Practical guide to bovine reproduction management
Reproductive efficacy is a major limiting factor in the economic success of cattle operations world wide.

The first problem faced is oestrus detection: oestrus of continuously decreasing duration, accompanied by less and less expressive behaviour is currently becoming characteristic in dairy cows. Abnormal cycles, in particular those with a persistent corpus luteum, are becoming more frequent in herds (up to 40% of cycles), making it difficult for the farmer to meet breeding time targets.

Secondly, the success rate of artificial insemination in dairy cows is decreasing by 1 percentage point every year, this indicates an urgent need for easy to follow treatment protocols that address problems such as ovulation failure, early embryonic mortality and chronic endometritis. This practical guide presents the main solutions for treatment and prevention of the majority of reproductive disorders frequently diagnosed by the veterinary practitioner in the cattle herds.

Sylvie Chastant-Maillard

Docteur Vétérinaire, Maître de conférences, Responsable de l’Unité de Reproduction Ecole Vétérinaire d’Alfort.
Proper reproduction management is widely acknowledged as a key to successful cattle breeding, high quality veterinary advice is of prime importance to achieve this. At Intervet Schering Plough AH, we strive to provide veterinarians with therapeutic and management solutions to contribute to the economic success of their clients, the farmers, as well as their own professional success.

Intervet Schering Plough AH supports veterinarians with:
- A wide range of products that demonstrate our leadership in the field of reproduction management in domestic animals.
- Training activities by invited opinion leaders and Intervet experts, bringing you the latest technical information and its applications in the field, including luteal support during early pregnancy.

This practical guide, focused on reproduction management of dairy cattle, has been created to assist veterinarians in their daily work.

The following sections are covered:
- Prophylactic and treatment schemes adapted to various situations encountered in the field.
- Zootechnical protocols – oestrus management made as clear and simple as possible.
- Latest knowledge on physiology of reproduction and its practical applications.
- Practical information on the use of Intervet products in reproduction management in cattle.

Intervet Schering Plough AH – your partner in reproduction
Reproductive disorders in the cow: preventive and therapeutic approaches

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# Diagnostic guide
When are certain disorders of the female reproduction tract suspected?

<table>
<thead>
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<th>Signs of decreased reproduction performance of the cow</th>
<th>Possible underlying reproductive disorders</th>
<th>Remarks</th>
</tr>
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<tbody>
<tr>
<td>Abnormal vaginal discharge within first two weeks post calving</td>
<td>Acute metritis</td>
<td>In general characterised by abundant foul smelling vaginal discharge. Often accompanied by general clinical signs of illness.</td>
</tr>
<tr>
<td>Abnormal vaginal discharge from 14 days post calving</td>
<td>Clinical endometritis/Chronic endometritis</td>
<td>In general the vaginal discharge is limited and is observed mainly during oestrus. Vaginoscopic/speculum examination is sometimes required for diagnosis. Often associated with AI failure.</td>
</tr>
<tr>
<td>Absence of behavioural signs of oestrus</td>
<td>True anoestrus</td>
<td>Acyclia. Inactive (smooth) ovaries. Developmental abnormalities should be ruled out in heifers.</td>
</tr>
<tr>
<td>Sub-oestrus/silent heat</td>
<td></td>
<td>Ovarian cyclic activity present but oestrus not accompanied by adequate behavioural signs of heat. Failure to detect heat signs should be ruled out.</td>
</tr>
<tr>
<td>Ovarian cysts</td>
<td></td>
<td>Common cause of oestrus irregularities</td>
</tr>
<tr>
<td>Corpus luteum persistent</td>
<td></td>
<td>Often seen in highly producing dairy cows. May be associated with pyometra.</td>
</tr>
</tbody>
</table>

