29.37 - Hormones, prostaglandins, thromboxanes and leukotrienes, natural or reproduced by synthesis; derivatives and structural analogues thereof, including chain modified polypeptides, used primarily as hormones.

- Polypeptide hormones, protein hormones and glycoprotein hormones, their derivatives and structural analogues :

2937.11 - - Somatotropin, its derivatives and structural analogues

2937.12 - - Insulin and its salts

2937.19 - - Other

- Steroidal hormones, their derivatives and structural analogues :

2937.21 - - Cortisone, hydrocortisone, prednisone (dehydrocortisone) and prednisolone (dehydrohydrocortisone)

2937.22 - - Halogenated derivatives of corticosteroidal hormones

2937.23 - - Oestrogens and progestogens

2937.29 - - Other

2937.50 - Prostaglandins, thromboxanes and leukotrienes, their derivatives and structural analogues

2937.90 - Other

This heading includes :

(I) **Natural hormones,** which are active substances produced in the living tissues of man or animals, extremely small amounts of which are capable of inhibiting or stimulating the functioning of particular organs by acting directly on them or controlling the synthesis or secretion of secondary or tertiary hormone systems. A fundamental defining characteristic of a hormone is that it binds to a stereospecific molecular receptor to activate a response**.** The secretion of these substances, usually by the endocrine glands, is governed by the sympathetic and para-sympathetic systems. Hormones are carried by the blood, lymph or other fluids of the body. They may also originate in glands which are both endo- and exocrinal or in various cellular tissues. Transport in the blood is not a requisite for a hormonal response. Responses can occur after release of hormones into the interstitial fluid with binding to receptors in nearby cells (paracrine control) or to receptors on the cell that released the hormone (autocrine control).

(II) **Natural prostaglandins, thromboxanes and leukotrienes**, compounds which are secreted by the body and behave like locally-acting hormones. Prostaglandins are a class of hormones or hormone-like substances which are synthesised by the tissue in which they act (or act in the local cellular environment) by binding to specific cellular receptors and act as important modulators of cell activity in many tissues. These three related chemical families (arachidonic acid derivatives) are said to have “hormone-like action”.

(III) **Natural hormones, prostaglandins, thromboxanes and leukotrienes reproduced by synthesis (including biotechnological processes)**, that is, having the same chemical structure as the natural substance.

(IV) **Derivatives of natural or synthetically reproduced hormones, prostaglandins, thromboxanes and leukotrienes**, such as salts, halogenated derivatives, cyclic acetals, esters, etc., including mixed **derivatives** (e.g., esters of halogenated derivatives), **provided that** they are used primarily as hormones.

(V) **Analogues of hormones, prostaglandins, thromboxanes and leukotrienes**. The term "analogue" refers to chemicals having a close structural relationship to the parent compound, but which are not considered to be derivatives. It includes compounds which have a structural resemblance to the natural compounds, but have had one or more atoms in the structure replaced by others.

(a) Analogues of polypeptide hormones are formed by adding, separating, replacing or altering certain amino acids in the natural polypeptide chain. **Somatrem** (INN)**,** an analogue of the growth hormone somatotropin, is the result of adding a terminal amino acid to the natural somatotropin molecule. **Ornipressin** (INN), an analogue of natural argipressin (INN) and lypressin (INN), is the result of replacing an internal amino acid in the argipressin or lypressin molecule. The synthetic gonadoliberins, **buserelin** (INN), **nafarelin** (INN), **fertirelin** (INN), **leuprorelin** (INN) and **lutrelin** (INN), analogues of **gonadorelin** (INN) are the result of altering and replacing certain amino acids in the polypeptide chain of natural gonadorelin**. Giractide** (INN), an analogue of **corticotropin** (INN) has the same structure as the first 18 amino acids of natural corticotropin, with the first amino acid replaced. **Metreleptin** (INN), an analogue of leptin, is the recombinant methionyl derivative of human leptin. **Saralasin** (INN), which contains three different amino acids in comparison to the molecule of angiotensin II, should be considered as a structural analogue of angiotensin II, although with antagonist effects (the former is a hypotensor and the latter an hypertensor).

(b) Analogues of steroid hormones must have the gonane structure, which can be altered by ring contraction or extension or by replacing some atoms in the ring by others (hetero-atoms). **Domoprednate** (INN) and **oxandrolone** (INN) represent two examples of this kind of analogues. The family of analogues and derivatives, which retain the fundamental structure of the gonane described, contains a large number of substances used as hormone inhibitors and antagonists (antihormones). Examples are **cyproterone** (INN), an antiandrogen, **danazol** (INN), an antigonadotropin, **epostane** (INN), which inhibits progesterone production.

