PHYSICIAN LEAFLET

HEMABATE® Sterile Solution
(Carboprost tromethamine)

Presentation

Colourless, sterile, aqueous solution containing carboprost tromethamine equivalent to carboprost 250 micrograms/ml.

This medicine contains 9.45 mg benzyl alcohol in each ampoule which is equivalent to 9.45 mg/ml. This medicine also contains sodium chloride, sodium hydroxide, hydrochloric acid, tromethamine and water for injections.

Uses

Treatment of post-partum haemorrhage due to uterine atony and refractory to conventional methods of treatment with oxytocic agents and ergometrine used either alone or in combination.

Conventional therapy should usually consist of 0.5 - 1 mg ergometrine with up to 50 units of oxytocin infused intravenously over periods of time from 20 minutes to 12 hours. The dosage and duration of administration should reflect the seriousness of the clinical situation.

Dosage and administration

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

An initial dose of 250 micrograms (1.0 ml) of Hemabate should be administered as a deep intramuscular injection.

If necessary, further doses of 250 micrograms may be administered at intervals of approximately 1.5 hours. In severe cases the interval between doses may be reduced at the discretion of the attending physician, but it should not be less than 15 minutes. The total dose of Hemabate should not exceed 2 mg (8 doses).

Elderly: Not applicable

Paediatric population: Not applicable

Contraindications

1. Hemabate should not be used where the patient is sensitive to carboprost tromethamine or to any of the excipients listed in section 6.1.2. Acute pelvic inflammatory disease.
3. Patients with known active cardiac, pulmonary, renal, or hepatic disease.

4. Hemabate is contra-indicated in pregnancy.

Special warnings and precautions for use

Hemabate should be used by medically trained personnel and is available only to hospitals and clinics with specialised obstetric units where 24 hour resident medical cover is provided. Hemabate, as with other potent oxytocic agents, should be used only with strict adherence to recommended dosages.

This preparation should not be used for induction of labour.

Hemabate must not be given intravenously.

Special caution is necessary in patients with history of asthma, hypo- or hypertension, cardiovascular, renal, or hepatic disease, glaucoma or raised intra-ocular pressure, anaemia, jaundice, diabetes, or epilepsy.

Benefit/risk ratio should be assessed in patients with cardiovascular disease (risk of decreased blood pressure up to cardiovascular collapse, bradycardia), and in patients with a history of asthma (risk of bronchoconstriction) and pulmonary disease (possibility of decreased pulmonary blood flow and increased arterial pulmonary pressure).

Very rare cases of cardiovascular collapse have been reported following the use of prostaglandins. This should always be considered when using Hemabate.

Decreases in maternal arterial oxygen content have been observed in patients treated with carboprost tromethamine. A causal relationship to carboprost tromethamine has not been established, however, it is recommended that patients with pre-existing cardio-pulmonary problems receiving Hemabate are monitored during treatment and given additional oxygen if necessary.

As with any oxytocic agent, Hemabate should be used with caution in patients with previously compromised (scarred) uteri.

Prior treatment with, or concomitant administration of anti-emetics and antidiarrhoeal drugs significantly reduces the very high incidence of the gastrointestinal side effects common to all prostaglandins. Their use should be considered an integral part of the management of patients.

Transient pyrexia that may be due to hypothalamic thermoregulation has been observed after intramuscular Hemabate. Temperature elevations exceeding 1.1 °C were observed in approximately one-eighth of patients who received the recommended dosage regimen but if not complicated by endometritis, the temperature elevation will usually return to normal within several hours of the last injection.

Animal studies lasting several weeks at high doses have shown that prostaglandins of the E and F series can induce proliferation of bone. Such effects have also been noted in newborn infants who have received prostaglandin E_1 during prolonged treatment.

There is no evidence that short-term administration of Hemabate can cause similar bone effects.

Benzyl alcohol:
This medicine contains 9.45 mg benzyl alcohol in each ampoule which is equivalent to 9.45 mg/ml. Benzyl alcohol may cause allergic reactions.

The preservative benzyl alcohol has been associated with serious adverse events, including the "gasping syndrome", and death in paediatric patients. The minimum amount of benzyl alcohol at which toxicity may occur is not known. The risk of benzyl alcohol toxicity depends on the quantity administered and the liver and kidneys' capacity to detoxify the chemical. Premature and low-birth weight infants may be more likely to develop toxicity. High volumes should be used with caution and only if necessary, especially in subjects with liver or kidney impairment because of the risk of accumulation and toxicity (metabolic acidosis).

