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.

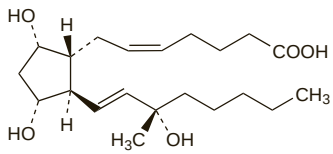
Multi-ingredient: ***Cz.:*** Duratocin.

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)

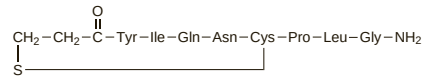
Belg.: Prostin/15M; ***Canad.:*** Hemabate; ***Cz.:*** Prostin 15M; ***Denm.:*** Prostinfenem; ***India:*** Prostodin; ***Neth.:*** Prostin/15M; ***NZ:*** Prostin 15M; ***Swed.:*** Prostinfenem; ***UK:*** Hemabate; ***USA:*** Hemabate.

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.



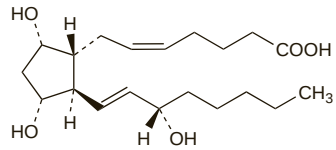
Profile
Demoxytocin is a synthetic analogue of oxytocin (p.2015) and has similar properties. It has been given as buccal tablets for the induction and augmentation of labour. It has also been given before nursing to stimulate milk ejection, although it is generally recommended that oxytocics should not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

mole, and intra-uterine fetal death. Dinoprost has also been given for the induction of labour but has a higher incidence of adverse effects than dinoprostone, and is no longer routinely recommended; more appropriate treatment is discussed on p.2002.

Dinoprost is usually given intra-amniotically for termination of pregnancy. It has been given intravenously, but with a high incidence of adverse effects. The extra-amniotic route has also been used. Dinoprost is given as the trometamol salt, but doses are described in terms of the base; 1.3 mg of dinoprost trometamol is equivalent to about 1 mg of dinoprost.

For the termination of pregnancy during the second trimester 40 mg of dinoprost is given intra-amniotically by slowly injecting 8 mL of a solution containing 5 mg/mL into the amniotic sac. A further dose of 10 to 40 mg may be given after 24 hours if the termination process has not been established or completed and the membranes are still intact. It should not be given continuously for more than 2 days.

Ileus. Ileus induced by vinca alkaloids in 3 patients with carcinoma of the lung was successfully relieved by the intravenous infusion of dinoprost 300 to 500 nanograms/kg per minute for 2 hours twice daily.[1]

1. Saito H, *et al.* Prostaglandin F in the treatment of vinca alkaloid-induced ileus. *Am J Med* 1993; **95:** 549–51.

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Prostin F2 Alpha; ***Cz.:*** Enzaprost F; ***Ger.:*** Minprostin F α; ***Gr.:*** Enzaprost; ***Hong Kong:*** Prostin F2 Alpha; ***Hung.:*** Enzaprost F; ***Irl.:*** Prostin F2†; ***Israel:*** Prostin F2 Alpha; ***NZ:*** Prostin F2 Alpha; ***Pol.:*** Enzaprost; ***Rus.:*** Enzaprost F (Энзапрост Ф); Prostin F2 Alfa (Простин F2-Альфа)†; ***S.Afr.:*** Prostin F2 Alpha.

Dinoprostone *(BAN, USAN, rINN)*

Dinoproston; Dinoprostona; Dinoprostonas; Dinoprostoni; Dinoprostonum; Dinoproszton; PGE_2; Prostaglandin E_2; U-12062. (5*Z*,13*E*)-(8*R*,11*R*,12*R*,15*S*)-11,15-Dihydroxy-9-oxoprosta-5,13-dienoic acid; (*Z*)-7-{(1*R*,2*R*,3*R*)-3-Hydroxy-2-[(*E*)-(3*S*)-3-hydroxyoct-1-enyl]-5-oxocyclopentyl}hept-5-enoic acid.

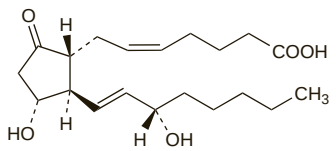
Динопростон

$C_{20}H_{32}O_5$ = 352.5.

CAS — 363-24-6.

ATC — G02AD02.

ATC Vet — QG02AD02.



