



Australian Government
Repatriation Medical Authority

Statement of Principles
concerning
CUSHING SYNDROME
(Balance of Probabilities)
(No. 44 of 2018)

The Repatriation Medical Authority determines the following Statement of Principles under subsection 196B(3) of the *Veterans' Entitlements Act 1986*.

Dated 27 April 2018

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

A handwritten signature in black ink, appearing to read 'Nicholas Saunders'.

Professor Nicholas Saunders AO
Chairperson

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1 Name

This is the Statement of Principles concerning *Cushing syndrome (Balance of Probabilities)* (No. 44 of 2018).

2 Commencement

This instrument commences on 28 May 2018.

3 Authority

This instrument is made under subsection 196B(3) of the *Veterans' Entitlements Act 1986*.

4 Revocation

The Statement of Principles concerning Cushing's syndrome No. 34 of 2009 made under subsection 196B(3) of the VEA is revoked.

5 Application

This instrument applies to a claim to which section 120B of the VEA or section 339 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 Cushing syndrome and death from Cushing syndrome.

Meaning of Cushing syndrome

- (2) For the purposes of this Statement of Principles, Cushing syndrome means an endocrine disorder resulting from an excess of endogenous or exogenous glucocorticoids.

Note: Features of Cushing syndrome may include proximal muscle weakness, facial plethora, wasting of the extremities with increased fat in the abdomen (centripetal fat) and face ("moon facies"), wide (> 1 cm) purplish striae, bruising with no obvious trauma, supraclavicular fat pads and dorsocervical fat pad ("buffalo hump").

- (3) While Cushing syndrome attracts ICD-10-AM code E24.0, E24.2, E24.3, E24.8 or E24.9, in applying this Statement of Principles the meaning of Cushing syndrome is that given in subsection (2).
- (4) For subsection (3), a reference to an ICD-10-AM code is a reference to the code assigned to a particular kind of injury or disease in *The International Statistical Classification of Diseases and Related Health*

Problems, Tenth Revision, Australian Modification (ICD-10-AM), Tenth Edition, effective date of 1 July 2017, copyrighted by the Independent Hospital Pricing Authority, ISBN 978-1-76007-296-4.

Death from Cushing syndrome

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

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

8 Basis for determining the factors

On the sound medical-scientific evidence available, the Repatriation Medical Authority is of the view that it is more probable than not that Cushing syndrome and death from Cushing syndrome can be related to relevant service rendered by veterans 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 exist before it can be said that, on the balance of probabilities, Cushing syndrome or death from Cushing syndrome is connected with the circumstances of a person's relevant service:

- (1) having a specified condition at the time of the clinical onset of Cushing syndrome;

Note: *specified condition* is defined in the Schedule 1 - Dictionary.

- (2) having glucocorticoid therapy as specified before the clinical onset of Cushing syndrome, and where the glucocorticoid therapy as specified has ceased or decreased, the last dose of the therapy was received within the 30 days before the clinical onset of Cushing syndrome;

Note: *glucocorticoid therapy as specified* is defined in the Schedule 1 - Dictionary.

- (3) being treated with medroxyprogesterone acetate or megestrol acetate for a malignant disease or human immunodeficiency virus infection:

- (a) for at least four weeks before the clinical onset of Cushing syndrome; and
(b) where treatment has ceased, the clinical onset of Cushing syndrome has occurred within 30 days of cessation;

- (4) inability to obtain appropriate clinical management for Cushing syndrome.

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 factor set out in subsection 9(4) applies only to material contribution to, or aggravation of, Cushing syndrome where the person's Cushing syndrome 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(3) 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:

adrenal neoplasm means a primary neoplasm, either benign (adenoma) or malignant (carcinoma), arising from the adrenal gland.

