

livery of the infant; contractions are reported to occur within 2 to 7 minutes. Delivery of the placenta is actively assisted while the uterus is firmly contracted.

In the prevention or treatment of **postpartum haemorrhage**, a similar dose of ergometrine maleate with oxytocin is given intramuscularly following delivery of the placenta or when bleeding occurs. A combined intravenous preparation of ergometrine maleate with oxytocin has been used but is no longer recommended. Ergometrine maleate alone is used for prevention or treatment of postpartum or postabortal haemorrhage in a usual intramuscular dose of 200 micrograms. The dose may be repeated in severe bleeding, but is rarely needed more often than once in 2 to 4 hours. In emergencies such as excessive uterine bleeding, ergometrine maleate has been given intravenously in a dose of 200 micrograms; single doses of 250 to 500 micrograms have also been used. Intravenous doses should be given over at least 1 minute to reduce the risk of adverse effects, particularly hypertension. Parenteral treatment of haemorrhage may be followed by ergometrine maleate 200 to 400 micrograms orally 2 to 4 times daily until the danger of atony and haemorrhage has passed, which is usually 48 hours. Tablets have also been given sublingually.

In the treatment of mild secondary postpartum haemorrhage, ergometrine maleate has been given orally. Ergometrine tartrate was formerly used.

**Diagnosis and testing.** Ergometrine maleate<sup>1-8</sup> or methylergometrine maleate<sup>9,10</sup> have been used in a provocation test for the diagnosis of Prinzmetal's angina (variant angina) (p.1157).

1. Waters DD, et al. Ergonovine testing in a coronary care unit. *Am J Cardiol* 1980; **46**: 922-30.
2. Health and Public Policy Committee, American College of Physicians. Performance of ergonovine provocative testing for coronary artery spasm. *Ann Intern Med* 1984; **100**: 151-2.
3. Song J-K, et al. Safety and clinical impact of ergonovine stress echocardiography for diagnosis of coronary vasospasm. *J Am Coll Cardiol* 2000; **35**: 1850-6.
4. Kashima K, et al. Long-term outcome of patients with ergonovine induced coronary constriction not associated with ischemic electrocardiographic changes. *J Cardiol* 2001; **37**: 301-8.
5. Palinkas A, et al. Safety of ergot stress echocardiography for non-invasive detection of coronary vasospasm. *Coron Artery Dis* 2001; **12**: 649-54.
6. Song JK, et al. Prognostic implication of ergonovine echocardiography in patients with near normal coronary angiogram or negative stress test for significant fixed stenosis. *J Am Soc Echocardiogr* 2002; **15**: 1346-52.
7. Sueda S, et al. Clinical impact of selective spasm provocation tests: comparisons between acetylcholine and ergonovine in 1508 examinations. *Coron Artery Dis* 2004; **15**: 491-7.
8. Coma-Canella I, et al. Ergonovine test in angina with normal coronary arteries: is it worth doing it? *Int J Cardiol* 2006; **107**: 200-6.
9. Bertrand ME, et al. Frequency of provoked coronary arterial spasm in 1089 consecutive patients undergoing coronary arteriography. *Circulation* 1982; **65**: 1299-1306.
10. Lablanche JM, et al. Réflexions d'un comité d'experts de la Société française de cardiologie concernant l'usage du maléate de méthyle-ergométrine (Methergin) dans la détection d'une vasomotricité coronaire anormale. *Arch Mal Coeur Vaiss* 1995; **88**: 247-53.

## Preparations

**BP 2008:** Ergometrine and Oxytocin Injection; Ergometrine Injection; Ergometrine Tablets.

**USP 31:** Ergonovine Maleate Injection; Ergonovine Maleate Tablets.

**Proprietary Preparations** (details are given in Part 3)

**Arg.:** Evina; **Metregina;** **Braz.:** Ergotrate; **Gr.:** Mitrotran; **Mex.:** Ergotrate; **Thai.:** Gynaemine; **USA:** Ergotrate.

**Multi-ingredient:** **Austral.:** Syntometrine; **Hong Kong:** Syntometrine; **Irl.:** Syntometrine; **Malaysia:** Syntometrine; **NZ:** Syntometrine; **S.Afr.:** Syntometrine; **UK:** Syntometrine.

## Ergot

Comezuelo del centeno; Secale Cornutum.