Always rule out possible pregnancy
<table>
<thead>
<tr>
<th>Irregular oestrus</th>
<th>Pseudo-anoestrus/silent heat</th>
<th>Poor oestrus demonstration and/or inadequate oestrus detection can lead to a diagnosis of oestrus irregularities.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian cysts</td>
<td>Common cause of oestrus irregularities. Nymphomaniac behaviour can also be present.</td>
<td></td>
</tr>
<tr>
<td>Late embryonic mortality</td>
<td>Cows losing their embryos after the initial recognition of pregnancy repeat oestrus more than 21 days post service.</td>
<td></td>
</tr>
<tr>
<td>Corpus luteum persistent</td>
<td>Not uncommon in highly producing dairy cows. May be associated with pyometra.</td>
<td></td>
</tr>
</tbody>
</table>

Always remember that inadequate oestrus detection is most often responsible for the diagnosis of oestrus irregularities

<table>
<thead>
<tr>
<th>Regular oestrus but failure to conceive after insemination in more than two consecutive cycles</th>
<th>Repeat breeding</th>
<th>The underlying cause is often difficult to diagnose</th>
</tr>
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<tr>
<td>Cause 1 Endometritis</td>
<td></td>
<td>Always rule out endometritis in repeat breeders</td>
</tr>
<tr>
<td>Cause 2 Hormonal disorders</td>
<td></td>
<td>Adequate corrections in the nutritional status of the cows and AI timing should precede any pharmaceutical treatment. Simple hormonal programs exist to address some of the underlying hormonal problems</td>
</tr>
<tr>
<td>• Failure of fertilisation (delayed ovulation)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Early embryonic mortality (precocious luteolysis, luteal insufficiency)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other causes:</td>
<td></td>
<td>Adequate corrections in the nutritional status of the cows and AI timing should precede any pharmaceutical treatment. All cows should be monitored and subjected to BVD and IBR prophylaxis.</td>
</tr>
<tr>
<td>• Nutritional deficiencies and metabolic diseases (elevated urea levels in circulation etc.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Certain infectious diseases (BVD, IBR etc.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Poor heat detection and insemination of cows not in oestrus</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
(Endo)metritis

Definition of the problem:
• Uterine infections

Actions:
Clinical metritis: adequate intrauterine therapy. In cows with elevated body temperature (>39° C) parenteral therapy with antibiotics and NSAIDs should be considered.
Clinical/subclinical endometritis:
- intrauterine antibiotics according to the bacterial sensitivity
- in the presence of corpus luteum - PGF2α

Remarks on clinical/subclinical endometritis:
- Can be difficult to diagnose by external examination alone.
- Should be treated as soon as possible after diagnosis to avoid continuous reproduction failure and irreversible morphological changes in the endometrium

Acute metritis:
- occurs within the first 2 weeks post partum
- predominantly caused by E.coli
- can be associated with systemic clinical signs
**Clinical/subclinical endometritis:**
- within 21 days or more post partum not accompanied by systemic signs
- predominantly caused by *Arcanobacterium pyogenes* and Gram negative anaerobes

**Pyometra**
- uterine infection with closed cervix
- accumulation of pathological discharge (pus) in the uterine lumen
- persistent corpus luteum

As the effect of Metricure on the sperm survival and function is not known it is not advisable to use the product simultaneously with insemination.

When diagnosing repeat breeding syndrome always consider uterine infections as possible cause.
**True anoestrus**

**Definition of the problem:**
In general two clinical pictures are possible:
- inactive ovaries, with no functional structures detected during rectal examination (smooth ovaries)
- ovaries with larger follicular structures (persistent anovulatory follicles or follicular cysts)

**Action:**
Induction of oestrus and ovulation. In both cases growth, maturation and ovulation of a dominant follicle originating from a new follicular wave needs to be induced.

