least 3 months; or
- (b) having a urinary iodine concentration of greater than 300 micrograms per litre, or greater than 500 micrograms per litre for pregnant women.

MRCA means the Military Rehabilitation and Compensation Act 2004.

relevant service means:

- (a) operational service under the VEA;
- (b) peacekeeping service under the VEA;
- (c) hazardous service under the VEA:
- (d) British nuclear test defence service under the VEA;
- (e) warlike service under the MRCA; or
- (f) non-warlike service under the MRCA.

Note: MRCA and VEA are also defined in the Schedule 1 - Dictionary.

specified list of drugs means:

- (a) immune checkpoint inhibitors;
- (b) interferon alpha;
- (c) interleukin-2;
- (d) lenalidomide;
- (e) lithium carbonate; or
- (f) tyrosine kinase inhibitors.

specified list of forms of thyroiditis means:

- (a) acute radiation thyroiditis;
- (b) drug-induced thyroiditis;
- (c) infectious thyroiditis;
- (d) silent thyroiditis; or
- (e) subacute thyroiditis.

Note 1: Infectious thyroiditis may be due to a bacterial or fungal infection of the thyroid gland. Organisms that can cause infectious thyroiditis include:

- (a) Salmonella species;
- (b) bacteria belonging to the Mycobacterium tuberculosis complex; and
- (c) Pneumocystis jirovecii and fungi belonging to the species Aspergillus, Candida or Coccidioides.

Note 2: Subacute thyroiditis is also known as de Quervain thyroiditis, granulomatous thyroiditis, giant cell thyroiditis or non-suppurative thyroiditis.

struma ovarii means an ovarian neoplasm defined by the presence of thyroid tissue comprising more than half of the overall mass, that usually occurs as part of a teratoma, but may also occur with a serous or mucinous cystadenoma.

terminal event means the proximate or ultimate cause of death and includes the following:

- (a) pneumonia;
- (b) respiratory failure;
- (c) cardiac arrest;
- (d) circulatory failure; or
- (e) cessation of brain function.

thyrotoxic crisis means a constellation of severe and life-threatening symptoms of rapid onset in a patient with biochemical evidence of elevated thyroid hormones. Characteristic symptoms and signs are fever, marked tachycardia, heart failure, tremor, nausea and vomiting, diarrhoea, dehydration, restlessness, extreme agitation, delirium and coma.

Note 1: Thyrotoxic crisis is also known as thyroid storm.

Note 2: Thyrotoxic crisis may be the first presentation of undiagnosed hyperthyroidism or thyrotoxicosis, or may complicate existing hyperthyroidism or thyrotoxicosis.

thyrotoxicosis—see subsection 7(3).

trauma involving the thyroid gland means:

- (a) a blunt injury or burn injury resulting in soft tissue damage adjacent to or overlying the thyroid gland; or
- (b) a penetrating injury, including surgery, to the region of the thyroid gland; or
- (c) direct trauma to the thyroid gland.

VEA means the Veterans' Entitlements Act 1986.