Yttrium-90

Itrio 90.

CAS — 10098-91-6.

ATC — V10AA01 (yttrium citrate colloid (^{90}Y)); V10AA02 (yttrium ferrihydroxide colloid (^{90}Y)); V10AA03 (yttrium silicate colloid (^{90}Y)); V10XX02 (ibritumomab tiuxetan (^{90}Y)).

ATC Vet — QV10AA01 (yttrium citrate colloid (^{90}Y)); QV10AA02 (yttrium ferrihydroxide colloid (^{90}Y)); QV10AA03 (yttrium silicate colloid (^{90}Y)); QV10XX02 (ibritumomab tiuxetan (^{90}Y)).

HALF-LIFE. 64.1 hours.

Yttrium-90 conjugated to ibritumomab tiuxetan (p.730) is used in the treatment of non-Hodgkin's lymphoma. Conjugates with various other monoclonal antibodies and compounds are also under investigation for malignant neoplasms.

Yttrium-90, in the form of a colloidal suspension of yttrium silicate (^{90}Y) has been used for instillation into pleural or peritoneal cavities in the treatment of malignant pleural effusion (p.659) or malignant ascites.

Yttrium-90, as either yttrium citrate (^{90}Y) or yttrium silicate (^{90}Y), has also been used in the treatment of arthritic conditions of joints.

Yttrium-90 enclosed in glass microspheres has been used for the local treatment of malignant neoplasms of the liver.

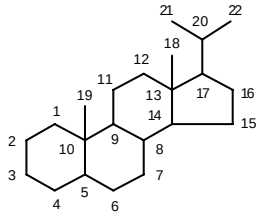
Preparations

USP 31: Yttrium Y 90 Ibritumomab Tiuxetan Injection.

Proprietary Preparations (details are given in Part 3)
Cz.: Ytracis; Yttriga; ***Hung.:*** Ytracis; ***Neth.:*** Theryttrex†; Ytracis; ***Port.:*** Ytracis; ***Spain:*** Ytracis; ***UK:*** Ytracis.

Sex Hormones and their Modulators

The male and female sex organs, the adrenal cortex, and the placenta produce steroidal hormones that influence the development and maintenance of structures directly and indirectly associated with reproduction. The secretion of these sex hormones is controlled by gonadotrophic hormones of the anterior lobe of the pituitary gland (and in pregnancy, from the placenta); the secretion of pituitary gonadotrophic hormones is in turn influenced by the hypothalamus and also by the concentration of circulating sex hormones. There are 3 groups of endogenous sex hormones, androgens, oestrogens, and progestogens, all of which are derived from the same steroidal precursors. The progestogenic hormone, progesterone, is formed from pregnenolone, and both of these compounds may be converted to androgen precursors such as androstenedione. Androstenedione is converted to the androgenic hormone testosterone by hydroxysteroid dehydrogenases. Oestrogenic hormones are synthesised from androstenedione (and also from testosterone) by the action of aromatase.



steroidal skeleton

Testosterone is the main androgenic hormone formed in the interstitial (Leydig) cells of the testes. A small proportion of circulating testosterone is also derived from the metabolism of less potent androgens secreted by the adrenal cortex and ovaries. In many target tissues testosterone is then converted to the more active dihydrotestosterone by 5α-reductase. Some testosterone also undergoes peripheral conversion to oestradiol.

Testosterone controls the development and maintenance of the male sex organs and the male secondary sex characteristics. It also produces systemic anabolic effects, such as increased retention of nitrogen, calcium, sodium, potassium, chloride, and phosphate. This leads to an increase in water retention and bone growth. The skin becomes more vascular and less fatty and erythropoiesis is increased.

Numerous derivatives of testosterone have been developed. Alkylation at the 17α position results in derivatives that are orally active, but associated with a risk of hepatotoxicity (see Table 1, below). Esterification of the 17β-hydroxyl group increases lipid solubility and is used to prepare long-acting intramuscular preparations (e.g. testosterone enantate). Removal of the 19-methyl group is reported to improve the anabolic to androgenic ratio (e.g. nandrolone). The derivatives also vary in their plasma protein binding affinity, and degree of conversion to dihydrotestosterone and aromatic conversion to oestrogen. Numerous other structural modifications have been made.

Oestradiol is the most active of the naturally occurring oestrogens formed from androgen precursors in the ovarian follicles of premenopausal women. In men and postmenopausal women (and to an insignificant extent in premenopausal women) oestrogens are also formed in adipose tissue from adrenal androgens.

Table 1. 17α-Alkylated testosterone derivatives

Danazol	Norethandrolone
Ethylestrenol	Oxandrolone
Fluoxymesterone	Oxymetholone
Methandienone	Stanozolol
Methyltestosterone	

Oestrogens control the development and maintenance of the female sex organs, secondary sex characteristics, and mammary glands as well as certain functions of the uterus and its accessory organs (particularly the proliferation of the endometrium, the development of the decidua, and the cyclic changes in the cervix and vagina). Large amounts of oestradiol are also formed in the placenta; in late pregnancy, this increases the spontaneous activity of the uterine muscle and its response to oxytocic drugs. The additional activity of progesterone is essential for the complete biological function of the female sex organs. Oestrogens also have some direct effects on metabolic processes, including those affecting bone mass, lipids, carbohydrates, and proteins.