**Progestagens: Crestar®**

Insemination timing in heifers – 48h after implant removal
Insemination timing in cows – 56h after implant removal
(independent of production type)
**Dose of PMSG (Folligon®) used with the Crestar® method**

- Adjust the dose of PMSG according to the age of the cow or heifer, production type and breed
- You can skip the PMSG injection in dairy heifers that are in good body condition

<table>
<thead>
<tr>
<th>Dairy cows and heifers</th>
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<tr>
<td>Holstein, Jersey, crosses of HF with other <em>Bos Taurus</em> breeds</td>
</tr>
<tr>
<td><em>Bos Indicus</em> breeds (zebu)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Beef heifers</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Bos Taurus</em> breeds (Charolais, Hereford, Angus, Limousine, Salers etc)</td>
</tr>
<tr>
<td><em>Bos Indicus</em> breeds (Nelore, Brahman)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Beef cows</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Bos Taurus</em> breeds non lactating</td>
</tr>
<tr>
<td><em>Bos Taurus</em> breeds nursing calves</td>
</tr>
<tr>
<td><em>Bos Indicus</em> breeds</td>
</tr>
</tbody>
</table>
### Recommended timing for initiation of Crestar® treatment in cattle in relation to age of the animals and time post partum

<table>
<thead>
<tr>
<th>Cattle Type</th>
<th>Timing</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dairy heifers</strong></td>
<td>From 15-18 months of age onwards</td>
<td>Attention! Heifers should have obtained at least 75% of their adult body weight.</td>
</tr>
<tr>
<td><strong>Dairy cows</strong></td>
<td>From 45 days post partum</td>
<td>Cows should have a BCS of at least 2.5 or greater.</td>
</tr>
<tr>
<td><strong>Beef heifers</strong></td>
<td></td>
<td>Heifers should have obtained at least 75% of their adult body weight.</td>
</tr>
<tr>
<td><strong>Beef cows</strong></td>
<td>From 60 days post partum</td>
<td>Cows should have a BCS of at least 2.5 or greater.</td>
</tr>
</tbody>
</table>
GnRH – Receptal® (providing that follicles larger than 10mm are present on the ovary)

More than 50 days post calving →

**Stage 1**

In the absence of heat within 10 days after the treatment with Receptal →

**Stage 2**
Rectal examination/ultrasonography

- CL present on the ovary

- No CL detected
Pseudo-anoestrus/Sub-oestrus

Definition:
Cow with normal cyclic ovarian activity, heat is however not detected due to:
• the absence of behavioural signs of oestrus (pseudo-anoestrus), or
• poorly expressed oestrus signs (sub-oestrus/silent heat)

Action:
During the luteal phase, an injection of PGF2α (Estrumate) induces luteolysis and initiates the next oestrus cycle. The cow will come into heat within an average of 3-5 days.
The cows should be inseminated at detected heat.

Protocol 1

PGF2α

This system is especially recommended for heifers
Protocol 2

Ovsynch

This system has an important advantage of possible fixed time insemination without the necessity for oestrus detection. This system is not recommended for heifers and nursing beef cows.

Protocol 3

Crestar

This system allows for insemination without heat detection. The Crestar system is especially recommended in beef cows as it causes an effective artificial luteal phase that is beneficial for corpus luteum function.
Cystic Ovarian Disease

Definition:
Ovarian cysts are defined as:
- Fluid filled ovarian structures of a diameter larger than 2.5cm that persist on the ovary for more than 8-10 days in the absence of a normal corpus luteum.
- They frequently appear during the early post partum period, intervention is not considered necessary before 40 days post calving
- They are associated with various oestrus cycle abnormalities such as anoestrus, irregular oestrus signs or nymphomania
- Thought to be caused by inadequate LH release from the pituitary gland and consequent ovulation failure or a lack of reactivity of the follicular cells to physiological LH stimulation. Negative energy balance and lack of previous exposure to adequate progesterone concentrations (in the previous oestrus cycle) are listed as the most important predisposing factors.
- Two types of ovarian cysts can be distinguished:
  - follicular (can be estrogenically active or not)
  - luteal (produce progesterone)

Diagnosis is by rectal palpation, ultrasound examination or measurement of progesterone in milk or serum.

