Hypophysin® LA
35 µg/ml

Hypophysin® LA
70 µg/ml

Gentle and long lasting rhythmic stimulation of uterus contractions in case of uterine inertia and interrupted involution of the uterus post partum

Compressing the onset of parturition in swine
Compared to exogenously introduced oxytocin, Hypophysin® LA has the advantage of a prolonged effect. Due to the long lasting stimulation of rhythmic uterine contractions, the uterine inertia is effectively treated in various species.

With respect to pigs, the commencement of farrowings for a group of animals can be successfully confined to a few hours through the additional administration of Hypophysin® LA (24 hours following the PGF$_{20}$ treatment) within the scope of partus synchronisation with PGF$_{20}$ (i.e. PGF Veyx®). However, for the piglet’s developmental maturity it is recommended that PGF$_{20}$ is administered at the earliest on the 114$^{th}$ day of pregnancy (the day following the first insemination is to be taken as the first day of pregnancy). Only 35 µg Carbetocin is to be given for synchronising of parturition in the pig.

In addition, placental expulsion and the progression of the postpartal period are positively influenced following the treatment with Hypophysin® LA in cattle and pigs.

Both Hypophysin® LA products are approved for cattle and pigs. With 1 ml of the finished product Hypophysin® LA 35 µg/ml the recommended dosage of the active ingredient is administered to pigs for the synchronisation of parturition. The traditional product Hypophysin® LA 70 µg/ml is to be administered in the usual dosage rates.
Hypophysin® LA 35 µg/ml solution for injection for cattle and pigs
Hypophysin® LA 70 µg/ml solution for injection for cattle and pigs,
Carbetocin

Statement of the active substance and other ingredients
Hypophysin® LA is a clear colourless solution for injection containing:

Hypophysin® LA 35 µg/ml
Active substance:
Carbetocin 35.00 µg/ml
Excipients:
Chlorocresol 1.00 mg/ml

Hypophysin® LA 70 µg/ml
Active substance:
Carbetocin 70.00 µg/ml
Excipients:
Chlorocresol 1.00 mg/ml

Indications
Cow:
- Uterine atony during the puerperal period
- Placental retention as a consequence of uterine atony
- Initiation of milk ejection in stress-induced agalactia or other conditions requiring udder emptying

Sow:
- Acceleration or restart of parturition after disruption of uterine contractions (uterine atony or inertial) following the expulsion of at least 1 piglet
- Supportive therapy of mastitis-metritis-agalactia (MMA-) syndrome
- Initiation of milk ejection
- Shortening of total parturition duration as a component of synchronisation of parturition in sows. The product may be applied to sows which have previously been administered an appropriate PGF₂α (e.g. cloprostenol) not prior to day 114 of pregnancy and have not started farrowing within 24 hours after the PGF₂α injection (day 1 of pregnancy is the last day of insemination).

Contraindications
Do not administer to accelerate parturition if cervix is not opened or if there is a mechanical cause for the delayed parturition such as physical obstruction, positional and postural abnormalities, convulsive labour, threatened rupture of uterus, uterine torsion, relative foetal oversize or deformities of the birth canal.
Do not use in case of hypersensitivity to the active substance or to any of the excipients.

Adverse reactions
Carbetocin may have an uterotonic effect in the late pregnancy.
If you notice any serious effects or other effects not mentioned in this package leaflet, please inform your veterinary surgeon.

Target species
Cattle, pigs.

Dosage for each species, routes and method of administration
For intramuscular and intravenous injection. Treatment takes place as a rule only once.