Спорынья

**Description.** Ergot consists of the sclerotium of the fungus *Claviceps purpurea* (Hypocreaceae) developed in the ovary of the rye, *Secale cereale* (Gramineae). It contains not less than 0.15% of total alkaloids, calculated as ergotoxine, and not less than 0.01% of water-soluble alkaloids, calculated as ergometrine. Some authorities have expressed alkaloidal content in terms of ergotamine and ergometrine.

## Adverse Effects and Treatment

As for Ergotamine Tartrate, p.620.

Epidemic ergot poisoning, arising from the ingestion of ergotised rye bread, is now seldom seen. Two forms of epidemic toxicity, which rarely occur together, have been described: a gangrenous form characterised by agonising pain of the extremities of the body followed by dry gangrene of the peripheral parts, and a rar-

er nervous type giving rise to paroxysmal epileptiform convulsions.

**Poisoning.** A report of an outbreak of ergotism, attributed to the ingestion of infected wild oats (*Avena abyssinica*), in Ethiopia.<sup>1</sup>

1. King B. Outbreak of ergotism in Wollo, Ethiopia. *Lancet* 1979; **ii**: 1411.

## Uses and Administration

Ergot has the vasoconstricting and oxytocic actions of its constituent alkaloids, especially ergotamine (p.620) and ergometrine (above). A liquid extract or tablets of prepared ergot were formerly used as an oxytocic. Preparations containing ergot extracts have been promoted for use in dyspepsia and nervous disorders.

## Preparations

**Proprietary Preparations** (details are given in Part 3)

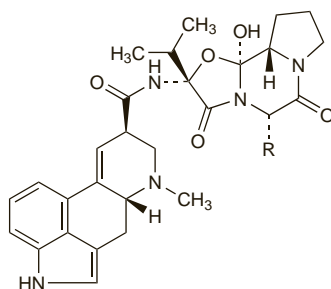
**India:** Ergotab.

## Ergotoxine

Ecboline; Ergotoxina.

Эрготоксин

CAS — 8006-25-5 (ergotoxine); 8047-28-7 (ergotoxine esilate); 8047-29-8 (ergotoxine phosphate); 564-36-3 (ergocornine); 511-08-0 (ergocristine); 511-09-1 ( $\alpha$ -ergocryptine); 20315-46-2 ( $\beta$ -ergocryptine).



Ergocornine	R = CH(CH <sub>3</sub> ) <sub>2</sub>
Ergocristine	R = CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>
$\alpha$ -Ergocryptine	R = CH <sub>2</sub> CH(CH <sub>3</sub> ) <sub>2</sub>
$\beta$ -Ergocryptine	R = CH(CH <sub>3</sub> )CH <sub>2</sub> CH <sub>3</sub>

## Profile

Ergotoxine is a mixture of naturally occurring ergot alkaloids. It contains equal proportions of ergocornine (C<sub>31</sub>H<sub>39</sub>N<sub>3</sub>O<sub>5</sub> = 561.7), ergocristine (C<sub>35</sub>H<sub>39</sub>N<sub>3</sub>O<sub>5</sub> = 609.7), and ergocryptine (C<sub>33</sub>H<sub>41</sub>N<sub>3</sub>O<sub>5</sub> = 575.7) as the  $\alpha$ - and  $\beta$ -isomers. The esilate was formerly used as an oxytocic and in the treatment of migraine. Ergotoxine phosphate has also been used.

## Gemeprost (BAN, USAN, rINN)

16,16-Dimethyl-trans- $\Delta^2$ -prostaglandin E<sub>1</sub> methyl ester; Géméprost; Gemeprost; Gemeprostum; ONO-802; SC-37681. Methyl (2E,13E)-(8R,11R,12R,15R)-11,15-dihydroxy-16,16-dimethyl-9-oxoprostano-2,13-dienoate; Methyl (E)-7-((1R,2R,3R)-3-hydroxy-2-[(E)-(3R)-3-hydroxy-4,4-dimethylcyclopentyl]-5-oxocyclopentyl)hept-2-enoate.

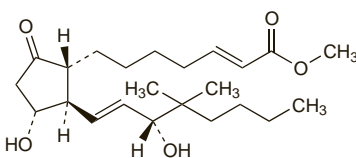
Гемепрост

C<sub>23</sub>H<sub>38</sub>O<sub>5</sub> = 394.5.