Follicular cysts
Action: restore follicular turnover and induce ovulation of the dominant follicle from a new follicular wave
→ GnRH or hCG

Important tip: the physical disappearance of the cyst is not necessary for successful treatment. Induction of oestrus and ovulation is the outcome that we are looking for!
The time from treatment to oestrus depends on the stage of follicular development at the moment of injection. The cows can be inseminated during the first detected heat.
Luteal cyst

**Action:** Induce luteolysis and restore cyclicity

Important tip: The time from treatment to oestrus depends on the stage of follicular development at the moment of injection. The cows can be inseminated during the first detected heat.

Shortening the time to oestrus & treatment of cysts of uncertain nature

With this system both types of cysts can be addressed while a combination of GnRH/hCG and PGF2α ensures induction of ovulation of the dominant follicle from a new follicular wave in a predictable and controlled time. Treated cows can thus be inseminated at a relatively short time after diagnosis.
Repeat breeding/Early Embryonic Mortality

Definition:
Cows with normal cyclic ovarian activity and no apparent disorders of reproductive tract that do not fall pregnant after insemination during more than two consecutive oestrus cycles. Thought to be caused by early embryonic losses.

Pattern of returns

Possible actions:
- Induction of ovulation to avoid delay of failure of ovulation → GnRH/hCG at AI
- Prevention of precocious luteolysis and creation of additional CL → GnRH at 11-12 d post AI
**Induction of Ovulation for AI**

This system is especially recommended in highly producing dairy cows exposed to high ambient temperatures.

**GnRH at 11-12 day post AI**

This system is especially recommended in cases of so called “late repeats”.

---

**Repeat breeding**
Selected infectious causes of fertility problems and abortions in cattle

<table>
<thead>
<tr>
<th>Affected function</th>
<th>Infectious disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative influence on ovarian activity and the function of higher endocrine regulatory centres</td>
<td>BVD, IBR, mastitis, endometritis</td>
</tr>
<tr>
<td>Negative effect on semen and oocyte quality</td>
<td>♂️BVD, IBR, acute phase of almost all infectious diseases accompanied by fever</td>
</tr>
<tr>
<td></td>
<td>♀️BVD, IBR, Hemophilus (?)</td>
</tr>
<tr>
<td>Direct negative influence on the embryo development (≤42d of pregnancy) and placental function</td>
<td>BVD, IBR, Neospora caninum, Trichomonas foetus, Leptospira, Campylobacter foetus</td>
</tr>
<tr>
<td>Direct negative influence on foetal development (&gt;42d of pregnancy) and placental function causing abortion</td>
<td>Leptospira Brucella abort. Listeria Campylobacter Hemophilus Ureaplasma Epizootic bovine abortion Mycoplasma Anaplasma Salmonella IBR BVD Bluetongue Vesiviruses Cache Valley virus Trichomonas Neospora can. Sarcocystis neuroni Aspergillus fum. Mucor spp. Mortierella wolfii</td>
</tr>
</tbody>
</table>

Remember: Careful monitoring of BVD and IBR status of the herd and vaccination against BVD with vaccines providing foetal protection and preventing cell free viraemia as well as against IBR should form an integral part of a modern reproduction management program in cattle herds.
Oestrus Management

The critical requirements for any effective oestrus cycle control system are predictable and high oestrus and ovulation responses during a specified 12-24h period followed by a high pregnancy rate to a single pre-programmed AI after treatment.

Pharmacological systems used in oestrus management in cattle should be perceived as useful tools that facilitate:
1. Successful insemination of cows
2. Improved management of females
3. Organisation of service
4. Corrections of problems such as inadequate oestrus detection, irregular oestrus cycles, silent heat or ovulation induction

Benefits of pharmacological oestrus management in cattle – why we want to induce and synchronize oestrus in cows

- **To improve the organisation of breeding**
  - improve reproduction results
  - maintain the same results but with less labour

- **To correct only certain elements of reproductive management**
  - improve heat detection
  - eliminate heat detection

- **To correct certain reproductive disorders in the herd**
  - silent heat
  - anoestrus
  - repeat breeding
Oestrus Management

Pharmacological systems used for oestrus induction and synchronization in cattle can be divided as follows:

- Systems that control only luteal function
  - prostaglandins used alone

- Systems that control only follicular function
  - progestagens used alone

- Systems that control both luteal function and follicular dynamics
  - combinations of prostaglandins and GnRH
  - combinations of progestagens with gonadotrophins and prostaglandins
Oestrus synchronization with prostaglandins

Injection of prostaglandin causes luteolysis and allows for the final growth and maturation of the dominant follicle followed by ovulation at a predictable time post injection.