Sodium:
This medicine contains less than 1 mmol sodium (23 mg) per ml of solution, that is to say essentially 'sodium-free'.

Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

There have been reports of undesirable effects such as syncope, dizziness and somnolence which could impair the ability to drive or use machines.

Therefore patients should refrain from driving until they know that Hemabate does not affect their ability to drive or use machines.

Undesirable effects

Hemabate can cause serious breathing difficulties as well as asthma and wheezing.

Less frequent, but potentially more serious, adverse effects are elevated blood pressure, dyspnoea and pulmonary oedema. Other less serious adverse effects noted include chills, headache, diaphoresis, dizziness and injection site erythmea and pain.

Adverse drug reactions reported during clinical trials and post marketing experience are presented below.

Very common: may affect more than 1 in 10 people.

These include:

Diarrhoea*, nausea*, vomiting*, body temperature increased.

Common: may affect up to 1 in 10 people.

These include:

Headache*, flushing, hot flush, chills, cough, uterine haemorrhage, retained placenta or membranes, endometritis*.

Uncommon: may affect up to 1 in 100 people.

These include:

Septic shock, urinary tract infection, sleep disorder, syncope vasovagal, dizziness*, dystonia, paraesthesia, somnolence, dysgeusia, vision blurred, eye pain, vertigo, tinnitus, tachycardia, hypertension, asthma, respiratory distress, dyspnoea, hyperventilation*, wheezing, hiccups, haematemesis, upper abdominal pain, dry mouth, hyperhidrosis, torticollis, back pain, myalgia, uterine rupture, uterine cervical laceration, pelvic pain*, breast tenderness, lethargy, chest discomfort, injection site pain.

Not known: frequency cannot be estimated from the available data.

Thyrotoxic crisis†, anxiety†, nervousness, syncope†, palpitations, bronchospasm, pharyngeal oedema†, choking sensation†, epistaxis†, dry throat, upper respiratory tract infection†, retching, rash†, muscle spasms, blepharospasm, uterine disorder, chest pain†, asthenia†, excessive thirst†, hypersensitivity reactions† (e.g. anaphylactic reaction, anaphylactic shock, anaphylactoid reaction, angioedema).

* Events reported for both intramuscular and intra-amniotic routes of administration are marked with an asterisk. All other events were reported only for the intramuscular route.
† Identified from post-marketing experience.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

Overdose

Treatment of overdosage must be symptomatic at this time, as clinical studies with prostaglandin antagonists have not progressed to the point where recommendations may be made.

If evidence of excessive side-effects appears, the frequency of administration should be decreased or administration discontinued.

How to store Hemabate

Store in a refrigerator at 2 - 8°C.

Legal category

POM

Package quantities

Pack containing 10 x 1 ml ampoules of Hemabate Sterile Solution 250 micrograms/ml.

Further information

Carboprost tromethamine stimulates the myometrium of the gravid uterus to contract in a manner that is similar to that observed in the term uterus during labour. Whether or not this action results from a direct effect of carboprost tromethamine on the myometrium has not been determined with certainty at this time.

When Hemabate is given post-partum, the resulting myometrial contractions provide haemostasis at the site of placentation and hence prevent further blood loss.

Product licence number

PL 00057/1000

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Pfizer Limited, Ramsgate Road, Sandwich, Kent CT13 9NJ, UK.

Manufacturer's name and address
Pfizer Service Company BV, 10 Hoge Wei, 1930 Zaventem, Belgium.

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05/2022

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Package Leaflet: Information for the patient
HEMABATE® Sterile Solution for Injection
Carboprost tromethamine 250 mcg/ml

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
Keep this leaflet. You may need to read it again.
If you have any further questions, ask your doctor or nurse.
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Hemabate Sterile Solution is and what it is used for

Therapeutic group*

- This medicine contains carboprost tromethamine, which belongs to a group of medicines called prostaglandins. Prostaglandins are produced naturally in your body and are very important for a variety of activities, including childbirth. After childbirth they make the womb contract and to help it stay contracted, which stops heavy bleeding from the womb. Hemabate given after childbirth increases the contraction of your womb which helps to control bleeding after delivery.