(c) Analogues of prostaglandins, thromboxanes and leukotrienes may be formed by substitution of atoms in a chain, or formation or elimination of rings. In **tilsuprost** (INN), a prostaglandin analogue, oxygen and carbon atoms are replaced by nitrogen and sulphur atoms and one ring is closed.

(VI) **Natural mixtures of hormones** or their derivatives or of steroids recognised as having a hormonal effect (e.g., a natural mixture of corticosteroid hormones or of conjugated oestrogens). Deliberate mixtures or preparations are excluded (generally **heading 30.03** or **30.04**).

Hormone-releasing factors (hormone-stimulating factors), hormone inhibitors and hormone antagonists (antihormones) are also included in this heading (see Note 8 to this Chapter). The heading also includes derivatives and structural analogues of hormones, provided that they are based on natural hormones, or on those reproduced by synthesis, and that they act using mechanisms similar to those of hormones.

A list of the products of this heading, arranged according to chemical structure, is given below. This list is not exhaustive.

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List of products which are to be classified as products of heading 29.37 (*)

(A) POLYPEPTIDE HORMONES, PROTEIN HORMONES AND GLYCOPROTEIN HORMONES, THEIR DERIVATIVES AND STRUCTURAL ANALOGUES

This part includes, *inter alia* :

(1) **Somatotropin, its derivatives and structural analogues**. **Somatotropin** (growth hormone, GH, STH (somatotropic hormone)). Water soluble protein which promotes growth of tissues and is involved in the regulation of other phases of protein metabolism. It is secreted by the somatotropic cells of the anterior pituitary gland. Secretion is regulated by a releasing factor (growth hormone-releasing hormone) and by an inhibitory factor, somatostatin. Human growth hormone (hGH) is a single polypeptide chain of 191 amino acids manufactured almost exclusively by recombinant DNA technology. This part also includes derivatives and analogues such as **somatrem** (INN) (methionyl hGH), **acetylated hGH**, **desamido hGH** and **somenopor** (INN) and antagonists such as **pegvisomant** (INN).

(2) **Insulin and its salts.** Insulin is a polypeptide containing 51 amino-acid groups and is produced in the islets of Langerhans of the pancreas of numerous animals. Human insulin can be obtained by extraction from the pancreas, by modification of bovine or porcine insulin or by biotechnological processes involving bacteria or yeasts to produce recombinant human insulin. Insulin is a factor in the cellular uptake of circulating glucose and other nutrients, as well as their storage as glycogen and fat. Pure insulin is a white, non-hygroscopic amorphous powder or shiny crystals, soluble in water. Its clinical use is in the treatment of diabetes. Insulin salts include insulin hydrochloride.

(3) **Corticotropin** (INN) (ACTH (adrenocorticotropic hormone), adrenocorticotropin). A polypeptide, soluble in water. It stimulates increased production of adrenocortical steroids. **Giractide** (INN) is an analogue of corticotropin.

(4) **Lactogenic hormone** (LTH, galactin, galactogene hormone, luteotrophin, mammotrophin, prolactin). A polypeptide which can be crystallised. Activates milk secretion and influences the activity of the *corpus luteum*.

(*) If a name is used in the International Nonproprietary Names or the International Nonproprietary Names (Modified) for pharmaceutical substances published by the World Health Organization, this name is mentioned first and marked (INN) or (INNM), respectively.

(5) **Thyrotrophin** (INN) (thyrotrophic hormone, TSH (thyroid-stimulating hormone)). A glycoprotein which intervenes in the action of the thyroid gland on the blood and in the removal of iodine. It affects growth and secretion.

(6) **Follicle-stimulating hormone** (FSH). A glycoprotein, soluble in water. It activates sexual functions.

(7) **Luteinising hormone** (LH, ICSH (interstitial-cell-stimulating hormone), luteinostimulin). A glycoprotein, soluble in water. It stimulates sexual functions by stimulating steroid secretion, ovulation and interstitial cell development.

(8) **Chorionic gonadotrophin** (INN) (hCG (human chorionic gonadotrophin)). Formed in the placenta; it is a glycoprotein extracted from the urine of pregnant women. White crystals, relatively unstable in aqueous solution. Stimulates follicle maturity.