Hypophysin® LA 35 µg/ml
Cows
For all indications:
6.0 - 10.0 ml/animal, corresponding to 210 – 350 µg carbetocin/animal

Sows
For shortening of total parturition duration as a part of the synchronisation of parturition:
1.0 ml/animal, corresponding to 35 µg carbetocin/animal
For acceleration or restart of parturition after disruption of uterine contractions (uterine atony or inertial) following the expulsion of at least 1 piglet:
1.0 - 2.0 ml/animal, corresponding to 35 - 70 µg carbetocin/animal
For MMA and milk ejection:
3.0 – 6.0 ml/animal, corresponding to 105 – 210 µg carbetocin/animal

Hypophysin® LA 70 µg/ml
Cows
For all indications:
3.0 – 5.0 ml/animal, corresponding to 210 – 350 µg carbetocin/animal

Sows
For shortening of total parturition duration as a part of the synchronisation of parturition:
0.5 ml/animal, corresponding to 35 µg carbetocin/animal
For acceleration or restart of parturition after disruption of uterine contractions (uterine atony or inertial) following the expulsion of at least 1 piglet:
0.5 - 1.0 ml/animal, corresponding to 35 - 70 µg carbetocin/animal
For MMA and milk ejection:
1.5 – 3.0 ml/animal, corresponding to 105 – 210 µg carbetocin/animal

The dosage requirements can be variable within the indicated limits based on the assessment of the veterinarian.
In case of treatment for milk ejection in the cow and sow or supportive therapy in MMA-syndrome in sow, a repeated administration is possible after 1 to 2 days.
The rubber stopper of the vial may be safely punctured up to 25 times. Otherwise, automatic syringe equipment, or a suitable draw-off needle, should be used for the 20 and 50 ml vials to avoid excessive puncturing of the closure.

Advice on correct administration
See “Dosage for each species, routes and method of administration”

Withdrawal period
Cattle, pigs: Meat and offal Zero days
Cattle: Milk Zero days
Special storage precautions
Keep out of the sight and reach of children. Store in a refrigerator (2 - 8 °C). Keep the vial in the outer carton in order to protect from light. Do not use this veterinary medicinal product after the expiry date which is stated on the carton and vial label after "EXP". The expiry date refers to the last day of that month. Shelf life after first opening the immediate packaging: 28 days. When the container is broached [opened] for the first time, using the in-use shelf life which is specified on this package insert, the date on which any product remaining in the vial should be discarded should be worked out. This discard date should be written in the space provided on the label.

Special warnings
Special warnings for each target species:
The responsiveness to carbetocin of the myometrium is likely to be close to zero from the 5th to the 11th day post partum. Therefore, the administration of the veterinary medicinal product during this period is likely to be inefficient and should be avoided. If treatment with carbetocin should fail, then it is advisable to reconsider the aetiology of the condition, specifically if hypocalcaemia could be a complicating factor. In case of severe septic metritis, appropriate concomitant therapy should be instigated when administering the veterinary medicinal product.

Special precautions for use:
Special precautions for use in animals:
The interval between two injections should not be shorter than 24 hours.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
In case of an accidental self-injection of the veterinary medicinal product in non-pregnant women the following effects may occur: facial flushing and warmth, lower abdominal pain. These effects usually disappear within a short span of time. Pregnant women, women post partum and breast-feeding women should not use this product, in order to avoid an accidental exposure. In case of accidental self-injection uterine contractions could be induced in pregnant women. In the case of accidental self-injection, seek medical advice and show the package leaflet to the doctor. In case of accidental contact with the skin, the corresponding area should be thoroughly cleaned with soap and water, as carbetocin may be absorbed through the skin. In case of contact with the eyes, they should be thoroughly rinsed with water. Persons with a known hypersensitivity to carbetocin or any of the excipients should not administer the product. Women of childbearing age should administer the product with special caution.

Use during pregnancy, lactation or lay:
The veterinary medicinal product is indicated to induce milk ejection. See also “Contraindications”.

Interaction with other medicinal products and other forms of interaction:
The administration of oxytocin after the administration of the veterinary medicinal product is unnecessary. Due to a possible intensification of the effect of oxytocin, undesirable uterine spasms may be induced.

Overdose (symptoms, emergency procedures, antidotes):
An overdosing of more than 400 μg of carbetocin/animal could increase the stillbirth rate in older sows if administered during prolonged parturition. An overdosing of 600 μg of carbetocin/animal may induce profuse lactation in sows that may result in diarrhoea, reduced weight gain and increased mortality in their piglets. Carbetocin is considered as moderately irritant. At the injection sites of treated animals, focal lymphocytic infiltration was observed at higher doses (1000 μg of carbetocin/animal).