CAS — 64318-79-2.

ATC — G02AD03.

ATC Vet — QG02AD03.



## Adverse Effects and Precautions

As for Dinoprostone, p.2007. Vaginal bleeding and mild uterine pain may occur. Pulse and blood pressure should be monitored in patients given gemeprost.

The effects of gemeprost on the fetus are not known. 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.

**Incidence of adverse effects.** The incidence of vomiting (19 or 35%) and diarrhoea (12 or 19%) in 2 studies of patients treated with gemeprost pessaries was similar to that seen with other prostaglandins, but gemeprost was reported to cause less uterine pain.<sup>1,2</sup>

1. Cameron IT, Baird DT. The use of 16,16-dimethyl-trans- $\Delta^2$  prostaglandin E<sub>1</sub> methyl ester (gemeprost) vaginal pessaries for the termination of pregnancy in the early second trimester: a comparison with extra-amniotic prostaglandin E<sub>1</sub>. *Br J Obstet Gynaecol* 1984; **91**: 1136-40.
2. Andersen LF, et al. Termination of second trimester pregnancy with gemeprost vaginal pessaries and intra-amniotic PGF<sub>2</sub> : a comparative study. *Eur J Obstet Gynecol Reprod Biol* 1989; **31**: 1-7.

**Effects on the cardiovascular system.** Periods of ventricular standstill of up to 6 seconds were seen in a patient during treatment with gemeprost vaginal pessaries.<sup>1</sup> The patient required temporary cardiac pacing, but no persistent cardiac rhythm disturbances were detected on follow-up. Severe cardiogenic shock due to vasospasm, and subsequent stroke, has been reported in a patient who had received gemeprost pessaries some hours earlier; myocardial infarction ensuing from coronary spasm was reported in a second patient.<sup>2</sup>

1. Kalra PA, et al. Cardiac standstill induced by prostaglandin pessaries. *Lancet* 1989; **i**: 1460-1.
2. Schulte-Sasse U. Life threatening myocardial ischaemia associated with the use of prostaglandin E<sub>1</sub> to induce abortion. *Br J Obstet Gynaecol* 2000; **107**: 700-2.

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

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

## Interactions

As for Dinoprostone, p.2008.

## Uses and Administration

Gemeprost is a synthetic analogue of alprostadil (prostaglandin E<sub>1</sub>; p.2183). It is used to soften and dilate the cervix and as a uterine stimulant in the termination of pregnancy (p.2004). In the first trimester, a pessary containing gemeprost 1 mg is inserted into the vagina 3 hours before surgery to ripen the cervix. Gemeprost may also be used for termination of pregnancy in the second trimester when a 1-mg pessary is inserted every 3 hours to a maximum of 5 pessaries. If this is ineffective, one further course may be given starting 24 hours after the beginning of the first course. If termination is not well established after 10 pessaries, alternative treatment should be used to complete uterine evacuation. In the case of intra-uterine fetal death in the second trimester, only one course of up to 5 pessaries should be given. Vaginal gemeprost is also used after oral mifepristone (p.2012) in the termination of pregnancy.

## Preparations

**Proprietary Preparations** (details are given in Part 3)

**Austral.:** Cervagem; **Denm.:** Cervagem; **Fin.:** Cervagem; **Fr.:** Cervagem; **Ger.:** Cergem; **Hong Kong:** Cervagem; **Ital.:** Cervidil; **Jpn.:** Preglandin; **Malaysia:** Cervagem; **Norw.:** Cervagem; **NZ:** Cervagem; **Singapore:** Cervagem; **Swed.:** Cervagem.

## Meteneprost (USAN, rINN)

9-Deoxo-16,16-dimethyl-9-methylene-prostaglandin E<sub>2</sub>; Méténéprost; Meteneprostum; U-46785. (5Z,13E)-(8R,11R,12R,15R)-11,15-Dihydroxy-16,16-dimethyl-9-methylene-prosta-5,13-dienoic acid; (Z)-7-((1R,2R,3R)-3-hydroxy-2-[(E)-(3R)-3-hydroxy-4,4-dimethylcyclopentyl]-5-methylenecyclopentyl)hept-5-enoic acid.

Метенепрост

C<sub>23</sub>H<sub>38</sub>O<sub>4</sub> = 378.5.

CAS — 61263-35-2.