(9) **Serum gonadotrophin** (INN) (equine chorionic gonadotropin (eCG)). It is a gonad-stimulating glycoprotein produced in the placenta and endometrium of pregnant mares. Originally called pregnant mare serum gonadotropin.

(10) **Oxytocin** (INN) (α-hypophamin). A polypeptide, soluble in water. Its chief action is on the contraction of the uterus and on milk ejection from the mammary gland. Also included are the analogues **carbetocin** (INN), **demoxytocin** (INN), etc.

(11) **Vasopressins** : **argipressin** (INN) and **lypressin** (INN), their derivatives and structural analogues. Vasopressins are polypeptides which raise blood pressure and cause an increase in water retention by the kidney. Also included here are polypeptide analogues such as **terlipressin** (INN), **desmopressin** (INN), etc.

(12) **Calcitonin** (INN). (TCA (thyrocalcitonin)). A hypocalcaemic and hypophosphatemic polypeptide.

(13) **Glucagon** (INN) (HGF (hyperglycaemic-glycogenolytic factor)). A polypeptide which has the property of increasing the blood-glucose concentration.

(14) **Thyroliberin** (TRF, TRH). This polypeptide stimulates the secretion of thyrotropin.

(15) **Gonadorelin** (INN) (gonadoliberin, gonadotrophin releasing hormone, LRF, GnRH). This polypeptide promotes the secretion of follicle-stimulating and lutein-stimulating hormones in the pituitary gland. Also included are the polypeptide analogues **buserilin** (INN), **goserilin** (INN), **fertirelin** (INN), **sermorelin** (INN), etc.

(16) **Somatostatin** (INN) (SS, SRIH, SRIF). This polypeptide inhibits the release of growth hormone and TSH from the pituitary gland and has a neurotropic action.

(17) **Atrial natriuretic hormone** (ANH, ANF), a polypeptide hormone secreted from the atria of the heart. When the cardiac atrium is stretched by increased blood volume, secretion of ANH is stimulated. ANH in turn increases salt and water excretion and reduces blood pressure.

(18) **Endothelin**, a polypeptide hormone secreted by endothelial cells throughout the vasculature. Although endothelin is released into the blood circulation, it acts locally in a paracrine fashion to constrict adjacent vascular smooth muscle and to increase blood pressure.

(19) **Inhibin** and **activin,** hormones found in gonadal tissue.

(20) **Leptin**, a polypeptide hormone produced by adipose tissue that is thought to act on receptors in the brain to regulate body weight and fat deposition. Also included here is **metreleptin** (INN), the recombinant methionyl derivative of leptin, which has a similar activity and which is considered to be an analogue of leptin.

(B) STEROIDAL HORMONES, THEIR DERIVATIVES AND STRUCTURAL ANALOGUES

(1) **Corticosteroid hormones**, secreted in the cortical zone of the adrenal glands, play an important role in the functioning of the body's metabolism. They are also known as adrenal cortical hormones or corticoids, and are generally divided into two groups, depending upon their physiological action : (i) glucocorticoids, which regulate protein and carbohydrate metabolism and (ii) mineralocorticoids, which cause the retention of sodium and water by the body and hasten the excretion of potassium. The properties of mineralocorticoids are utilised in the treatment of kidney deficiencies and of Addison's disease. These include the following corticosteroid hormones, derivatives and analogues :

(a) **Cortisone** (INN). A glucocorticoid which regulates protein and carbohydrate metabolism and also has a local anti-inflammatory effect.

(b) **Hydrocortisone** (INN) (cortisol). A glucocorticoid with effects similar to those of cortisone.

(c) **Prednisone** (INN) (dehydrocortisone). Glucocorticoid. A derivative of cortisone.

(d) **Prednisolone** (INN) (dehydrohydrocortisone). Glucocorticoid. A derivative of hydrocortisone.

(e) **Aldosterone** (INN). A mineralocorticoid.

(f) **Cortodoxone** (INN).

Some derivatives are modified so as to suppress their cortical hormone effect in favour of their anti-inflammatory effect, which is regarded as being a hormonal effect. These are principally derivatives of cortisone (INN), hydrocortisone (INN), prednisone (INN) and prednisolone (INN), which are used as anti-inflammatory and antirheumatism agents.

(2) **Halogenated derivatives of corticosteroid hormones** are steroids in which the hydrogen atom generally at the 6- or 9-position on the gonane ring is substituted by a chlorine or fluorine atom (e.g., **dexamethasone** (INN)) and which greatly enhance the glucocorticoid and anti-inflammatory effect of the corticoids from which they are derived. These derivatives are often further modified and marketed in the form of esters, acetonides (e.g., **fluocinolone acetonide** (INN)), etc.

