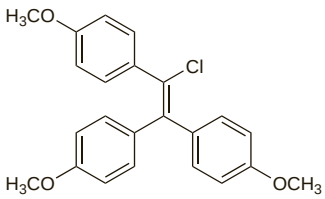
### Chlorotrianisene *(BAN, rINN)*

Chlorotrianisène; Chlorotrianisenum; Clorotrianiseno; Klooritrianiseeni; Klortrianisen; NSC-10108; Tri-*p*-anisylchloroethylene. Chlorotris(4-methoxyphenyl)ethylene.

Хлоротрианизен

$C_{23}H_{21}ClO_3$ = 380.9.
*CAS — 569-57-3.*
*ATC — G03CA06.*
*ATC Vet — QG03CA06.*




**Pharmacopoeias.** In *Chin.*

#### Profile

Chlorotrianisene is a synthetic nonsteroidal oestrogen structurally related to diethylstilbestrol (p.2094). It has a prolonged action, and has been given orally for the treatment of menopausal symptoms, female hypogonadism, and prostatic carcinoma.

## Chorionic Gonadotrophin *(BAN, rINN)* ⊗

CG; Choriogonadotrophin; Chorionic Gonadotropin; Chorioninis gonadotropinas; Gonadotrofina coriónica; Gonadotrophine Chorionique; Gonadotrophinum Chorionicum; Gonadotropin choriový; Gonadotropine chorionique; Gonadotropinum chorionicum; hCG; Human Chorionic Gonadotrophin; Koriongonadotropiini; Koriongonadotropin; Korion-gonadotropin; Koriyonik Gonadotrofin; Pregnancy-urine Hormone; PU.

Гонадотропин Хорионический
*CAS — 9002-61-3.*
*ATC — G03GA01.*
*ATC Vet — QG03GA01.*

**Pharmacopoeias.** In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.

**Ph. Eur. 6.2** (Gonadotrophin, Chorionic). A dry preparation of placental glycoproteins extracted from the urine of pregnant women. The potency is not less than 2500 units/mg. A white to yellowish-white, amorphous powder. Soluble in water. Store at 2° to 8° in airtight containers. Protect from light.

**USP 31** (Chorionic Gonadotropin). A gonad-stimulating polypeptide hormone obtained from the urine of pregnant women. It has a potency of not less than 1500 USP units/mg. A white or practically white, amorphous powder. Freely soluble in water. Store in airtight containers at 2° to 8°.

### Choriogonadotropin Alfa *(BAN, USAN, rINN)* ⊗

Choriogonadotropine Alfa; Choriogonadotropinum Alfa; Coriogonadotropina alfa.

Хориогонадотропин Альфа
*CAS — 177073-44-8 (choriogonadotropin alfa); 56832-30-5 (α subunit); 56832-34-9 (β subunit).*
*ATC — G03GA08.*
*ATC Vet — QG03GA08.*

### Adverse Effects and Precautions

Adverse effects that have been reported with chorionic gonadotrophin include headache, tiredness, changes in mood, depression, restlessness, oedema (especially in males), and pain on injection. Treatment for cryptorchidism may produce premature epiphyseal closure or precocious puberty. Gynaecomastia has been reported. Ovarian hyperstimulation may occur, with marked ovarian enlargement or cyst formation, acute abdominal pain, ascites, pleural effusion, hypovolaemia, shock, and thromboembolic disorders in severe cases.

Chorionic gonadotrophin should be given with care to patients in whom androgen-induced fluid retention might be a hazard as in asthma, epilepsy, migraine, or cardiovascular disorders, including hypertension, or renal disorders. Hypersensitivity reactions may occur and it is recommended that patients suspected to be susceptible should be given skin tests before treatment. It should not be given to patients with disorders that might be exacerbated by androgen release such as carcinoma of the prostate or precocious puberty. Use should also be avoided in the presence of breast, uterine, ovarian, and testicular tumours, as well as tumours of the hypothalamus, pituitary, thyroid, and adrenal glands.

### Pharmacokinetics

Peak concentrations of chorionic gonadotrophin occur about 6 hours after an intramuscular dose and 16 to 20 hours after a subcutaneous injection. It is distributed primarily to the gonads. Blood concentrations decline in a biphasic manner, with half-lives of about 6 to 11 hours and 23 to 38 hours, respectively. Chorionic gonadotrophin is metabolised mainly in the kidneys. About 10 to 12% of an intramuscular dose is excreted in urine within 24 hours.

After subcutaneous doses, choriogonadotropin alfa has a bioavailability of about 40%. It is metabolised and excreted similarly to chorionic gonadotrophin.

### Uses and Administration

Chorionic gonadotrophin is a hormone produced by the placenta and obtained from the urine of pregnant women. Its effects are mainly those of the gonadotrophin, luteinising hormone (p.2112), which is responsible for triggering ovulation and formation of the corpus luteum in women, and stimulates the production of testosterone by the testes in men. It is usually given by intramuscular injection although the subcutaneous route has also been used. Choriogonadotropin alfa is a recombinant form of chorionic gonadotrophin.