Incompatibilities:
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

Special precautions for disposal of unused product or waste materials, if any
Medicines should not be disposed of via wastewater or household waste. Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment. Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

To be supplied only on veterinary prescription.

Package sizes
Hypophysin® LA 35 μg/ml
50 ml vial
100 ml vial

Hypophysin® LA 70 μg/ml
20 ml vial
50 ml vial

The information given in this product brochure conform to the state of knowledge on completion.

Please read the package leaflet before using the veterinary medicinal product!
Basic physiological principles
Oxytocin is a hormone comprising of 9 amino acids. It is produced in the hypothalamus and is carried to the posterior lobe of the pituitary gland via neuro-secretion and is stored there bound to neurophysin. This protein bond is released in the presence of calcium ions by nervous stimulation. During the dilation stage of parturition, the distension of the cervix by the foetus triggers the stimuli that induce the increased secretion of oxytocin (FERGUSON reflex).

Suckling, mechanical stimulation of the udder, as well as the placing of teat cups (in cattle), are additional releasing stimuli. Oxytocin effects contractions of the smooth uterine muscles as well as of the myoepithelial basket cells of the mammary gland. The responsiveness of the uterine muscles to oxytocin varies during the various phases of the oestrous cycle or pregnancy. The highest degree of efficacy is achieved when the level of oestrogen is high and the level of progesterone is low. Oxytocin only becomes effective if it is bound to specific receptors. The receptors, in turn, are developed as a consequence of the increase in the oestrogen levels. Oxytocin effects a contraction of the muscles via membrane depolarisation. After the contraction is achieved the muscle cell remains refractory for a certain period of time until oxytocinase enzymes have degraded the hormone. After repolarisation, the muscle cell regains its sensitivity to oxytocin. This rhythmics comprises a period of 3 to 5 minutes (i.e. GRUNERT 1993; KROKER 1997). Due to its short half-life, preparations containing oxytocin have severely limited therapeutic application possibilities within the scope of obstetrics. The application of Hypophysein® LA presents an alternative in this case, because of its substantially longer duration of effect.

Chemistry
Carbetocin is a synthetic analogue of the original oxytocin with a prolonged effect. The molecular weight is 988.17 g/mol.

The structural formula of carbetocin is as follows:

![Chemical Structure of Carbetocin](image)

Pharmacology
Carbetocin has basically the same principal effect as oxytocin. Characteristic of Carbetocin is the longer–acting effect on the myometrium and the myoepithelial basket cells of the mammary gland (i.e. CORT et al. 1981; STROHBACH and STROHBACH 1989; BERNHARD et al. 1993; EULENBERGER et al. 1993). Carbetocin is bound to the oxytocin receptors at the action site (ATKE and VILHARDT 1987).

In the uterus, carbetocin primarily stimulates the longitudinal muscle fibres, whilst the impact on the sphincter muscles (in the region of the cervix and the vaginal) is marginal. The effect of carbetocin on the uterus is strictly receptor-bound; it is neither affected by adrenalin nor by ergometrine. The pharmacodynamics of carbetocin is more pronounced in a gravid uterus than in the non-gravid organ. Uterine efficiency of carbetocin was proven in various species (l.a. BARTH et al. 1980; EULENBERGER et al. 1986, 1987; STROHBACH and STROHBACH 1989; TAURA et al. 1992; BERNHARD et al. 1993; EULENBERGER 1993; SCHULZ 1993). Like oxytocin, carbetocin already intensifies uterine-muscle contractions within a few minutes following parenteral application. The effectivity of carbetocin in terms of intensity and frequency of induced labour is very similar to that of endogenous oxytocin secretion. Tetanic or high-frequency contraction activities - a possible complication in repeated parenteral administration of oxytocin - are not to be expected with the application of carbetocin. As electro-hysterographic examinations in cattle and pigs have shown, carbetocin results in several hours of intensified uterine motor activity (up to a maximum of 6 hours).