(3) **Oestrogens and progestogens**. These are two major groups of sex hormones secreted by the male and female genital organs. They may also be obtained by synthesis. These hormones are also called progestins and gestagens.

Oestrogens are female sex hormones produced by the ovaries, testes, adrenal glands, placenta and other steroid-producing tissues. They are characterised by their ability to produce oestrus in the female mammal. Oestrogens are responsible for the development of female sex characteristics and are used in the treatment of menopause or in the preparation of contraceptive drugs. They include the following oestrogens, derivatives and analogues :

(a) **Estrone** (INN). A principal oestrogen in humans.

(b) **Estradiol** (INN). An important natural oestrogen.

(c) **Estriol** (INN). A natural oestrogen.

(d) **Ethinyl estradiol** (INN). An important synthetic oestrogen which is orally active and used as a main oestrogenic component in combination oral contraceptives.

(e) **Mestranol** (INN). Ether derivative of ethinyl estradiol. Used as an oral contraceptive.

Progestogens are a class of steroids named for their progestational effects, which are essential for the initiation and continuation of pregnancy. These female sex hormones prepare the uterus for pregnancy and for the maintenance of pregnancy. Because they suppress ovulation, many progestins are used as components of contraceptive drugs. They include :

(a) **Progesterone** (INN). The primary progestin in humans and an intermediate in the biosynthetic pathways of oestrogens, androgens and corticosteroids. It is produced by the *corpus luteum* after release of the ovum and in the adrenal gland, the placenta and the testes.

(b) **Pregnandiol**. Naturally occurring progestin with a much weaker biological activity than that of progesterone.

(4) **Other steroidal hormones**.

Androgens are a major group of sex hormones not included above, which are produced mainly by the testes and, to a lesser extent, by the ovaries, adrenal glands and placenta. Androgens are responsible for the development of male sex characteristics. Androgens influence metabolism, i.e., have an anabolic effect. **Testosterone** (INN) is one of the most important androgens.

This part also includes synthetic steroids used to inhibit or counteract the effects of hormones, such as anti-oestrogens, anti-androgens, and anti-progestogens (antiprogestins, antiestagens). Steroidal antiprogestins are progestin antagonists which have found many uses in the treatment of some diseases. Examples of this group include **onapristone** (INN) and **aglepristone** (INN).

The most important of these steroids in international trade are listed below. The products are cited in alphabetical order, according to their short names, followed by an indication of their main hormonal function. If several names exist, the name used is that of the International Nonproprietary Names for pharmaceutical preparations (INN) published by the World Health Organization or that of the International Nonproprietary Names Modified (INNM). The **chemical names** given are in accordance with the IUPAC 1957 Rules for Nomenclature of Steroids.

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List of steroids used primarily for their hormone function

Short name Chemical name	Main hormonal function
Adrenosterone androst-4-ene-3,11,17-trione	Androgen
Aldosterone (INN) 11β,21-dihydroxy-3,20-dioxopregn-4-en-18-al	Corticosteroid
Allylestrenol (INN) 17α-allyloestr-4-en-17β-ol	Progestogen
(No short name) 5α-androstane-3,17-dione	Androgen intermediate
Androstanolone (INN) 17β-hydroxy-5α-androstan-3-one	Androgen
Androstenediols androst-5-ene-3β,17β-diol androst-5-ene-3β,17α-diol	Anabolic intermediate
(No short name) androst-4-ene-3,17-dione	Androgen intermediate
Androsterone 3α-hydroxy-5α-androstan-17-one	Androgen
Betamethasone (INN) 9α-fluoro-11β,17α,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione	Corticosteroid
Bolasterone (INN) 17β-hydroxy-7α,17α-dimethylandrost-4-en-3-one	Anabolic
Chlormadinone (INN) 6-chloro-17α-hydroxypregna-4,6-diene-3,20-dione	Progestogen