Therapeutic indications

- Hemabate is a sterile solution for injection. It is available in ampoules and contains 250 mcg of the active ingredient, carboprost, per ml of solution.
- Hemabate is used to stop excessive bleeding in women who have just given birth, when bleeding is due to the womb failing to return to its normal size.

* A therapeutic group is one in which a drug is classified depending on its actions and the part(s) of the body it affects.

2. What you need to know before you are given Hemabate Sterile Solution

Do not take Hemabate

Hemabate is not suitable for all women. Your doctor may decide to give you a different medicine if any of these apply to you.

You should not be given Hemabate

- if you are allergic to carboprost tromethamine or to any of the other ingredients of this medicine listed in section 6, in particular benzyl alcohol which can cause problems in some people – see section 4 of this leaflet for more details.
- if you currently have an infection of your womb, ovaries or fallopian tubes (this may be causing pain in your pelvis or vaginal discharge).
- if you have any problems with your heart, lung, kidney or liver.
- if you are pregnant.

Warnings and precautions

Talk to your doctor or nurse before you are given Hemabate if you currently have, or have had in the past any of the following, as Hemabate will have to be used more carefully;

- lung disease, including asthma
- high or low blood pressure (including high blood pressure in pregnancy)
- heart disease or anaemia (low blood count)
- kidney or liver disease (including jaundice)
- glaucoma (raised pressure in your eyes)
- diabetes or epilepsy
- a caesarean section or any other operation on your womb

In very rare cases heart and circulation failure have been reported following the use of prostaglandins (the active ingredient of this medicine).

It is possible that this medicine may lower the oxygen levels in your blood. If you have previously suffered from conditions affecting your heart and lungs your doctor will monitor you and may give you additional oxygen as necessary.

Your doctor may give you other medicines to reduce the side effects of being sick or having diarrhoea as these are the common side effects of all prostaglandins (the active ingredient of this medicine).

Raised temperature has been observed with treatment from Hemabate. This will usually return to normal several hours after the last injection.

Other medicines and Hemabate

Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines.

Treatments that strengthen contraction of the womb, including oxytocin and ergometrine, can be affected by Hemabate. Medical staff will watch over you very carefully if you have had these treatments as well as Hemabate.

Pregnancy, breast-feeding and fertility

Hemabate will only be given shortly after you have delivered your baby and not while you are still pregnant as it could put the embryo or foetus at risk.

It is not known if carboprost is excreted in human breast milk. As your own body produces prostaglandins during childbirth, Hemabate is not expected to cause any harm to your baby.

It is not known what effects Hemabate has on your fertility.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

Do not drive, use any tools or operate machinery soon after receiving Hemabate as it may affect your ability to do so safely. Hemabate may make you lose consciousness, feel dizzy or drowsy.

Hemabate contains sodium and benzyl alcohol.
This medicine contains less than 1 mmol sodium (23 mg) per ml of solution, that is to say essentially 'sodium-free'. This medicine contains 9.45 mg benzyl alcohol in each ampoule which is equivalent to 9.45 mg/ml. Benzyl alcohol may cause allergic reactions. Benzyl alcohol has been linked with the risk of severe side effects including breathing problems (called "gasping syndrome") in young children.
Ask your doctor or pharmacist for advice if you are pregnant or breast-feeding. This is because large amounts of benzyl alcohol can build-up in your body and may cause side effects (called "metabolic acidosis").

Ask your doctor or pharmacist for advice if you have a liver or kidney disease. This is because large amounts of benzyl alcohol can build-up in your body and may cause side effects (called "metabolic acidosis").

3. How you are given Hemabate Sterile Solution

This product should be used only in hospitals and clinics with specialised units for pregnancy and childbirth. Medical staff should be available in the hospital at all times. Hemabate may be given by a doctor or a midwife.

The staff will make sure that this medicine is used in the right way and at the right time. You should never be given Hemabate while you are pregnant, only after the birth. It must never be given by injection into a vein.

- Hemabate is given by injection deep into a muscle.
- The first dose is usually 1 ml of solution (250 micrograms of carboprost). Your doctor may give you more doses of 1 ml if you need them. You should not have

doses more often than once every 15 minutes. Usually you would have them less often, about once in one-and-a-half hours.
- You should not be given more than 8 doses (2 mg of carboprost) altogether.