In *women* with **anovulatory infertility** due to absent or low concentrations of gonadotrophins, chorionic gonadotrophin is given to induce ovulation after follicular development has been stimulated with follicle-stimulating hormone or human menopausal gonadotrophins. A single dose of 5000 to 10 000 units of chorionic gonadotrophin is given by intramuscular injection to mimic the midcycle peak of luteinising hormone which normally stimulates ovulation. Up to 3 repeat injections of up to 5000 units each may be given within the next 9 days to prevent insufficiency of the corpus luteum. Chorionic gonadotrophin is also given with menotrophin as an adjunct to IVF procedures and other assisted conception techniques involving superovulation and oocyte collection.

Choriogonadotropin alfa is used similarly to induce ovulation in the treatment of anovulatory infertility, or as an adjunct to IVF procedures and other assisted conception techniques. A single dose of 250 micrograms is given, by subcutaneous injection, when optimal stimulation of follicular growth is achieved.

In *males*, chorionic gonadotrophin has been used in the treatment of prepubertal **cryptorchidism**. Regimens vary widely, but doses usually range from 500 to 4000 units three times weekly by intramuscular injection. Treatment should continue for 1 to 2 months after testicular descent.

Chorionic gonadotrophin is also given for male infertility associated with hypogonadotrophic **hypogonadism**. Again, there is considerable variation in the dosage regimen, and doses have varied from 500 to 4000 units two or three times weekly by intramuscular injection. A drug with follicle-stimulating activity such as menotrophin is often added to enable normal spermatogenesis.

In the treatment of **delayed puberty** associated with hypogonadism in males, an initial dose of chorionic gonadotrophin 500 to 1500 units is given twice weekly by intramuscular injection; the dose should be titrated against plasma-testosterone concentration.

**Cryptorchidism.** Although surgery remains the treatment with the best success rate, primary hormonal therapy with chorionic gonadotrophin is widely used for cryptorchidism (p.2079). Systematic reviews[1,2] suggest a success rate of about 20% overall, although this may be reduced when care is taken to exclude retractile testes. There is some suggestion that medical treatment given either before or after surgery can improve the patient's fertility index, a predictor of future fertility.[3] Chorionic gonadotrophin may also be used as an adjuvant before surgery, to render the testes palpable,[4] but changes suggestive of inflammation in the testis have been reported following such treatment.[5]

1. Pyöräläinen S, *et al.* A review and meta-analysis of hormonal treatment of cryptorchidism. *J Clin Endocrinol Metab* 1995; **80:** 2795–9.
2. Henna MR, *et al.* Hormonal cryptorchidism therapy: systematic review with metanalysis of randomized clinical trials. *Pediatr Surg Int* 2004; **20:** 357–9.
3. Tekgül S, *et al.* European Society for Paediatric Urology, European Association of Urology. Guidelines on paediatric urology (issued March 2008). Available at: http://www.uroweb.org/fileadmin/user_upload/Guidelines/Paediatric%20Urology.pdf (accessed 31/03/08)
4. Polascik TJ, *et al.* Reappraisal of the role of human chorionic gonadotropin in the diagnosis and treatment of the nonpalpable testis: a 10-year experience. *J Urol (Baltimore)* 1996; **156:** 804–6.
5. Kaleva M, *et al.* Treatment with human chorionic gonadotrophin for cryptorchidism: clinical and histological effects. *Int J Androl* 1996; **19:** 293–8.

**Delayed puberty.** Use of chorionic gonadotrophin may be appropriate in boys with delayed puberty due to hypogonadotrophic hypogonadism (p.2079).

**Infertility.** In women with anovulatory infertility chorionic gonadotrophin and choriogonadotropin alfa can be used to provoke ovulation and provide luteal support once maturation of a suitable number of follicles has been stimulated by other means. They are used similarly in the various protocols for assisted reproduction. However, use is not recommended for assisted reproduction in patients at risk of ovarian hyperstimulation, such as those with polycystic ovary syndrome. In men with hypogonadotrophic hypogonadism chorionic gonadotrophin is used to stimulate and maintain spermatogenesis. The management of male and female infertility, including the role of chorionic gonadotrophin, is discussed on p.2080.