Requirements:
- oestrus induction and synchronization systems are only effective in cycling animals (animals must have a functional corpus luteum that is sensitive to prostaglandins at the time of PG injection)
- for satisfactory results animals must have an adequate body condition score of ≥ 3.0.

Target group:
Oestrus synchronization systems based on prostaglandins alone are recommended for:
- Cycling dairy and beef heifers
- Cycling dairy cows in good body condition
- Herds where labour resources for heat detection are limited (animals for heat observation are grouped and identified)
**Single prostaglandin injection**

**Attention:**
The presence of luteal tissue must be confirmed before synchronization systems based on a single prostaglandin injection are used. This can be done by rectal palpation, ultrasound examination, measurement of progesterone concentrations in milk (>2ng/ml) or blood (>5ng/ml) or based on the date of the last heat observed.

**Double prostaglandin injection**

**Attention:**
This system can be used without detection of a CL but still only applies to cycling animals.

**Multiple prostaglandin injection**
Efficacy of oestrous synchronization based on prostaglandin administration

Injection of prostaglandin modifies the lifespan of the corpus luteum and induces the final growth of a new follicular wave. It has however no influence on the time from injection to oestrus and ovulation. The time interval from treatment to ovulation depends on the degree of follicular development at the moment of PGF administration.

![Graph showing the distribution of oestrus in cows treated with PGF](image)

Distribution of oestrus in cows treated with PGF

Because of the variability of oestrus and ovulation post PGF injection, insemination at detected heat is recommended and gives the best results.
Combination of prostaglandins and GnRH – Ovsynch type systems

Systems combining luteolysis, induced with PGF, and induction of follicular growth and ovulation with GnRH, control the lifespan of the corpus luteum and the follicular growth dynamics. Some of these systems thus allow for fixed time AI.

Classical Ovsynch protocol

Target group
- Dairy cows
- Dairy cows exposed to heat stress

Attention:
- Ovsynch system allows for insemination at fixed time without observation of behavioural signs of heat
- The classical Ovsynch is not recommended for heifers and animals in anoestrus
Modifications of the classical Ovsynch

Co Synch

Pre Synch

hCG Synch
**Progestagens**

Progestagens combined with prostaglandins and GnRH/PMSG modify both the CL function and follicular dynamics. Thanks to the creation of an artificial luteal phase oestrus synchronization with progestagens can also be used in anoestrous animals. System Crestar allows for fixed time insemination. Heat detection is not necessary.

**Crestar**

**AI:**
Heifers of dairy and beef type – 48h post implant removal
Cows of dairy and beef type: 56h post implant removal

PMSG dosage: see page 10

**Target group:**
- Dairy and beef cows regardless of their cycling status
- Synchronisation of donors and recipients in ET programs
Unwanted pregnancy
Pharmacological pregnancy termination is undesirable in general but may be necessary in certain cases such as the accidental mating of heifers in feedlot units.
Abortion with prostaglandins can be achieved up to 150 days of pregnancy.

Attention:
- Between 100 and 150 days of pregnancy the efficacy of prostaglandins can be reduced. It might be necessary to administer more than one dose in order to terminate pregnancy.
- After day 150, prostaglandins alone are not effective abortifacients in cattle as the placenta produces enough progesterone to maintain pregnancy.
Induction of calving

Reasons for calving induction in cattle:
- To shorten calving intervals or to tighten the calving pattern.
- To reduce the incidence of dystocia by preventing foetal oversize.
- To terminate abnormal pregnancies.
- To advance the date of calving in late-conceiving cows, where breeding and production is seasonal.