Hemabate is not indicated for use in children.

If you are given more Hemabate than you should be
If you get very bad sickness and diarrhoea, your doctor may delay the next injection of Hemabate, or may not give you any more doses. Your doctor will treat the symptoms that the Hemabate has caused.

If you continue to bleed
If you continue to bleed heavily after being given Hemabate you may be given other medicines to help control the bleeding. Your doctor or midwife will be watching you closely to help them decide whether Hemabate is working for you.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible Side Effects

Like all medicines, this medicine can cause side effects although not everybody gets them.

- **Effects on your respiratory system and immune system**: Hemabate can very occasionally cause serious breathing difficulties as well as asthma and wheezing. If you have any difficulty breathing after receiving Hemabate **tell your doctor or midwife immediately.**
- The benzyl alcohol in Hemabate solution can cause an allergic reaction in some people. If you suffer from wheezing together with any itching or swelling of the face or tongue **tell your doctor or midwife immediately.**

The following side effects are listed by frequency.

Very common: may affect more than 1 in 10 people.
These include: diarrhoea, nausea, vomiting, increased body temperature.

Common: may affect up to 1 in 10 people.
These include: headache, flushing, hot flush, chills, coughing, bleeding from the uterus, retained placenta or membranes, and inflammation of the uterus.

Uncommon: may affect up to 1 in 100 people.
These include: septic shock, urinary tract infection, irregular sleep patterns or general feeling of drowsiness, dizziness, muscle contractions affecting your posture and positioning of the head, general muscle pain, pins and needles, abnormal taste, increased levels of sweating, chest discomfort, severe shortness of breath, asthma and general breathing difficulties such as rapid breathing or wheezing, general pain especially in regions such as the upper abdomen, back and pelvis, tenderness of the breasts, blurred vision, eye pain, dry mouth, hiccups, vertigo, ringing in the ears, increased heart rate, high blood pressure, vomiting blood, uterine rupture, uterine

cervical laceration, fluid retention, general feeling of being unwell and injection site pain.

Not known: frequency cannot be estimated from the available data.
These include: a rare but severe form of hyperthyroidism, anxiety, nervousness, fainting, temporary loss of consciousness caused by a fall in blood pressure, palpitations, muscle spasm in the walls of the bronchioles, swelling of the throat, choking sensation, nose bleeds, dry throat, infection affecting the nose sinuses and throat, retching, rash, muscle spasms, uncontrolled abnormal contraction or twitch of the eyelid, uterine disorder, chest pain, abnormal physical weakness or lack of energy, excessive thirst and hypersensitivity reactions (e.g. anaphylactic reaction, anaphylactic shock, anaphylactoid reaction, angioedema).

Most effects are mild and short-lived and will wear off quickly after treatment.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Hemabate Sterile Solution

Keep this medicine out of the sight and reach of children.

Do not use Hemabate after the expiry date which is stated on the carton and on the ampoule after EXP. Your pharmacist will check this before the injection is given. The expiry date refers to the last day of the month.

Store in a refrigerator between 2 – 8°C. Your pharmacist will check the ampoules are still clear and colourless before use.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Hemabate contains

The active substance in each ampoule is 250 mcg of carboprost.

The other ingredients are sodium chloride (sodium content approximately 4.0 mg/ml), water for injections, tromethamine and a preservative, benzyl alcohol (9.45 mg/ml). Small amounts of hydrochloric acid and sodium hydroxide, (used to regulate the acidity or alkalinity of the solution) may also be present.

What Hemabate looks like and contents of the pack

Hemabate is a colourless solution available in glass ampoules containing 1 ml of solution. Hemabate comes in packs of two or ten ampoules.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer:

Marketing Authorisation Holder:
Pfizer Limited,
Ramsgate Road,
Sandwich, Kent,
CT13 9NJ
UK

Manufacturer:
Pfizer Service Company BV,
10 Hoge Wei,
1930 Zaventem,
Belgium.

For more information about this medicine, please contact the local representative of the local Marketing Authorisation Holder:

Medical Information,
Pfizer Limited,
Walton Oaks,
Dorking Road,
Tadworth,
Surrey,
KT20 7NS,
UK
Telephone 01304 616161

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