An even longer mode of action was ascertained after the administration of various carbetocin-dosage rates in sows approx. 5 hours after birth of the last piglet. The intrauterine pressure was measured for a period of 10 hours following administration. Rhythmic uterine contractions were seen over the whole measuring period and that after the administration of 70 µg Carbetocin as well as after the administration of 35 µg. However, in the initial phase considerably stronger contractions were measured with the higher dosage rate in comparison to the lower dosage rate. With 35 µg a very rhythmic contraction model is achieved immediately (figure 1). The use of a physiologic salt solution did not lead to a considerable increase of the intrauterine pressure (figure 2).

![Figure 1: Development of intrauterine pressure after intramuscular application of 70 µg or 35 µg Carbetocin (extract from the pressure curve)](image)
Figure 2: Development of intrauterine pressure after intramuscular application of 1 ml NaCl (extract from the pressure curve)

However, after administration of oxytocin, the intensified activity lasts for up to only 20 minutes. The stimulation of milk ejection in pigs by intensified contraction of the alveolar muscle fibres in the mammary gland also begins a few minutes after carbetocin application and the effect lasts on average for 6 to 7 hours (see table 1). In contrast, upon administration of oxytocin, the effect on milk flow is only short-term (CORT et al. 1982).

Table 1: Influence of carbetocin and oxytocin on the duration of stimulation of milk ejection in sows (CORT et al. 1982)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number of animals</th>
<th>Average duration (hours)</th>
<th>Confidence interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbetocin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>200 µg i.v.</td>
<td>4</td>
<td>6.00</td>
<td>3.30 - 7.00</td>
</tr>
<tr>
<td>200 µg i.m.</td>
<td>4</td>
<td>6.00</td>
<td>4.00 - 7.00</td>
</tr>
<tr>
<td>400 µg i.v.</td>
<td>4</td>
<td>6.50</td>
<td>3.30 - 8.30</td>
</tr>
<tr>
<td>400 µg i.m.</td>
<td>4</td>
<td>6.30</td>
<td>4.00 - 9.00</td>
</tr>
<tr>
<td>600 µg i.v.</td>
<td>10</td>
<td>6.15</td>
<td>4.00 - 9.00</td>
</tr>
<tr>
<td>600 µg i.m.</td>
<td>10</td>
<td>7.00</td>
<td>4.30 - 9.00</td>
</tr>
<tr>
<td>Oxytocin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 - 10 IU i.v.</td>
<td>4</td>
<td>0.14</td>
<td>0.10 - 0.20</td>
</tr>
</tbody>
</table>

As a result of acute toxicity examinations in rats, it was found that the LD50 for intravenous application is exceeding 0.875 mg/kg live weight. The mean lethal dose using intramuscular or subcutaneous administration is in each case higher than 1.75 mg/kg live weight. As this dosage exceeds the therapeutic dose 500- to 1,000-fold the therapeutic dose, carbetocin may be classified as a substance with a minimal toxicological risk. This opinion is supported by other partially subchronic research into undesirable or toxic effects. carbetocin does not have any impact on diuresis and blood pressure. There are no relevant effects from a biological residue point of view, which justifies why there is no requirement to observe a withdrawal period.
Pharmacotherapy
Tolerance and action of Hypophysin® LA were tested inter alia in cows, sows, mares, small ruminants and bitches with a normal or disturbed course of labour.

Application in cattle
The application of Hypophysin® LA is indicated sub partu in cattle because of its effect in protracting the uterine mobility in primary and if necessary, secondary uterine inertia. Moreover, if it is administered during the dilation stage, Hypophysin® LA results in an acceleration of the remainder of labour by shortening the dilation and expulsion phase of parturition (i.e. STROHBACH and STROHBACH 1989, see table 2). In the presence of uterine inertia and/or prolonged duration of labour, Hypophysin® LA can only be used if dystocia (e.g. malpresentation of the foetus, torsio uteri) can be excluded or is eliminated. The stimulation of uterine contractions by subpartial administration of Hypophysin® LA further results in shortening the placental stage as well as in lowering the incidence of foetal membrane retention, as research of the aforementioned authors has shown in a herd of cattle with a high percentage of placental retention (see also table 2).