Cushing syndrome—see subsection 7(2).

equivalent glucocorticoid therapy means a glucocorticoid in the following table, at the doses specified in the table, or a therapeutically equivalent dose of another glucocorticoid:

Glucocorticoid	Minimum cumulative dose (milligram)	Minimum average rate (milligram/day)
betamethasone	45	1.5
cortisone	1 875	62.5
dexamethasone	55	1.8
methylprednisolone	300	10
paramethasone	150	5
prednisolone	375	12.5
prednisone	375	12.5
triamcinolone	300	10

equivalent inhaled glucocorticoid means:

- (a) 2 000 micrograms of beclometasone;
- (b) 1 600 micrograms of ciclesonide;
- (c) 2 500 micrograms of fluticasone propionate;
- (d) 1 000 micrograms of fluticasone furoate;
- (e) 10 000 micrograms of triamcinolone; or
- (f) a therapeutically equivalent dose of another inhaled glucocorticoid.

glucocorticoid therapy as specified means:

- (a) applying a high or very high potency topical glucocorticoid to at least 30% of total skin surface area, daily, for at least six months; or
- (b) inhaling at least 4 000 micrograms of budesonide, or equivalent inhaled glucocorticoid, daily, for at least six months; or
- (c) taking:
 - (i) hydrocortisone, orally or by injection:
 - (A) to a cumulative dose of at least 1 500 milligrams; and
 - (B) at a minimum dose rate averaging 50 milligrams per day, or
 - (ii) equivalent glucocorticoid therapy, orally or by injection; or
- (d) using a glucocorticoid concurrently with a drug, daily, for at least 4 weeks, where that drug can inhibit the activity of the metabolising enzyme cytochrome P450 3A4 by at least 30% (moderate to strong inhibition); or

- (e) using a glucocorticoid concurrently with a drug from the specified list of drugs, daily, for at least four weeks; or
- (f) using a clobetasol containing oral preparation, daily, for at least four weeks; or
- (g) using glucocorticoid containing enemas, daily, for at least six months.

Note: *equivalent glucocorticoid therapy*, *equivalent inhaled glucocorticoid*, *high or very high potency topical glucocorticoid* and *specified list of drugs* are also defined in the Schedule 1 – Dictionary.

high or very high potency topical glucocorticoid means:

- (a) betamethasone dipropionate 0.05%;
- (b) betamethasone valerate 0.1%;
- (c) clobetasol proprionate 0.05%;
- (d) diflucortolone valerate 0.1%;
- (e) fluocinolone acetonide 0.025%;
- (f) methylprednisolone 0.1%;
- (g) mometasone 0.1%;
- (h) triamcinolone acetonide 0.5%; or
- (i) another topical glucocorticoid of equivalent potency.

MRCA means the *Military Rehabilitation and Compensation Act 2004*.

neuroendocrine neoplasm means a non-pituitary neoplasm that secretes polypeptides functionally equivalent to adrenocorticotrophic hormone (ACTH) or corticotropin-releasing hormone (CRH), and includes oat cell or small cell lung carcinoma, carcinoid tumour, islet cell tumour, tumours of the thymus, medullary carcinoma of the thyroid, and pheochromocytoma.

relevant service means:

- (a) eligible war service (other than operational service) under the VEA;
- (b) defence service (other than hazardous service and British nuclear test defence service) under the VEA; or
- (c) peacetime service under the MRCA.

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

specified condition means one of the following:

- (a) adrenal neoplasm;
- (b) adrenocorticotrophic hormone (ACTH) secreting neoplasm of the pituitary gland;
- (c) macronodular adrenal hyperplasia;
- (d) micronodular adrenal hyperplasia; or
- (e) neuroendocrine neoplasm.

Note: ***adrenal neoplasm*** and ***neuroendocrine neoplasm*** are also defined in the Schedule 1 - Dictionary.

specified list of drugs means:

- (a) amprenavir;
- (b) atazanavir;
- (c) boceprevir;
- (d) clarithromycin;
- (e) darunavir;

- (f) delavirdine;
- (g) erythromycin;
- (h) fosamprenavir;
- (i) indinavir;
- (j) isoniazid;
- (k) itraconazole;
- (l) ketoconazole;
- (m) lopinavir;
- (n) nelfinavir;
- (o) posaconazole;
- (p) ritonavir;
- (q) saquinavir;
- (r) telaprevir;
- (s) telithromycin;
- (t) tipranavir; or
- (u) voriconazole.

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.

VEA means the *Veterans' Entitlements Act 1986*.