NOTE. In *Martindale* the term dinoprostone is used for the exogenous substance and prostaglandin E_2 for the endogenous substance.

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

Ph. Eur. 6.2 (Dinoprostone). A white or almost white, crystalline powder or colourless crystals. Practically insoluble in water; freely soluble in alcohol; very soluble in methyl alcohol. Store at a temperature not exceeding –15°.

USP 31 (Dinoprostone). A white to off-white, crystalline powder. Freely soluble in alcohol, in acetone, in dichloromethane, in ether, in ethyl acetate, in isopropyl alcohol, in methyl alcohol; soluble in diisopropyl ether and in toluene; practically insoluble in hexanes. Protect from light.

Adverse Effects

The incidence and severity of adverse reactions to dinoprostone are dose-related and also depend to some extent on the route; the intravenous route has been associated with a high incidence of adverse effects. Nausea, vomiting, diarrhoea, and abdominal pain are common by all routes. Back pain and rash can occur. Transient cardiovascular (vasovagal) symptoms have included flushing, shivering, headache, dizziness, and hypotension; there have been rare reports of myocardial infarction and cardiac arrest. Hypertension has also been reported. Convulsions and EEG changes have occurred rarely. Local tissue irritation and erythema, as well as pyrexia and raised white cell count, may follow intravenous doses but generally revert to normal after termination of the infusion. Transient pyrexia and raised white cell count may also occur after intravaginal use. Local infection may follow intra- or extra-amniotic therapy. Excessive uterine activity may occur and there have been occasional reports of uterine rupture after the use of prostaglandins to terminate pregnancy or induce labour; fetal distress and, rarely, fetal death have occurred during induction. Disseminated intravascular coagulation has occurred rarely.

Dinoprostone, although generally acting as a bronchodilator, may cause bronchoconstriction in some individuals. Hypersensitivity reactions have occurred.

Incidence of adverse effects. Adverse effects were evaluated in 626 patients[1] undergoing abortion (usually in the second trimester), using extra-amniotic or intra-amniotic dinoprost or dinoprostone, often with oxytocin. Vomiting occurred in 291, diarrhoea in 28, pyrexia in 34, transient hypotension (fall in systolic blood pressure of at least 20 mmHg) in 25, transient bronchospasm in 2 patients given extra-amniotic dinoprost, and blood loss exceeding 250 mL in 68 (38 lost more than 500 mL). No patients had convulsions even though 8 were being treated for epilepsy. Three patients sustained lacerations to the cervix. Five patients complained of breast soreness or lactation; these symptoms may have been under-reported. Overall 14 patients were re-admitted; 13 because of excessive vaginal bleeding and 1 because of pelvic infection.

A later report describes the cumulative experience in 3313 pregnancies[2] in which dinoprostone gel was used for induction of term labour or cervical ripening. Adverse effects were rare. Vomiting, fever, and diarrhoea occurred in about 0.2% of mothers and were difficult to distinguish from the effects of concurrent drug therapy. Detectable myometrial activity was dose-related and more common after intravaginal than after intracervical use. Myometrial activity was reported in 0.6 to 6% of patients following intravaginal application and hyperstimulation was virtually non-existent at an intracervical dose of 500 micrograms. Fetal effects were negligible in the absence of uterine hyperstimulation.

1. MacKenzie IZ, *et al.* Prostaglandin-induced abortion: assessment of operative complications and early morbidity. *BMJ* 1974; **4:** 683–6.
2. Rayburn WF. Prostaglandin E gel for cervical ripening and induction of labor: a critical analysis. *Am J Obstet Gynecol* 1989; **160:** 529–34.

Effects on the bones. Reversible periosteal reactions of the long bones and bone thickening have occurred in infants receiving long-term therapy with prostaglandins of the E series (see Alprostadil, p.2183). In addition, reversible widening of cranial sutures was reported[1] in 2 neonates given dinoprostone intravenously for 95 and 97 days respectively.

1. Hoevels-Guerich H, *et al*. Widening of cranial sutures after long-term prostaglandin E therapy in two newborn infants. *J Pediatr* 1984; **105:** 72–4.

