Enzaprost® T
The natural Prostaglandin

Uterotonic and luteolytic, naturally
Enzaprost® T:
The uterotonic and luteolytic prostaglandin, naturally!
The active compound of **Enzaprost** is Dinoprost, a tromethamine (organic buffered solution) salt of the native prostaglandin F2α.

Prostaglandins (PGF2α) of uterine origin are necessary to cause Corpus Luteum (CL) regression in bovines, which in turn will set the length of the oestrus cycle.

Dinoprost has luteolytic effect (causing the regression of the CL) and uterotonic effect (inducing myometrium contraction) as the natural PGF2α.

**Enzaprost** indications in cattle are:

1. Oestrus synchronisation.
2. Treatment of sub-oestrus or silent heat in cows which have a functional corpus luteum, but do not express behavioural oestrus.
3. Induction of abortion until day 120 of pregnancy.
4. Induction of parturition.
5. As an aid in the treatment of chronic metritis or pyometra where there is a functional or persistant corpus luteum.
Prostaglandins mode of action

Natural PGF2α half-life a natural protective mechanism!

Their main action is to cause luteolysis of a CL but it is important to highlight that newly formed CLs (less than 5 days old) are refractory to luteolytic effects of prostaglandins.

Mammals have developed mechanisms to avoid having excessive concentrations of PGF2α in blood for unnecessary periods. Therefore PGF2α is metabolized very rapidly after a single pass through the lungs. Thus, the short half-life of the natural PGF2α is in fact a protective mechanism of the normal physiology developed by mammals [1]. The natural PGF2α produced by the endometrium triggers a CL-induced oxytocin release in mature CLs, which in turn will cause more PGF2α release from the endometrium and this self-sustained endocrine loop (feedback loop, in blue in the picture shown below) will culminate with CL regression. Additionally, it has been recently demonstrated that PGF2α will induce PGF2α production in the CL in another self-sustained loop (Auto-amplification loop, in red in the picture shown below).

Luteolysis mechanisms

Auto-amplification loop
PGF2α from endometrium or exogenous origin induces PGF2α production in the CL in a self-sustaining loop

Feedback loop
PGF2α from uterus or exogenous origin induces Oxytocin production in the CL, which induces more PGF2α release from the endometrium
Analogues versus natural Prostaglandins

Prostaglandins can be natural like Enzaprost®T (dinoprost) or agonists like synthetic analogues.

Analogues have only limited action on the smooth muscles as this was considered to be a harmful side-effect when these synthetic PGF2α were originally developed.

Analogue compounds include cloprostenol and d-cloprostenol, luprostiol, etiproston, alfaprostol and others and they are normally dosed at 2ml/animal.

Enzaprost®T (dinoprost) is a natural prostaglandin so it has an enhanced action on uterine contraction with an equivalent luteolytic effect. Dinoprost is dosed at 5ml/animal.

**Enzaprost®T has a greater uterotonic effect than prostaglandin analogues with the same luteolytic effect!**
Enzaprost® T exerts greater activity than d-cloprostenol and alfaprostol on both longitudinal and circular muscle of bovine myometrium during the luteal phase in an *in vitro* model [5].

An *in vivo* study measuring intra-uterine pressure, Dinoprost exerts greater uterotonic activity in all stages of the cycle particularly during dioestrous when there is an active corpus luteum [6].

Interestingly, the enhanced activity of the natural PGF_2α_ is thought to be related to its much greater binding affinity to myometrial and CL cell receptors than for synthetic analogues. This affinity has been reported to be roughly 10 times greater than dl-Cloprostenol for myometrial cells and staggeringly 150 times greater than dl-Cloprostenol for PGF_2α_ receptors in CL cells [7].
2. Equivalent luteolytic effect in oestrus induction in beef cattle!

A very large (>1,000 animals enrolled) and well designed trial [8] to compare oestrus responses and conception results between dinoprost and cloprostenol using beef heifers as experimental units, found no significant effects on percentage and synchrony of oestrus or conception results for both PGF2α products tested.

3. Superior luteolytic effect in fixed-time artificial insemination in dairy cattle!

A recent publication [9] reporting results from two large field studies done in multiple herds in synchronised-lactating dairy cows showed a significant improvement in luteolysis rates in cows bearing a responsive CL that were treated with dinoprost as compared to cloprostenol (Exp 1: dinoprost 91.3% vs cloprostenol 86.6%, P<0.05). The same study also reported that dairy cows with unknown pregnancy status receiving a Re-synchronization program also presented greater (P<0.05) luteolysis rates after dinoprost treatment (78.5%) than after cloprostenol (69.1%).