Table 2: Influence of the administration of Hypophysin® LA in cattle in the dilation phase* under consideration of clinically significant parameters [STROHBACH and STROHBACH 1989]

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Hypophysin® LA 70 µg/ml (n = 70)</th>
<th>Placebo (n = 44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interval between application and birth of the calf (in minutes)</td>
<td>43</td>
<td>75</td>
</tr>
<tr>
<td>Dystocia (%)</td>
<td>15.7</td>
<td>15.9</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>0</td>
<td>2.3</td>
</tr>
<tr>
<td>Vitality of live born calves (average score on a scale with a maximum of 10 points)</td>
<td>9.8</td>
<td>9.4</td>
</tr>
<tr>
<td>Delay in the expulsion of the placenta (%)</td>
<td>17.1</td>
<td>29.5</td>
</tr>
<tr>
<td>Placental retention (%)</td>
<td>8.6</td>
<td>17.5</td>
</tr>
</tbody>
</table>

* Administration of 5.0 ml Hypophysin® LA 70 µg/ml approximately 40 minutes after rupture of the membranes

Even if Hypophysin® LA is only administered shortly after parturition, the frequency of disorders related to placental retentions is reduced (STROHBACH and STROHBACH 1989). On the basis of the aforementioned trial results, metaphylactic application of Hypophysin® LA during the dilation stage or shortly after calving in herds of cattle with a high prevalence of placental retention is recommended. Puerperal disorders in cattle are frequently manifested in the form of uterine atony with a delay in involution and an intensive accumulation of lochia. Under these circumstances, contractions of the myometrium are stimulated and the expulsion of lochia is promoted by administration of Hypophysin® LA during the first 5 days after parturition [EULENBERGER et al. 1987]. However, between the 6th and 10th day post partum, the responsiveness of the myometrium to Hypophysin® LA is extremely marginal. Only from the 11th day post partum the uterine muscles are sensitive to Hypophysin® LA again due to the influence of the restarted follicular activity. However, in clinically manifest puerperal endometritis the treatment with Hypophysin® LA has only a supportive function. In this process of disease the additional supportive treatment of the uterus to depress pathogenic organisms is very essential.
Application in pigs
In sows, a delayed period of parturition is often associated with an increased percentage of stillborn piglets. Moreover, a prolonged period of parturition favours the occurrence of puerperal diseases (i.a. SCHNURRBUSCH and HÜHN 1994). The stimulation of insufficient uterine motility sub partu or post partum by one single application of oxytocin must be considered as inadequate due to its short duration of effect. In contrast the administration of Hypophysin® LA has a prolonged and thus more intense effect. The duration of parturition is significantly reduced upon administration of Hypophysin® LA (I. a. UDLUFT and UDLUFT 2003, see table 3).

<table>
<thead>
<tr>
<th>Labour stimulating injection</th>
<th>Sows (n)</th>
<th>Timing of the injection (min after parturition began)</th>
<th>Duration of parturition per piglet born (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Before injection</td>
</tr>
<tr>
<td>20 IU Oxytocin</td>
<td>44</td>
<td>126.0</td>
<td>42.9</td>
</tr>
<tr>
<td>140 µg carbetocin</td>
<td>47</td>
<td>178.4</td>
<td>46.5*</td>
</tr>
<tr>
<td>70 µg carbetocin</td>
<td>52</td>
<td>140.4</td>
<td>41.2*</td>
</tr>
</tbody>
</table>

a, b: The differences between the groups were significant (p < 0.05).
A, B: The differences between the values before and after injection were significant (p < 0.05).

Subject to the exclusion of any other complications of parturition the best results are to be achieved if Hypophysin® LA is administered upon the occurrence of interruption of birth. The sustained efficacy of Hypophysin® LA is also manifested in the significantly lower rate of puerperal diseases in pigs (see table 4), in comparison with that associated with the administration of oxytocin.

