Interactions
Although reports are lacking, carbetocin may be involved in similar interactions to those that can occur with oxytocin (p.2016).

Pharmacokinetics
After intravenous injection of carbetocin, firm uterine contraction occurs within 2 minutes and lasts for several hours. Carbetocin undergoes a biphasic elimination, with a terminal elimination half-life of about 40 minutes. Less than 1% of a dose is excreted unchanged by the kidney. Carbetocin is distributed into breast milk.

Uses and Administration
Carbetocin is a synthetic analogue of oxytocin (p.2016) reported to have a longer duration of action. For the prevention of uterine atony and excessive bleeding after caesarean section under epidural or spinal anaesthesia, a single dose of 100 micrograms may be given by slow intravenous injection over 1 minute. Carbetocin must only be given after delivery of the infant, preferably before removal of the placenta.

◊ References.

1. Hunter DJS, *et al.* Effect of carbetocin, a long-acting oxytocin analog on the postpartum uterus. *Clin Pharmacol Ther* 1992; **52:** 60–7.
2. Dansereau J, *et al.* Double-blind comparison of carbetocin versus oxytocin in prevention of uterine atony after cesarean section. *Am J Obstet Gynecol* 1999; **180:** 670–6.
3. Boucher M, *et al.* Comparison of carbetocin and oxytocin for the prevention of postpartum hemorrhage following vaginal delivery: a double-blind randomized trial. *J Obstet Gynaecol Can* 2004; **26:** 481–8.
4. Leung SW, *et al.* A randomised trial of carbetocin versus syntometrine in the management of the third stage of labour. *BJOG* 2006; **113:** 1459–64.

Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Duratocin; ***Austral.:*** Duratocin; ***Canad.:*** Duratocin; ***Fr.:*** Pabal; ***Hong Kong:*** Duratocin; ***Hung.:*** Pabal; ***Malaysia:*** Duratocin; ***Mex.:*** Lonactene; ***Port.:*** Pabal; ***Singapore:*** Duratocin; ***UK:*** Pabal.

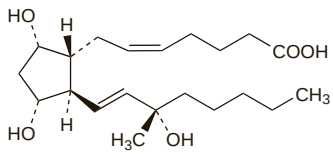
Multi-ingredient: ***Cz.:*** Duratocin.

Carboprost *(BAN, USAN, rINN)*

Carboprostum; 15-Me-PGF_2 ; Methyldinoprost; (15*S*)-15-Methylprostaglandin F_2 ; U-32921. (5*Z*,13*E*)-(8*R*,9*S*,11*R*,12*R*,15*S*)-9,11,15-Trihydroxy-15-methylprosta-5,13-dienoic acid; (*Z*)-7-{(1*R*,2*R*,3*R*,5*S*)-3,5-Dihydroxy-2-[(*E*)-(3*S*)-3-hydroxy-3-methyloct-1-enyl]cyclopentyl}hept-5-enoic acid.

Карбопрост

$C_{21}H_{36}O_5$ = 368.5.
CAS — 35700-23-3.
ATC — G02AD04.
ATC Vet — QG02AD04.



Carboprost Methyl *(BANM, USAN, rINNM)*

Carboprost Méthyle; Carboprostum Methylis; Methyl Carboprost; Metil carboprost; U-36384. The methyl ester of carboprost.

Карбопрост Метил

$C_{22}H_{38}O_5$ = 382.5.
CAS — 35700-21-1.
ATC — G02AD04.
ATC Vet — QG02AD04.

Pharmacopoeias. In *Chin.*

Carboprost Trometamol *(BANM, rINNM)*

Carboprost trométamol; Carboprost Tromethamine *(USAN)*; Carboprostum Trometamoli; Carboprostum trometamolum; Kaboprosttrometamol; Karboprost z trometamolem; Karboprostas trometamolis; Karboprostitrometamoli; Karboprost-trometamol; U-32921E.

Карбопрост Трометамол

$C_{21}H_{36}O_5.C_4H_{11}NO_3$ = 489.6.
CAS — 58551-69-2.
ATC — G02AD04.
ATC Vet — QG02AD04.