Attention:
- Induction of calving with prostaglandins is associated with an increased incidence of placental retention.
- Induction of parturition should not be attempted more than 7 days before the expected calving date to avoid the birth of premature and weak calves.
Reproductive problems in the bull

Cryptorchidism

**Definition:** one or both testes fail to descend normally into the scrotal sac. The testis/testes can be located in the abdominal cavity or inguineal canal.

**Attention:**
- Pharmacological treatment is usually unsuccessful
- If a hereditary cause is suspected treatment and use of the male for breeding is not recommended.

Poor libido:

**Definition:** weak or absent sexual drive in a sexually mature bull

**Treatment:** Injection of hCG (Chorulon, 2 injections/week for 4-6 weeks at a dose of 500-1000iu)

**Attention:** Before any pharmacological treatment is initiated, morphological (painful conditions of muscles and bones, systemic diseases) and managerial causes (stress, inappropriate handling) of poor libido should be ruled out or corrected
Oligospermia

**Definition:** insufficient number of sperm cells in the ejaculate

**Treatment:** improvement of semen quality can be attempted with prolonged treatment with PMSG. Results are however variable and dependant on the underlying physiological causes.

**Attention:** Before any pharmacological treatment is initiated, functional disorders such as systemic diseases accompanied by elevated body temperature, nutritional deficiencies and genital tract infections as well as the influence of a high ambient temperature should be ruled out.
Physiology

Follicular dynamics and its practical implications

In cattle, ovarian follicles grow and develop in so-called waves (two or three waves per cycle). Only the dominant follicle of the last wave ovulates.

Did you know that?

Duration of the oestrus cycle
The duration of the oestrus cycle can vary between 18 and 25 days depending on the number of follicular waves that develop during a cycle. An inter-oestrus interval of 25 days is still considered physiological!

Abnormal heats – the explanation:
- Between two consecutive ovulations typical oestrus behaviour may be observed due to the influence of oestrogens secreted by the growing dominant follicle

During gestation, the growth of follicular waves continues. In rare cases, behavioural signs of oestrus can be observed in pregnant cows.

Resumption of cyclicity post partum

<table>
<thead>
<tr>
<th>Dairy cows</th>
<th>Beef cows</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance of the first dominant follicle</td>
<td>Between 4 and 40 days post partum</td>
</tr>
<tr>
<td>Fate of the first dominant follicle</td>
<td>Between 5 and 40 days post partum</td>
</tr>
<tr>
<td></td>
<td>75% - ovulation, 20% - cyst formation, 5% -</td>
</tr>
<tr>
<td></td>
<td>atresia</td>
</tr>
<tr>
<td></td>
<td>10-20% ovulation, 10% - cyst formation, 70-80%</td>
</tr>
<tr>
<td></td>
<td>atresia</td>
</tr>
</tbody>
</table>
Hormonal regulation of reproductive function

Mechanism of hormonal regulation of reproductive function in cattle

Hormone levels during the Oestrus cycle of a cow.
The role of LH and Progesterone

Luteinising hormone and progesterone are crucial to reproduction function in cattle. LH support is necessary for:

- the final stage of follicular growth and maturation
- timely ovulation
- the formation and early function of corpus luteum.

The quantity of LH released and the release pattern determine successful ovulation and luteal function.

**Impaired LH secretion (quantitative and qualitative)**

- Delayed ovulation
- Poor oocyte quality
- Impaired corpus luteum function
- Early embryonic mortality
- Formation of follicular cyst
- Absence of follicular growth

**Progesterone is essential for high fertility of cows**

There are four main types of progesterone profiles in the early post partum period (source: Mann 2002)

- **Normal profile**
- **Abnormal profile**

Lack of rapid and adequate rise in progesterone concentrations is an important risk factor in early embryonic mortality
Relationship between the hormonal profile and infertility in cattle

Hormonal disorders leading to suboptimal fertility

<table>
<thead>
<tr>
<th>4 periods of risk</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk period</td>
<td>D-9</td>
<td>D0</td>
<td>D5</td>
<td>D12 D15</td>
</tr>
<tr>
<td>Risk</td>
<td>Ovulation failure</td>
<td>Insufficient luteal function</td>
<td>Increased risk of precocious luteolysis</td>
<td></td>
</tr>
</tbody>
</table>