Table 4: Influence of subpartal administration of Hypophysin® LA or oxytocin in pigs on the puerperal course (application upon expulsion of the 1st piglet) (STROHBACH and STROHBACH 1989)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Hypophysin® LA (n = 56)</th>
<th>Oxytocin (n = 55)</th>
<th>Placebo (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Puerperal disorders (%) (mastitis, endometritis, fever 3rd day post partum)</td>
<td>23.2</td>
<td>38.2</td>
<td>48.0</td>
</tr>
<tr>
<td>Treatments per sow (total)</td>
<td>0.25</td>
<td>0.69</td>
<td>0.58</td>
</tr>
<tr>
<td>Treatment per illness</td>
<td>1.1</td>
<td>1.7</td>
<td>1.2</td>
</tr>
</tbody>
</table>

On numerous pig breeding and piglet production farms with synchronised farrowing using PGF2α or its analogue constitutes a significant procedure within the herd management. The following objectives are to be achieved with the synchronisation of parturition: the concentration of farrowings for a group of sows within strictly limited time periods and thus improved birth monitoring, shifting births to daytime working hours and “farrowing-free” weekends. Approximately 12 to 36 hours after prostaglandin application, the expulsion stage in sows begins. On average, the response of gilts is slightly slower than that of adult sows. Due to the fact that foetuses gain a lot of weight during the last days of gestation, the injection for inducing parturition should be administered on the 114th day at the earliest in order to ensure an adequate development (the day after 1st insemination is considered to be the 1st day of pregnancy!).

Recommended that Hypophysin® LA is given to sows if farrowing has not commenced within approximately 24 hours after the prostaglandin injection. With the administration of Hypophysin® LA much better synchronisation effects are achieved than with the administration of oxytocin (I. a. GERICKE and HÜHN 1990; SCHNURRBUSCH and HÜHN 1994; UDLUFT 2004).

As can be seen from figure 3, the farrowing period following the administration of Hypophysin® LA is considerably shorter than with the administration of PGF2α alone. Induced farrowings are then concentrated within only a few hours, and as a consequence, births can be batched at a certain time of day. The farrowing process following induced parturition is normal. Extensive evaluations have also shown no indications that repeated induced births in consecutive farrowings produced any negative effects.

In order to compress the onset of parturitions even further, pursuant to extensive research, it is
Figure 3: Onset of parturition in sows without induction of parturition, after induction of parturition with PGF₂α as well as after combined PGF₂α and Hypophysin® LA treatment (acc. to LEIKE and HÜHN 1992). The batching of farrowing relative to the time following administration of Hypophysin® LA is clearly evident.

Without induction of parturition (n = 308)

Induction of parturition with PGF₂α (n = 407)

Induction of parturition with PGF₂α and Hypophysin® LA (n = 239)

As long years of experience have demonstrated, synchronisation effects are most efficient if the prostaglandin preparation [cloprostenol] is administered on the 114th day and if Hypophysin® LA is administered one day later [in each case, the preparations should be applied in the morning]. If, as shown in figure 3, the first insemination is carried out on Tuesday, then the 114th day of gestation will be a Thursday. If the sows are administered PGF₂α on Thursday morning and Hypophysin® LA approximately 24 hours later, the parturition of the sows of the respective group will in general be completed by Friday afternoon.
Within the framework of controlling parturition with PGF<sub>2α</sub>, UDLUFT (2004) tested different dosages of Hyophsyn<sup>®</sup> LA (see tables 5 – 7). These tests did not reveal any significant differences regarding the duration of parturition in adult sows and gilts between a dosage of 35 μg and 70 μg carbetocin per animal. At a higher dosage of carbetocin however, the practitioners identified a premature let-down or expulsion of colostrum in a relatively high percentage of the treated sows. Therefore only 35 μg carbetocin should be administered for synchronisation of parturition.

Extensive studies into this issue revealed that the avoidance of undesired prolonged gestation periods through the induction of farrowing has a prophylactic effect on puerperal diseases and has a positive influence on the rearing performance (i.a. SCHNURRBUSCH and HÜHN 1994; HÜHN and GEY 1999; UDLUFT 2004).

Table 5: Influence of varying parturition control measures on the onset and the duration of parturition and the proportion of piglets born dead (UDLUFT 2004).