**Malignant neoplasms.** Control of Kaposi's sarcoma (p.675) has been reported in a few patients given high-dose intramuscular chorionic gonadotrophin, but regrowth occurred when dosage was reduced or withdrawn.[1] Another study, using lower doses, was stopped due to toxicity and lack of benefit,[2] but others have confirmed benefit after intralesional injection.[3] There is some suggestion that preparations vary in their activity against the tumour and that it is not chorionic gonadotrophin itself, but some impurity (perhaps a ribonuclease[4] or the degradation product of the β-subunit[5]), that is the active principle.[3,6,7] Some contaminants may have a stimulant effect on the neoplasm, which might also contribute to the variable results.[5]

1. Harris PJ. Treatment of Kaposi's sarcoma and other manifestations of AIDS with human chorionic gonadotropin. *Lancet* 1995; **346:** 118–19.
2. Bower M, *et al.* Human chorionic gonadotropin for AIDS-related Kaposi's sarcoma. *Lancet* 1995; **346:** 642.
3. Gill PS, *et al.* The effects of preparations of human chorionic gonadotropin on AIDS-related Kaposi's sarcoma. *N Engl J Med* 1996; **335:** 1261–9. Correction. *ibid.* 1997; **336:** 1115.
4. Griffiths SJ, *et al.* Ribonuclease inhibits Kaposi's sarcoma. *Nature* 1997; **390:** 568.
5. Simonart T, *et al.* Treatment of Kaposi's sarcoma with human chorionic gonadotropin. *Dermatology* 2002; **204:** 330–3.
6. Gill PS, *et al.* Intralesional human chorionic gonadotropin for Kaposi's sarcoma. *N Engl J Med* 1997; **336:** 1188.
7. von Overbeck J, *et al.* Human chorionic gonadotropin for AIDS-related Kaposi's sarcoma. *Lancet* 1995; **346:** 642–3.

**Obesity.** A meta-analysis[1] involving 24 studies concluded that there was no evidence that chorionic gonadotrophin was effective in the treatment of obesity (p.2149).

1. Lijesen GKS, *et al.* The effect of human chorionic gonadotropin (HCG) in the treatment of obesity by means of the Simeons therapy: a criteria-based meta-analysis. *Br J Clin Pharmacol* 1995; **40:** 237–43.

**Testicular function.** Chorionic gonadotrophin is used in the assessment of testicular function in suspected primary hypogonadism and incomplete masculinisation. The *BNFC* states that for children 1 month to 18 years of age a dose of 1500 to 2000 units may be given once daily for 3 days (short stimulation test) or twice weekly for 3 weeks (prolonged test).

### Preparations

***BP 2008:*** Chorionic Gonadotrophin Injection;
***USP 31:*** Chorionic Gonadotropin for Injection.

**Proprietary Preparations** (details are given in Part 3)
***Arg.:*** Dinaron; Endocorion; Gonacor; Ovidrel; Pregnyl; Profasi†; ***Austral.:*** Ovidrel; Pregnyl; Profasi; ***Austria:*** Pregnyl; Profasi; ***Belg.:*** Choragon; Ovitrelle; Pregnyl; ***Braz.:*** Choragon†; Ovidrel; Pregnyl; Profasi HP; ***Canad.:*** Pregnyl†; Profasi HP; ***Chile:*** APL†; Gonacor; Ovidrel†; Pregnyl; Profasi†; ***Cz.:*** Ovitrelle; Praedyn†; Pregnyl; Profasi†; ***Denm.:*** Ovitrelle; Pregnyl; Profasi†; ***Fin.:*** Ovitrelle; Pregnyl; Profasi†; ***Fr.:*** Ovitrelle; ***Ger.:*** Choragon; Ovitrelle; Predalon; Pregnesin†; Primogonyl†; ***Gr.:*** Ovitrelle; Pregnyl; Profasi†; ***Hong Kong:*** Choragon; Choriomon; Ovidrel; Pregnyl; Profasi; ***Hung.:*** Choragon; Ovitrelle; Pregnyl; Profasi†; ***India:*** Corion; Profasi; Proligon†; Provigil; Pubergen; ***Indon.:*** Ovidrel; Pregnyl; ***Irl.:*** Ovitrelle; Pregnyl; Profasi; ***Israel:*** Chorigon†; Ovitrelle; Pregnyl; ***Ital.:*** Gonasi HP; Ovitrelle; Pregnyl; Profasi HP†; ***Malaysia:*** Choragon; Ovidrel; Pregnyl; Profasi†; ***Mex.:*** Choragon; Choriomon; Gonadotropyl C†; Ovidrel; Pregnyl; Profasi†; ***Neth.:*** Choragon; Ovitrelle; Pregnyl; Profasi†; ***Norw.:*** Ovitrelle; Pregnyl; Profasi†; ***NZ:*** Ovidrel; Profasi; ***Philipp.:*** Ovidrel; Pregnyl; ***Pol.:*** Choragon; Ovitrelle; Pregnyl; ***Port.:*** Ovitrelle; Pregnyl; Profasi HP†; ***Rus.:*** Choragon (Хорагон); Ovitrelle (Овитрель); Pregnyl (Прегнил); ***S.Afr.:*** APL; Pregnyl; Profasi; ***Singapore:*** Ovidrel; Pregnyl; Profasi†; ***Spain:*** Ovitrelle; Profasi HP†; ***Swed.:*** Ovitrelle; Pregnyl; Profasi†; ***Switz.:*** Choriomon; Ovitrelle; Pregnyl; Profasi†; ***Thai.:*** IVF-C; Ovidrel; Pregnyl; Profasi†; ***Turk.:*** Choragon; Ovitrelle; Pregnyl;