Improvement of fertility: therapeutic options

<table>
<thead>
<tr>
<th>Type of hormonal disorder</th>
<th>Risk</th>
<th>AI at risk</th>
<th>Therapeutic option</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asynchronous follicular development</td>
<td>Fertilisation failure</td>
<td>Especially 3rd AI and subsequent AI’s.</td>
<td>Induction and synchronization of follicular development and LH peak</td>
<td>Ovsynch protocol or Receptal - 7-9 days post PGF2α</td>
</tr>
<tr>
<td>Delayed ovulation or ovulation failure</td>
<td>Fertilisation failure or poor development of the embryo (early embryonic mortality)</td>
<td>Especially 3rd AI and subsequent AI’s</td>
<td>Induction of LH peak and ovulation within 24h before insemination</td>
<td>Receptal/Chorulon at AI, Complete Ovsynch protocol</td>
</tr>
<tr>
<td>Precocious luteolysis due to inadequate progesterone levels and stimulation of luteolytic cascade by luteal phase follicles</td>
<td>Early Embryonic Mortality</td>
<td>At any AI</td>
<td>Elimination of growing follicles, increase of progesterone levels through formation of additional corpora lutea</td>
<td>Receptal - 11-12 days post AI</td>
</tr>
</tbody>
</table>

Schematic evolution in the risk of hormonal disorders in subsequent inseminations

% of risk

Follicular origin – date of preovulatory LH peak

Luteal origin – progesterone deficiency
# Information about Intervet reproduction range

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<th>Product</th>
<th>Active ingredient</th>
<th>Indications for use in cattle</th>
<th>Posology</th>
<th>Presentations</th>
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<tr>
<td><strong>Hormonal products</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chorulon®</td>
<td>hCG</td>
<td>• Induction of ovulation at AI</td>
<td>• Induction of ovulation and improvement of fertility – 1.500 IU</td>
<td>Vials of 500, 1.500, 2.500, 5.000 and 10.000 IU with solvent</td>
</tr>
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<td></td>
<td></td>
<td>• Improvement of fertility and induction of ovulation at AI</td>
<td>• Treatment of cysts – 3.000 IU i.m. or slow i.v.</td>
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<td></td>
<td>• Treatment of Follicular cysts (preferably in combination with PGF at 7-9d later)</td>
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<tr>
<td>Crestar®</td>
<td>Norgestomet</td>
<td>Oestrus induction and synchronization for fixed time AI in cows and heifers (beef and dairy)</td>
<td>Implant insertion + injection, implant removal after 9-10 days accompanied with PMSG injection. In dairy cows PGF injection at 48h before implant removal</td>
<td>Boxes with 25 treatments (implants +injections)</td>
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<tr>
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<td>Oestradiol valerate</td>
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<tr>
<td>Estrumate®</td>
<td>Cloprostenol racemate (synthetic PGF2α)</td>
<td><strong>Zootecchnical:</strong> • Oestrus induction and synchronization • Induction and synchronization of calving</td>
<td>2ml/cow i.m.</td>
<td>Vials with 2, 20 and 50ml</td>
</tr>
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<td></td>
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<td><strong>Therapeutical:</strong> • Corpus lutum persistent and luteal cysts • Pyometra and as additional treatment in other uterine infections • Pseudo anoestrous/silent heat</td>
<td></td>
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</tr>
<tr>
<td>Folligon®</td>
<td>PMSG/eCG</td>
<td>• Oestrus induction</td>
<td>• Induction of oestrus 500-1.000 IU i.m.</td>
<td>Vials of 400, 500, 600, 700, 1.000, 5.000 and 6.000 IU with solvent</td>
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<td></td>
<td>• Improvement of fertility rate in progestagen-based oestrus synchronization systems</td>
<td>• In combination with progestagens – 300-750IU i.m. at removal of progestagen source</td>
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<tr>
<td></td>
<td></td>
<td>• Superovulation</td>
<td>• Superovulation – 3.000 IU i.m. on 8-13d of oestrus cycle</td>
<td></td>
</tr>
<tr>
<td>Product</td>
<td>Active ingredient</td>
<td>Indications for use in cattle</td>
<td>Posology</td>
<td>Presentations</td>
</tr>
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| Intertocine S® | Synthetic oxytocin       | • Stimulation of uterine contractions during labour  
• Improvement of post partum uterine involution  
• Stimulation of milk secretion              | 10-50IU s.c. or i.m.                  | Vials of 10, 25 and 50ml containing 10IU/ml       |
| Receptal® | Buserelin (GnRH analogue) | • Induction of ovulation at AI  
• Improvement of fertility post AI (10-12d post AI)  
• Treatment of ovarian cysts               | • Induction of ovulation and improvement of fertility – 2.5ml  
• Treatment of cysts – 5ml i.m., s.c., i.v. | Vials of 2.5ml, 5ml, 10ml and 50ml         |
| Metricure® | Cep Lapirin              | Treatment of subacute and chronic endometritis                                                | • Treatment of endometritis – 1 intrauterine injector | Box with 10 or 12 injectors                       |
We provide solution to all problems that take place during the reproduction season of the cows.
The information below provides the basic facts about Intervet products used for management of reproduction in cattle throughout the world. Please bear in mind that not all of these products will be present in all countries. With respect to withdrawal times, consult the product leaflet valid in your country.