<table>
<thead>
<tr>
<th>Group</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method of induction of parturition</td>
<td>Spontaneous commencement of birth</td>
<td>175 μg Cloprostenol</td>
<td>as B plus 20 IU Oxytocin 24 h after Cloprostenol</td>
<td>as B plus 70 μg Carbetocin 24 h after Cloprostenol</td>
<td>as B plus 35 μg Carbetocin 24 h after Cloprostenol</td>
</tr>
<tr>
<td>n (complete data sets, entire birth documented)</td>
<td>585</td>
<td>526</td>
<td>134</td>
<td>155</td>
<td>162</td>
</tr>
<tr>
<td>Birth commenced post injection (min)</td>
<td>-</td>
<td>781</td>
<td>145</td>
<td>96</td>
<td>85</td>
</tr>
<tr>
<td>Duration of parturition per piglet born (min)</td>
<td>21.1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>20.6&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>21.1&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>19.3&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>18.6&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Stillborn piglets (%)</td>
<td>8.9&lt;sup&gt;a&lt;/sup&gt;</td>
<td>6.6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>7.1&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>5.6&lt;sup&gt;b,c&lt;/sup&gt;</td>
<td>5.3&lt;sup&gt;b,c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

a, b, c: Differences between the groups were significant (p < 0.05).
Table 6: Influence of varying parturition control measures on the frequency of puerperal diseases (UDLUFT 2004).

<table>
<thead>
<tr>
<th>Group</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method of induction of parturition</td>
<td>Spontaneous commencement of birth</td>
<td>175 µg Cloprostenol</td>
<td>as B plus 20 IU Oxytocin 24 h after Cloprostenol</td>
<td>as B plus 70 µg Carbetocin 24 h after Cloprostenol</td>
<td>as B plus 35 µg Carbetocin 24 h after Cloprostenol</td>
</tr>
<tr>
<td>n (including incomplete data sets)</td>
<td>710</td>
<td>719</td>
<td>180</td>
<td>175</td>
<td>191</td>
</tr>
<tr>
<td>Proportion of sows with puerperal diseases [%]</td>
<td>12.8&lt;sup&gt;a&lt;/sup&gt;</td>
<td>10.4&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>9.4&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>8.6&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>7.9&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

a, b, c: Differences between the groups were significant (p < 0.05).

Table 7: Influence of varying parturition control measures on the piglet losses (UDLUFT 2004).

<table>
<thead>
<tr>
<th>Group</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method of induction of parturition</td>
<td>Spontaneous commencement of birth</td>
<td>175 µg Cloprostenol</td>
<td>as B plus 20 IU Oxytocin 24 h after Cloprostenol</td>
<td>as B plus 70 µg Carbetocin 24 h after Cloprostenol</td>
<td>as B plus 35 µg Carbetocin 24 h after Cloprostenol</td>
</tr>
<tr>
<td>n (valuable litters)</td>
<td>539</td>
<td>498</td>
<td>129</td>
<td>147</td>
<td>154</td>
</tr>
<tr>
<td>Piglet losses [%]</td>
<td>18.0&lt;sup&gt;a&lt;/sup&gt;</td>
<td>14.6&lt;sup&gt;b&lt;/sup&gt;</td>
<td>10.0&lt;sup&gt;c&lt;/sup&gt;</td>
<td>9.3&lt;sup&gt;c&lt;/sup&gt;</td>
<td>9.0&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

a, b, c: Differences between the groups were significant (p < 0.05).
The information given in this product brochure conforms to the state of knowledge on completion.

**Further information is available from the SPC. Please refer to the product package leaflet for full information concerning side effects, precautions, warnings and contra-indications.**

Authors:
Priv. Doz. Dr. Dr. habil. Wolfgang Zaremba
Dr. Silke Engl

Veyx-Pharma is GMP- and QS-certified.

Veyx-Pharma GmbH · Soehreweg 6 · 34639 Schwarzenborn · Germany
Phone 0049 5686 99860 · Fax 0049 5686 1489 · E-Mail zentrale@veyx.de
www.veyx.de · www.veyx.com