Short name Chemical name	Main hormonal function
Chloroprednisone (INN) 6α-chloro-17α,21-dihydroxypregna-1,4-diene-3,11,20-trione	Corticosteroid
Clocortolone (INN) 9α-chloro-6α-fluoro-11β,21-dihydroxy-16α-methylpregna-1,4-diene-3,20-dione	Corticosteroid
Clostebol (INN) 4-chloro-17β-hydroxyandrost-4-en-3-one	Anabolic
Corticosterone 11β,21-dihydroxypregn-4-ene-3,20-dione	Corticosteroid
Cortisol - see **Hydrocortisone**	
Cortisone (INN) 17α,21-dihydroxypregn-4-ene-3,11,20-trione	Corticosteroid
11-Dehydrocorticosterone 21-hydroxypregn-4-ene-3,11,20-trione	Corticosteroid
Deoxycorticosterone - see **Desoxycortone**	
Desoxycortone (INN) 21-hydroxypregn-4-ene-3,20-dione	Corticosteroid
Dexamethasone (INN) 9α-fluoro-11β,17α,21-trihydroxy-16α-methylpregna-1,4-diene-3,20-dione	Corticosteroid
Dihydroandrosterone 5α-androstane-3α,17β-diol	Androgen intermediate
Dydrogesterone (INN) 9β,10α-pregna-4,6-diene-3,20-dione	Progestogen
Equilenin 3-hydroxyoestra-1,3,5(10),6,8-pentaen-17-one	Oestrogen
Equilin 3-hydroxyoestra-1,3,5(10),7-tetraen-17-one	Oestrogen

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Short name Chemical name	Main hormonal function
Estradiol (INN) oestra-1,3,5(10)-triene-3,17β-diol	Oestrogen
Estriol (INNM) oestra-1,3,5(10)-triene-3,16α,17β-triol	Oestrogen
Estrone (INN) 3-hydroxyoestra-1,3,5(10)-trien-17-one	Oestrogen
Ethinylestradiol (INN) 17α-ethynyloestra-1,3,5(10)-triene-3,17β-diol	Oestrogen
Ethisterone (INN) 17α-ethynyl-17β-hydroxyandrost-4-en-3-one	Progestogen
Ethylestrenol (INN) 17α-ethyloestr-4-en-17β-ol	Anabolic
Etynodiol (INN) 17α-ethynyloestr-4-ene-3β,17β-diol	Progestogen
Fludrocortisone (INN) 9α-fluoro-11β,17α,21-trihydroxypregn-4-ene-3,20-dione	Corticosteroid
Flumetasone (INN) 6α,9α-difluoro-11β,17α,21-trihydroxy-16α-methylpregna-1,4-diene- 3,20-dione	Corticosteroid
Fluocinolone (INNM) 6α,9α-difluoro-11β,16α,17α,21-tetrahydroxy-pregna-1,4-diene-3,20-dione	Corticosteroid
Fluocortolone (INN) 6α-fluoro-11β,21-dihydroxy-16α-methylpregna-1,4-diene-3,20-dione	Corticosteroid
Fluorometholone (INN) 9α-fluoro-11β,17α-dihydroxy-6α-methylpregna-1,4-diene-3,20-dione	Corticosteroid
9α-**Fluoroprednisolone** 9α-fluoro-11β,17α,21-trihydroxypregna-1,4-diene-3,20-dione	Corticosteroid

Short name Chemical name	Main hormonal function
Fluoxymesterone (INN) 9α-fluoro-11β,17β-dihydroxy-17α-methylandrost-4-en-3-one	Androgen
Fluprednidene (INN) 9α-fluoro-11β,17α,21-trihydroxy-16-methylenepregna-1,4-diene-3,20-dione	Corticosteroid
Fluprednisolone (INN) 6α-fluoro-11β,17α,21-trihydroxypregna-1,4-diene-3,20-dione	Corticosteroid
Flurandrenolone 6α-fluoro-11β,16α,17α,21-tetrahydroxypregn-4-ene-3,20-dione	Corticosteroid
Formocortal (INN) 3-(2-chloroethoxy)-9α-fluoro-6-formyl-11β,21-dihydroxy-16α,17-isopropylidenedioxypregna-3,5-dien-20 one 21-acetate	Corticosteroid
Gestonorone (INNM) 17β-ethyl-17α-hydroxyoestr-4-ene-3,20-dione	Progestogen
Hydrocortisone (INN) 11β,17α,21-trihydroxypregn-4-ene-3,20-dione	Corticosteroid
Hydroxyprogesterone (INN) 17α-hydroxypregn-4-ene-3,20-dione	Progestogen
Lynestrenol (INN) 17α-ethynyloestr-4-en-17β-ol	Progestogen
Medroxyprogesterone (INN) 17α-hydroxy-6α-methylpregn-4-ene-3,20-dione	Progestogen
Megestrol (INN) 17α-hydroxy-6-methylpregna-4,6-diene-3,20-dione	Progestogen
Mestanolone (INN) 17β-hydroxy-17α-methyl-5α-androstan-3-one	Anabolic
Mesterolone (INN) 17β-hydroxy-1α-methyl-5α-androstan-3-one	Androgen