Effects on the cardiovascular system. Cardiovascular adverse effects are most common after intravenous dinoprostone but may also occur with other routes. Severe cardiovascular disorders reported with the intra-amniotic or intravaginal use of dinoprost or dinoprostone have included: cardiac arrhythmias in 3 patients,[1,2] fatal in 2 of them;[2] hypotension, tachypnoea, and tachycardia in 3 patients[3,4] with associated pyrexias in 2 patients;[3] and fatal myocardial infarction in a patient who had several high-risk factors for ischaemic heart disease.[5]

Severe hypertension occurred in a patient[6] who received dinoprostone by direct myometrial injection and by intravenous infusion concomitantly for postpartum haemorrhage.

Adverse cardiovascular effects have also been reported with other prostaglandins used in gynaecological or obstetric indications (see under Gemeprost, p.2010, and Sulprostone, p.2018).

1. Burt RL, *et al.* Hypokalemia and cardiac arrhythmia associated with prostaglandin-induced abortion. *Obstet Gynecol* 1977; **50:** 45S–46S.
2. Cates W, Jordaan HVF. Sudden collapse and death of women obtaining abortions induced with prostaglandin F . *Am J Obstet Gynecol* 1979; **133:** 398–400.
3. Phelan JP, *et al.* Dramatic pyrexic and cardiovascular response to intravaginal prostaglandin E . *Am J Obstet Gynecol* 1978; **132:** 28–32.
4. Cameron IT, Baird DT. Sudden collapse after intra-amniotic prostaglandin E injection. *Lancet* 1984; **ii:** 1046.
5. Patterson SP, *et al.* A maternal death associated with prostaglandin E . *Obstet Gynecol* 1979; **54:** 123–4.
6. Veber B, *et al.* Severe hypertension during postpartum haemorrhage after i.v. administration of prostaglandin E2. *Br J Anaesth* 1992; **68:** 623–4.

Effects on the fetus. A woman who failed to abort despite receiving carboprost intravaginally 7 weeks after conception gave birth at 34 weeks of gestation to an infant with hydrocephalus and abnormal digits.[1] There have been reports of 2 infants born, without congenital abnormality, to women who continued with the pregnancy after attempted mid-trimester termination using intravaginal gemeprost.[2,3] However, abnormalities including limb deformities, cleft palate, anencephaly, cerebellar atrophy, and heart malformation were reported in a review[4] of 71 cases of pregnancy that were continued after attempted termination using mifepristone either alone or with a prostaglandin. Of the 8 cases of abnormality that were reported, 7 occurred in the group of 10 women who had been given intravaginal gemeprost. A case of cerebellar agenesis has also been described[5] after a failed medical termination using mifepristone and gemeprost. For abnormalities reported after the failed misuse of misoprostol alone for termination of pregnancy, see p.2013.

For reports of adverse effects on the fetus due to hyperstimulation of the uterus during labour, see under Effects on the Uterus, below.

1. Collins FS, Mahoney MJ. Hydrocephalus and abnormal digits after failed first-trimester prostaglandin abortion attempt. *J Pediatr* 1983; **102:** 620–1.
2. Lakasing L, Spencer JAD. Continuation of pregnancy after mid-trimester gemeprost administration. *Br J Obstet Gynaecol* 1999; **106:** 1319–20.
3. Rolland P, Sinha A. Continuation of pregnancy after mid-trimester gemeprost administration. *Br J Obstet Gynaecol* 2000; **107:** 1184.
4. Sitruk-Ware R, *et al.* Fetal malformation and failed medical termination of pregnancy. *Lancet* 1998; **352:** 323.
5. Afadapa FK, Elsapagh K. Isolated one-sided cerebellar agenesis following an attempted medical termination of pregnancy. *J Obstet Gynaecol* 2006; **26:** 581–2.