A number of oestrogens are used therapeutically. Ethinyl substitution at the C17 position has led to the development of synthetic oestrogens such as ethinylestradiol and mestranol, which have greatly improved potency and oral activity. Oral activity of natural oestrogens is improved by esterification (e.g. estradiol valerate) or by conjugation (e.g. estrone sulfate). Esterification also increases solubility in lipid vehicles and is used to prepare long-acting intramuscular preparations.

A number of nonsteroidal oestrogens, including chlorotrianisene, dienestrol, and diethylstilbestrol, have also been used.

Progesterone is the main hormone secreted by the corpus luteum. It acts on the endometrium by converting the proliferative phase induced by oestrogen to a secretory phase thereby preparing the uterus to receive the fertilised ovum. Progesterone has a catabolic action and causes a slight rise in basal body temperature during the secretory phase of menstruation. During pregnancy the placenta produces large quantities of progesterone, which suppresses uterine motility and is responsible for the further development of the breasts.

Progestogens (gestagens, progestagens, progestins) are synthetic compounds with actions similar to those of progesterone. They are either progesterone derivatives or 19-nortestosterone analogues. The 19-nortestosterone analogues (such as norethisterone and norgestrel) possess some androgenic activity, but some newer norgestrel derivatives (desogestrel, gestodene, and norgestimate) have little androgenic activity. The progesterone derivatives dydrogesterone, hydroxyprogesterone, and medroxyprogesterone are less androgenic than the 19-nortestosterone analogues. The progesterone derivatives chlormadinone, and particularly cyproterone, have anti-androgenic activity.

The principal natural and synthetic sex hormones covered in this chapter are thus:

- **androgens and anabolic steroids**, typified by testosterone (p.2129)
- **oestrogens**, typified by estradiol (p.2097)
- **progestogens**, typified by progesterone (p.2125)

Other related substances also described in this chapter are:

- drugs with mainly **weak androgenic** properties such as danazol and gestrinone
- drugs that combine **oestrogenic and progestogenic** properties such as tibolone
- drugs with mainly **anti-androgenic** properties including the progesterone derivative cyproterone acetate. Those anti-androgens used principally in the hormonal treatment of prostate cancer are covered in the Antineoplastics chapter; they include the nonsteroidal drugs bicalutamide (p.686), flutamide (p.725), and nilutamide (p.756). The nonsteroidal 5α-reductase inhibitors finasteride (p.2188) and dutasteride (p.2188) and the plant extract saw palmetto (p.2192), used in the treatment of benign prostatic hyperplasia, are covered in the Urological Drugs chapter
- drugs with mainly **anti-oestrogenic** properties. These include the nonsteroidal anti-oestrogens clomifene, cyclofenil, and the more selective nonsteroidal anti-oestrogens ormeloxifene and raloxifene. Those anti-oestrogens used principally in the hormonal treatment of breast cancer are covered in the Antineoplastics chapter; they include the oestrogen receptor antagonists tamoxifen (p.772) and toremifene (p.781), and various aromatase inhibitors such as formestane (p.726) and anastrozole (p.681)
- **gonad-regulating hormones** (see below for more detail) include endogenous and recombinant forms of luteinising and follicle-stimulating hormones, and their releasing hormone gonadorelin and its analogues.

The therapeutic applications of sex hormones and related substances are broad and cover many circumstances where hormonal manipulation is desirable. Major applications are the use of oestrogens and progestogens for **contraception** (p.2070) and for the alleviation of **menopausal symptoms** (p.2077). A physiological application is the use of sex hormones or gonad-regulating hormones in the management of **delayed puberty** (p.2079) and **hypogonadism** (p.2079). Other clinical applications include the management of **benign prostatic hyperplasia** (p.2178), **endometriosis** (p.2091), **gynaecomastia** (p.2092), **hirsutism** (p.2089), **infertility** (p.2080), **mastalgia** (p.2092), **menorrhagia** (p.2126), and **premenstrual syndrome** (p.2099). Hormonal manipulation also has an important role in the treatment of **malignant neoplasms** of the breast (p.661), prostate (p.671), and endometrium (p.663).

Hormonal Contraceptives

Anticonceptivos hormonales; Contraceptifs Hormonaux; Hormonale Kontrazeptiva.

Гормональный Контрацептивы

Types of Contraceptive

Hormonal contraceptives are currently only available for women although preparations for men are being evaluated. Oral hormonal contraceptives for women are divided into 2 main types: 'combined' (containing an oestrogen and a progestogen) and 'progestogen-only'. Parenteral preparations have also been developed and include subcutaneous implants and depot intramuscular injections. Progestogen-releasing intra-uterine devices and a combined hormonal contraceptive vaginal ring are available. A combined hormonal transdermal patch has also been developed.

Parenteral progestogen-only contraceptives provide reliable suppression of ovulation by suppressing the necessary mid-cycle surge of luteinising hormone. However, the low doses in progestogen-only oral contraceptives do not suppress it reliably in all cycles. Contraceptive efficacy is instead achieved by thickening the cervical mucus so that it is not readily penetrated by sperm, and by preventing proliferation of the endometrium so that it remains unfavourable for implantation of any fertilised ova. Intra-uterine progestogen-only devices act similarly; the physical presence of the system in the uterus may also contribute to overall contraceptive efficacy.

Oestrogens inhibit ovulation by suppressing the mid-cycle release of follicle-stimulating hormone. They act synergistically with progestogens in combined oral contraceptives to provide regular and consistent suppression of ovulation.