Description. Carboprost trometamol is a compound of carboprost with trometamol in a ratio of 1:1.

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

Ph. Eur. 6.2 (Carboprost Trometamol). A white or almost white powder. Soluble in water. Store at a temperature below −15°.

USP 31 (Carboprost Tromethamine). A white to off-white powder. Soluble in water. Store at −25° to −10°.

Adverse Effects and Precautions
As for Dinoprostone, p.2007.

Carboprost may cause bronchospasm and, less frequently, dyspnoea and pulmonary oedema. Patients with cardiopulmonary disorders should be monitored for reductions in arterial-oxygen content.

Once a prostaglandin has been given to terminate pregnancy it is essential that termination take place; if the prostaglandin is unsuccessful other measures should be used.

Effects on the fetus. Congenital abnormalities have been reported in pregnancies carried to term after failed termination using prostaglandins, including carboprost (see under Dinoprostone, p.2007).

Effects on the neonate. For a report of inadvertent intramuscular administration of carboprost to a neonate, see under Dinoprostone, p.2007.

Effects on the uterus. For reference to hyperstimulation and uterine rupture after use of prostaglandins, including carboprost, for termination of pregnancy or induction of labour, see Dinoprostone, p.2007.

Uses and Administration
Carboprost is a synthetic 15-methyl analogue of dinoprost (prostaglandin $F_{2\alpha}$; below). It is a uterine stimulant with a more prolonged action than dinoprost; the presence of the methyl group delays inactivation by enzymic dehydrogenation.

Carboprost is used for the termination of pregnancy (p.2004) and for the treatment of refractory postpartum haemorrhage due to uterine atony (p.2003) that is not controlled by oxytocin and ergot preparations. It is usually given intramuscularly as the trometamol salt but doses are expressed in terms of carboprost. Carboprost trometamol 1.3 micrograms is equivalent to about 1 microgram of carboprost.

For the **termination** of second trimester pregnancy (between 13 and 20 weeks of gestation) the equivalent of 250 micrograms of carboprost is given by deep intramuscular injection and repeated every 1½ to 3½ hours depending on the uterine response. If necessary the dose may be increased to 500 micrograms, but the total dose given should not exceed 12 mg, and continuous use for more than 2 days is not recommended. If preferred, a test dose of 100 micrograms may be given initially. Carboprost trometamol has also been given intra-amniotically in a dose equivalent to 1 mg of carboprost over five minutes; this dose may be repeated after 24 hours if termination has not occurred and the membranes are intact. A total dose of 5 mg should not be exceeded.

Carboprost methyl given as vaginal pessaries has been tried for termination of pregnancy in the second trimester.

For the treatment of **postpartum haemorrhage** the equivalent of 250 micrograms of carboprost is given by deep intramuscular injection as the trometamol salt at intervals of about 90 minutes; the interval may be reduced if necessary, but should not be less than 15 minutes. A total dose of 2 mg should not be exceeded.

Haemorrhagic cystitis. Carboprost trometamol instilled into the bladder successfully controlled cyclophosphamide-induced haemorrhagic cystitis (p.702) in 15 of 24 bone marrow transplant patients.[1] The dose consisted of 50 mL of solutions containing 2 to 10 micrograms/mL instilled four times daily for 7 days.

1. Ippoliti C, *et al.* Intravesicular carboprost for the treatment of hemorrhagic cystitis after marrow transplantation. *Urology* 1995; **46:** 811–15.

Preparations
USP 31: Carboprost Tromethamine Injection.

Proprietary Preparations (details are given in Part 3)

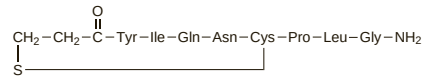
Belg.: Prostin/15M; ***Canad.:*** Hemabate; ***Cz.:*** Prostin 15M; ***Denm.:*** Prostinfenem; ***India:*** Prostodin; ***Neth.:*** Prostin/15M; ***NZ:*** Prostin 15M; ***Swed.:*** Prostinfenem; ***UK:*** Hemabate; ***USA:*** Hemabate.