Short name Chemical name	Main hormonal function
Mestranol (INN) 17α-ethynyl-3-methoxyoestra-1,3,5(10)-trien-17β-ol	Oestrogen
Metandienone (INN) 17β-hydroxy-17α-methylandrosta-1,4-dien-3-one	Anabolic
Metenolone (INN) 17β-hydroxy-1-methyl-5α-androst-1-en-3-one	Anabolic
Methandriol (INN) 17α-methylandrost-5-ene-3β,17β-diol	Anabolic
2-**Methylhydrocortisone** 11β,17α,21-trihydroxy-2β-methylpregn-4-ene-3,20-dione	Corticosteroid
6α-**Methylhydrocortisone** 11β,17α,21-trihydroxy-6α-methylpregn-4-ene-3,20-dione	Corticosteroid
Methylnortestosterone 17β-hydroxy-17α-methyloestr-4-en-3-one	Progestogen
17α-Methyloestradiol 17α-methyloestra-1,3,5(10)-triene-3,17β-diol	Oestrogen
Methylprednisolone (INN) 11β,17α,21-trihydroxy-6α-methylpregna-1,4-diene-3,20-dione	Corticosteroid
Methyltestosterone (INN) 17β-hydroxy-17α-methylandrost-4-en-3-one	Androgen
Nandrolone (INN) 17β-hydroxyoestr-4-en-3-one	Anabolic
Norethandrolone (INN) 17α-ethyl-17β-hydroxyoestr-4-en-3-one	Anabolic
Norethisterone (INN) 17α-ethynyl-17β-hydroxyoestr-4-en-3-one	Progestogen
Noretynodrel (INN) 17α-ethynyl-17β-hydroxyoestr-5(10)-en-3-one	Progestogen

Short name Chemical name	Main hormonal function
Norgestrel (INN) 13β-ethyl-17α-ethynyl-17β-hydroxygon-4-en-3-one	Progestogen
Normethandrone - see **Methylnortestosterone**	
Nortestosterone - see **Nandrolone**	
Oxabolone (INNM) 4,17β-dihydroxyoestr-4-en-3-one	Anabolic
Oxymesterone (INN) 4,17β-dihydroxy-17α-methylandrost-4-en-3-one	Anabolic
Oxymetholone (INN) 17β-hydroxy-2-hydroxymethylene-17α-methyl-5α-androstan-3-one	Anabolic
Paramethasone (INN) 6α-fluoro-11β,17α,21-trihydroxy-16α-methylpregna-1,4-diene-3,20-dione	Corticosteroid
Prasterone (INN) 3β-hydroxyandrost-5-en-17-one	Androgen
Prednisolone (INN) 11β,17α,21-trihydroxypregna-1,4-diene-3,20-dione	Corticosteroid
Prednisone (INN) 17α,21-dihydroxypregna-1,4-diene-3,11,20-trione	Corticosteroid
Prednylidene (INN) 11β,17α,21-trihydroxy-16-methylenepregna-1,4-diene-3,20-dione	Corticosteroid
Pregnenolone (INN) 3β-hydroxypregn-5-en-20-one	Corticosteroid
Progesterone (INN) pregn-4-ene-3,20-dione	Progestogen
Stanolone - see **Androstanolone**	

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Short name Chemical name	Main hormonal function
Testosterone (INN) 17β-hydroxyandrost-4-en-3-one	Androgen
Tiomesterone (INN) 1α,7α-di(acetylthio)-17β-hydroxy-17α-methylandrost-4-en-3-one	Anabolic
Triamcinolone (INN) 9α-fluoro-11β,16α,17α,21-tetrahydroxypregna-1,4-diene-3,20-dione	Corticosteroid

(C) PROSTAGLANDINS, THROMBOXANES AND LEUKOTRIENES, THEIR DERIVATIVES AND STRUCTURAL ANALOGUES

These products are derivatives of arachidonic acid.

(1) **Prostaglandins**.

The most important arachidonic acid derivatives are prostaglandins, endogenous substances operating in minute doses as hormones and containing the fundamental structure of prostanoic acid. Prostaglandins influence the regulation of blood circulation, kidney function and the endrocrine system (e.g., by reducing the production of progesterone by the *corpus luteum*); they also stimulate the contraction of smooth muscles or dilation of blood vessels, prevent platelet aggregation and regulate gastric secretions. These include the following prostaglandins, derivatives and analogues :

(a) **Alprostadil** (INN) (prostaglandin E_1). A primary prostaglandin crystallised from biological extracts. It is used as a vasodilator. It also functions to stimulate the release of erythropoietin from the renal cortex and inhibits blood platelet aggregation.