![Graph showing luteolysis rates comparison between dinoprost and cloprostenol](image_url)

Source: adapted from Stevenson and Phatak, 2010
Enzaprost® T uses

Most common uses of Enzaprost® T in bovine reproduction

- Uterine involution and treatment of uterine infections
- Induction of synchronous oestrus in non-pregnant/cycling cattle
- In synchronisation protocols for fixed-time insemination
- Improve luteolysis and conception
- Terminate undesirable pregnancies, induce labor, and other alternative uses during calving time

PGF2α used during Pre-synchronisation for 1st postpartum AI (artificial insemination)

PGF2α for cows detected non-pregnant and assigned to a Re-synch protocol for 2nd or later AIs

PGF2α towards the end of synchronisation programs for timed AI to induce CL regression
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References


Ask your Ceva representative for ReprodAction advice
ENZAPROST 5 mg/ml Solution for injection for cattle and pigs. COMPOSITION. Each 1ml contains: Active substance: Dinoprost (as trometamol) 5 mg. Excipients: Benzyl alcohol (E1519) 16.5 mg. INDICATIONS. The product is indicated for its luteolytic effects in cattle and pigs. Cattle: The luteolytic effect of the product can be exerted in the following therapeutic uses: 1. Oestrus synchronisation. 2. Treatment of sub-oestrus or silent heat in cows which have a functional corpus luteum, but do not express behavioural oestrus. 3. Induction of abortion until day 120 of pregnancy. 4. Induction of parturition. 5. As an aid in the treatment of chronic metritis or pyometra where there is a functional or persistent corpus luteum. Pigs: 1. Induction of parturition from day 111 of pregnancy. 2. Post partum use: reduction of the weaning to oestrus interval (WOI) and the weaning to fertility service interval (WFSI) in sows with puveral problems such as metritis in herds with reproductive problems. CONTRA-INDICATIONS. Do not treat animals if they suffer from either acute or subacute disorders of the vascular system, gastro-intestinal tract or respiratory system. Do not administer to pregnant animals, unless it is desirable to induce parturition or interruption of pregnancy. Do not use in cases of known hypersensitivity to the active substance or to any of the excipients. ADVERSE REACTIONS. Cattle: The most frequently observed side-effect is increased rectal temperature. However, rectal temperature changes have been transient in all cases observed and have been of no detriment to the animal. Limited salivation has been seen in some instances. The side-effects disappear within one hour after the instillation. In rare occasions, increased salivation, flushing of skin and restless behaviour (arching of back, pawing, and rubbing and graving the crate), dyspnea, slight ataxia, abdominal muscle spasms, vomiting and pruritus occur occasionally following the administration of dinoprost in pregnant sows and gilts. These effects tend to parallel the signs exhibited by sows prior to normal parturition, only to be condensed in these effects. They are usually seen within 10 minutes of injection and disappear within 3 hours. Nest building is a common behaviour 5 to 10 minutes after the administration of prostaglandin in sows that are housed in pen or pasture. In very rare occasions, anaphylactic-type reactions have been reported. Men, women of child-bearing age, asthmatics and persons with bronchial and other respiratory problems should not use the product or should wear disposable plastic gloves. Men, women who are pregnant, intending to become pregnant, or whose pregnancy status is unknown and to asthmatics and persons with bronchial or other respiratory problems. AS THMatics and persons with bronchial or other respiratory problems should handle the product with care to avoid accidental self-injection and skin contact. Pregnant women, women of child-bearing age, asthmatics and persons with bronchial and other respiratory problems should not use the product or should wear disposable plastic gloves. Use during pregnancy, lactation or lay. Pregnancy status should be determined prior to injection since Dinoprost has been demonstrated to result in abortion or parturition induction when administered at sufficiently high doses in many animal species. If pregnant, the unlikely possibility of uterine rupture should be borne in mind, especially if cervical dilation does not occur. Further indication of induction in parturition than 72 hours prior to predicted foetal membranes may occur more frequently, depending on the gestational age at treatment. Interaction with other medicinal products and other forms of interaction. As non-steroidal anti-inflammatory drugs may inhibit the endogenous prostaglandin synthesis, concomitant administration of these compounds with the product may exacerbate the luteolytic effects. Ovulatory suppression, emergency procedures, antidiabetes, if necessary increased rectal temperature and a slight transitory increase in heart rate can be observed at 5 or 10 times the recommended dosage in cows and heifers. In absence of compatibility studies do not mix with other veterinary medicinal products. PRESENTATIONS: Pack sizes: 10 vials of 5 ml. 5 vials of 10 ml. 1 vial of 30 ml. 1 vial of 50 ml. Not all pack sizes may be marketed. FOR ADDRESSES AND ADDRESS OF THE MARKETING AUTHORIZATION HOLDER: CEVA SANTE ANIMALE - 10 av. de la Ballastière - 33500 LIBOURNE. Indications featured in the product leaflet and product information sheet are subject to consultation and change. For more information about the specific use of this product refer to the SPC of your country.