Effects on the gastrointestinal system. Necrotising enterocolitis has been associated with the use of intravenous[1] or oral[2] dinoprostone, or intravenous alprostadil,[2] in infants with symptomatic congenital heart disease. It has been suggested that induced hypotension and apnoea may be responsible,[1] although others[3] did not support this view, or that pulmonary vasodilatation may produce systemic to pulmonary shunting, rendering the gastrointestinal tract relatively ischaemic.[2]

1. Leung MP, *et al.* Necrotizing enterocolitis in neonates with symptomatic congenital heart disease. *J Pediatr* 1988; **113:** 1044–6.
2. Singh GK, *et al.* Study of low dosage prostaglandin—usages and complications. *Eur Heart J* 1994; **15:** 377–81.
3. Miller MJS, Clark DA. Congenital heart disease and necrotizing enterocolitis. *J Pediatr* 1989; **115:** 335–6.

Effects on the neonate. Aspiration of the undissolved remnants of a dinoprostone vaginal tablet caused neonatal respiratory distress due to mechanical obstruction of the airways; there was no evidence to suggest absorption of dinoprostone from the tablet matrix.[1]

Inadvertent intramuscular injection of carboprost 250 micrograms caused hypertension, bronchospasm, diarrhoea, and hyperthermia in a neonate. There was also an adverse neurological effect that was either a dystonic reaction or seizure activity. The neonate was treated symptomatically and discharged 24 hours later; neurological and developmental examinations were normal at 3 months of age.[2] The authors of this report also learned of 2 other cases that had been reported to the manufacturer, in which neonates given injections of 125 micrograms and 63 micrograms remained asymptomatic.

1. Andersson S, *et al.* Neonatal respiratory distress caused by aspiration of a vaginal tablet containing prostaglandin. *BMJ* 1987; **295:** 25–6.
2. Mrvos R, *et al.* Carboprost exposure in a newborn with recovery. *J Toxicol Clin Toxicol* 1999; **37:** 865–7.

Effects on the nervous system. Convulsions and EEG changes have been occasionally reported during the use of prostaglandins for termination of pregnancy. Convulsions occurred[1] in 5 of 320 women after intra-amniotic dinoprost, but in other large series[2-4] of patients given dinoprost or dinoprostone by various routes no problems occurred despite the inclusion of patients with a history of epilepsy. However, convulsions were reported[5] in 3 of 4 epileptic patients given sulprostone intramuscularly.

1. Lyneham RC, *et al.* Convulsions and electroencephalogram abnormalities after intra-amniotic prostaglandin F . *Lancet* 1973; **ii:** 1003–5.
2. MacKenzie IZ, *et al.* Convulsions and prostaglandin-induced abortion. *Lancet* 1973; **ii:** 1323.
3. Thiery M, *et al.* Prostaglandins and convulsions. *Lancet* 1974; **i:** 218.
4. Fraser IS, Gray C. Electroencephalogram changes after prostaglandin. *Lancet* 1974; **i:** 360.
5. Brandenburg H, *et al.* Convulsions in epileptic women after administration of prostaglandin E derivative. *Lancet* 1990; **336:** 1138.

Effects on the uterus. Use of prostaglandins to induce labour or to terminate pregnancy is associated with an increased risk of hyperstimulation of the uterus. Uterine rupture has occurred with carboprost,[1] dinoprost or dinoprostone,[2-7] gemeprost,[8-10] misoprostol,[11-14] and sulprostone.[15-17] These effects have been reported with parenteral, local, and oral dosage. The risk of rupture and associated complications is increased in grand multiparae[4] and those with uterine scarring from previous caesarean section.[5,7] Studies have reported relative risks of between 6 and 10 times those of spontaneous labour after labour induction with dinoprostone in the latter group.[5,7] In addition to rupture, with the risk of potentially fatal maternal haemorrhage, hyperstimulation has been associated with fetal distress and death,[18-20] and maternal death due to amniotic fluid embolism.[18,21]

1. Vergote I, *et al.* Uterine rupture due to 15-methyl prostaglandin F . *Lancet* 1982; **ii:** 1402.
2. Claman P, *et al.* Uterine rupture with the use of vaginal prostaglandin E for induction of labor. *Am J Obstet Gynecol* 1984; **150:** 889–90.
3. Keller F, Joyce TH. Uterine rupture associated with the use of vaginal prostaglandin E suppositories. *Can Anaesth Soc J* 1984; **31:** 80–2.