(b) **Alfaprostol** (INN). A synthetic prostaglandin analogue used in the treatment of infertility in mares.

(c) **Tilsuprost** (INN). A prostaglandin analogue which has had an oxygen and a carbon atom replaced by a nitrogen and a sulphur atom with ring closure.

This group also includes other synthetic products such as **prostalene** (INN), **dinoprost** (INN), etc., which retain the basic structure of natural products and have similar physiological activity.

(2) **Thromboxanes and leukotrienes**.

Thromboxanes and leukotrienes, like prostaglandins, are synthesised in cells from arachidonic acid; although their function is comparable to that of prostaglandins and their structure is very similar, they do not contain the fundamental structure of prostanoic acid. Thromboxanes are biosynthetically derived from prostaglandins. They cause platelet aggregation and contraction of arteries, and are important regulators of the actions of polyunsaturated fatty acids. Leukotrienes received their name because of their origin in leukocytes and their conjugated triene structure. They are potent bronchoconstrictors and play an important role in hypersensitivity reactions.

(a) **Thromboxane B_2**. A vasoconstrictor, a bronchoconstrictor and an inducer of blood platelet aggregation.

(b) **Leukotriene C_4**. Found to be 100 to 1,000 times more potent than histamine or prostaglandins in their effects on pulmonary air passages.

(D) OTHER HORMONES

Classified here are other hormones whose structure differs from that of the hormones referred to above. An example is **melatonin**, which is found in the pineal gland and can be considered to be a derivative of indol. Other hormones classified here are the following :

(1) **Catecholamine hormones, their derivatives and structural analogues.**

This group of hormones includes those found in the medullar zone of the adrenal glands.

(a) **Epinephrine** (INN) (adrenaline or (-)-3,4-dihydroxy-α-[(methylamino)methyl]benzyl alcohol) and **racepinephrine** (INN) ((±)-3,4-dihydroxy-α-[(methylamino)methyl]benzyl alcohol). The structure of both of these hormones corresponds to the chemical name 1-(3,4-dihydroxyphenyl)-2-methylaminoethanol. Epinephrine is a light brown or nearly white crystalline powder, affected by light; it is slightly soluble in water and organic solvents. It may be derived from the adrenal glands of horses, but is obtained mostly by synthesis. A hypertension hormone, it stimulates the sympathetic nervous system, increases the number of corpuscles and the sugar content in blood; it also has a strong vasoconstrictive action.

(b) **Norepinephrine** (INN) (levarterenol, noradrenaline or (-)-2-amino-1-(3,4-dihydroxyphenyl)ethanol). Norepinephrine occurs as white crystals, soluble in water. Its physiological activity is intermediate between that of adrenaline and of ephedrine.

(2) **Amino-Acid Derivatives.**

(a) **Levothyroxine** (INNM) and **DL-thyroxine** (3-[4-(4-hydroxy-3,5-diiodophenoxy)-3,5-diiodophenyl]alanine or 3,5,3',5'-tetraiodothyronine). Thyroxine is extracted from the thyroid gland or obtained by synthesis. It is an aromatic amino acid; it occurs as white or yellowish crystals, insoluble in water or in any of the common solvents. It increases the basic metabolic rate and oxygen consumption, acts on the sympathetic system, controls the action of proteins and fats and makes up any iodine deficiency in the organism; used to treat goitre and cretinism. The L-ısomer is the active form. The sodium salt is a white powder, slightly soluble in water, with similar activity.

(b) **Liothyronine** (INN) and **rathyronine** (INN) (DL-3,5,3'-triiodothyronine) (3-[4-(4-hydroxy-3-iodophenoxy)-3,5-diiodophenyl]alanine). Triiodothyronine is also extracted from the thyroid gland; its physiological activity is greater than that of thyroxine.

EXCLUSIONS

The heading **excludes** :

(1) Products not having a hormonal effect, but having a hormone-like structure :

(a) Androst-5-ene-3α,17α-diol, androst-5-ene-3α,17β-diol (**heading 29.06**) and their diacetates (**heading 29.15**).

(b) Adrenalone (INN) (3',4'-dihydroxy-2-methylaminoacetophenone) (**heading 29.22**).