Demoxytocin *(rINN)*

Deamino-oxytocin; Demoksitosiini; Demoxitocina; Démoxytocine; Demoxytocinum; Desaminocitocina; Desamino-oxytocin; ODA-914. 1-(3-Mercaptopropionic acid)-oxytocin.

Демокситоцин

$C_{43}H_{65}N_{11}O_{12}S_2$ = 992.2.
CAS — 113-78-0.
ATC — H01BB01.
ATC Vet — QH01BB01.



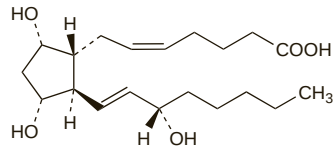
Profile
Demoxytocin is a synthetic analogue of oxytocin (p.2015) and has similar properties. It has been given as buccal tablets for the induction and augmentation of labour. It has also been given before nursing to stimulate milk ejection, although it is generally recommended that oxytocics should not be used for this purpose (see p.2003).

Dinoprost *(BAN, USAN, rINN)*

Dinoprosti; Dinoprostum; PGF_2 ; Prostaglandin F_2 ; U-14583. (5*Z*,13*E*)-(8*R*,9*S*,11*R*,12*R*,15*S*)-9,11,15-Trihydroxyprosta-5,13-dienoic acid; (*Z*)-7-{(1*R*,2*R*,3*R*,5*S*)-3,5-Dihydroxy-2-[(*E*)-(3*S*)-3-hydroxyoct-1-enyl]cyclopentyl}hept-5-enoic acid.

Динопрост

$C_{20}H_{34}O_5$ = 354.5.
CAS — 551-11-1.
ATC — G02AD01.
ATC Vet — QG02AD01.



NOTE. In *Martindale* the term dinoprost is used for the exogenous substance and prostaglandin F_2 for the endogenous substance.

Pharmacopoeias. In *Jpn.*

Dinoprost Trometamol *(BANM, rINNM)*

Dinoprost trométamol; Dinoprost Tromethamine *(USAN)*; Dinoprostas trometamolis; Dinoprostitrometamoli; Dinoprost-trometamol; Dinoprost-trometamol; Dinoprostum Trometamoli; Dinoprostum trometamolum; Dinoproszt-trometamol; PGF_2 THAM; Prostaglandin F_2 Trometamol; U-14583E.

Динопрост Трометамол

$C_{20}H_{34}O_5.C_4H_{11}NO_3$ = 475.6.
CAS — 38562-01-5.
ATC — G02AD01.
ATC Vet — QG02AD01.

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

Ph. Eur. 6.2 (Dinoprost Trometamol). A white or almost white powder. Very soluble in water; freely soluble in alcohol; practically insoluble in acetonitrile.

USP 31 (Dinoprost Tromethamine). A white to off-white crystalline powder. Very soluble in water; slightly soluble in chloroform; freely soluble in dimethylformamide; soluble in methyl alcohol. Store in airtight containers.

Adverse Effects and Precautions
As for Dinoprostone, p.2007.

Dinoprost can cause bronchoconstriction, and bronchospasm with wheezing and dyspnoea has occurred, especially in asthmatic patients.

Once a prostaglandin has been given to terminate pregnancy it is essential that termination take place; if the prostaglandin is unsuccessful other measures should be used.

Interactions
As for Dinoprostone, p.2008. Alcohol and beta agonists may reduce the efficacy of dinoprost.

◊ For a report of a severe reaction after the use of oxytocin, methylergometrine, and dinoprost, see under Dinoprostone, p.2008.

Uses and Administration
Dinoprost is a prostaglandin of the F series (p.2374) with actions on smooth muscle; the endogenous substance is termed prostaglandin F_2 and is rapidly metabolised in the body. It induces contraction of uterine muscle at any stage of pregnancy and is reported to act mainly as a vasoconstrictor on blood vessels and as a bronchoconstrictor on bronchial muscle.

Dinoprost is used principally for the termination of pregnancy (p.2004). It may also be used for missed abortion, hydatidiform