(c) The following products which are classified in **heading 29.22** :

(i) 2-Amino-1-(3,4-dihydroxyphenyl)butan-1-ol.

(ii) Corbadrine (INN) (2-amino-1-(3,4-dihydroxyphenyl)propan-1-ol, 3,4-dihydroxynorephedrine, homoarterenol).

(iii) Deoxyepinephrine (deoxyadrenaline,1-(3,4-dihydroxyphenyl)-2-methylaminoethane, epinin).

(iv) 3',4'-Dihydroxy-2-ethylaminoacetophenone (4-ethylaminoacetylcatechol).

(v) 1-(3,4-Dihydroxyphenyl)-2-methylaminopropan-1-ol (3,4-dihydroxyephedrine).

(vi) (±)-N-Methylepinephrine ((±)-1-(3,4-dihydroxyphenyl)-2-dimethylaminoethanol, methadrene, (±)-N-methyladrenaline).

(2) Products having a hormonal effect, but not having a hormone-like structure :

(a) Dienestrol (INN) (3,4-bis(*p*-hydroxyphenyl)hexa-2,4-diene) (**heading 29.07**).

(b) Hexestrol (INN) (3,4-bis(*p*-hydroxyphenyl)hexane) (**heading 29.07**).

(c) Diethylstilbestrol (INN) (*trans*-3,4-bis(*p*-hydroxyphenyl)hex-3-ene) (**heading 29.07**), its dimethyl ether (**heading 29.09**), its dipropionate (**heading 29.15**) and its furoate (**heading 29.32**).

(d) Clomifene (INN) (anti-oestrogen) (**heading 29.22**).

(e) Tamoxifen (INN) (anti-oestrogen) (**heading 29.22**).

(f) Flutamide (INN) (anti-androgen) (**heading 29.24**).

(g) Endothelin antagonists, such as darusentan (INN) (**heading 29.33**), atrasentan (INN) (**heading 29.34**) and sitaxentan (INN) (**heading 29.35**).

(3) Natural substances with hormonal effects, but which are not secreted in the bodies of humans or animals :

(a) Zearalenone, an anabolic agent (**heading 29.32**).

(b) Asperlicin, a cholecistoquinine antagonist (**heading 29.33**).

(4) The following products sometimes considered to be hormones but which have no real hormone activity :

(a) Cystine, cysteine (INN) and their hydrochlorides (**heading 29.30**).

(b) Methionine and its calcium salts (**heading 29.30**).

(c) Neurotransmitters and neuromodulators, such as dopamine (**heading 29.22**), acetylcholine (**heading 29.23**), serotonin (5-hydroxytryptamine or 5-hydroxy-3-(ß-aminoethyl)indole) (**heading 29.33**), histamine (**heading 29.33**) and related products, such as their receptor agonists and antagonists.

(d) Leukemia-inhibiting factor (human) growth factor emfilermin (INN) (**heading 29.33**) and fibroblast growth factor repifermin (INN) (**heading 29.33**).

(e) NMDA (N-methyl-D-aspartic acid) receptor antagonists, such as lanicemine (INN) (heading 29.33) and nebostinel (INN) (**heading 29.24**).

(f) Heparin (**heading 30.01**).

(g) Modified immunological products (**heading 30.02**).

(5) Plant-growth regulators (e.g., phytohormones), natural or synthetic, which are classified :

(A) When unmixed and not put up for retail sale, according to their chemical composition, for instance :

(a) α-Naphthylacetic acid and its sodium salt (**heading 29.16**).

(b) 2,4-Dichlorophenoxyacetic acid (2,4-D), 2,4,5-T (ISO) (2,4,5-trichlorophenoxyacetic acid) and 4-chloro-2-methyl-phenoxyacetic acid (MCPA) (**heading 29.18**).

(c) β-Indolylacetic acid and its sodium salt (**heading 29.33**).

(B) When put up in forms or packings for retail sale or as preparations or articles, in **heading 38.08**.

(6) Antagonists of thromboxanes and leukotrienes, which are classified according to their structure (e.g., seratrodast (INN) (**heading 29.18**) and montelukast (INN) (**heading 29.33**)).

(7) Antagonists of tumor necrosis factor, such as ataquimast (INN) (**heading 29.33**).

(8) Immunological products of **heading 30.02**.

(9) Medicaments of **heading 30.03** or **30.04**, in particular, " Retard Insulin " (zinc-insulin, protamin-zinc insulin, globin-insulin, zinc-globin insulin, histone-insulin).