**Chorulon®**
**Composition:** Chorulon contains human Chorionic Gonadotrophin (hCG) as a white freeze-dried crystalline powder. **Indications:** Chorulon can be used for the control of fertility problems in domestic animals: - improvement of conception rate in female animals (cattle); - induction of ovulation in female animals (horses, dogs, cattle); - cystic ovaries with irregular oestrous cycle, nymphomania or absence of oestrus in female animals (cattle); - anoestrus in female animals (horses, dogs); - delayed ovulation, prolonged oestrus in female animals (dogs); - deficiency of libido and cryptorchidism in male animals (dogs). **Dosage and administration:** cattle, horses: 1.500-3.000IU, dogs: 100-800IU. **Contraindications:** As with all protein-containing preparations, in rare cases anaphylactoid-type reactions may occur shortly after administration. In such circumstances, prompt medication with adrenaline (1:1000) or glucocorticosteroids may be indicated. **Withdrawal period:** Milk, meat – nil. **Storage conditions:** Store at 8-15° C. Protect from light.

**Crestar®**
**Description:** Crestar is a part of a system suitable to control oestrus in heifers and cows in order to apply a planned insemination program. Crestar consists of: Crestar implant containing 3 mg of the progestagen Norgestomet (17α-acetoxy-11β-methyl-19-norpregna-4-en-2.20-dione) and Crestar injection of 2 ml, containing 3 mg Norgestomet and 5 mg oestradiol valerate. **Mode of action:** Crestar injection: The oestrogen plus the Norgestomet compound shortens the luteal phase if treatment is given in an early stage of the cycle and induces so called follicular turnover (ovulation or luteinisation of any LH-sensitive follicle present on the ovary at the time of injection) preventing this way the formation of persistent dominant follicles. At the same time the Norgestomet compound suppresses oestrus and ovulation by pituitary inhibition. Crestar implant: The continuous release of Norgestomet maintains the suppression of oestrus and ovulation. After removal of the implant the blocking effect on the pituitary ceases and a new follicular phase starts. In non-cyclic animals the priming effect of Norgestomet is enhanced by combining the removal of the implant with an intramuscular PMSG injection that stimulates synchronized follicular development. **Indications:** Oestrus control in both cyclic and non-cyclic cattle (heifers and cows). **Posology:** Place the implant under the skin of the outer surface of the ear and inject the Crestar injection. In dairy cows administer a dose of prostaglandin 48h before implant removal. After 9-10 days remove implant and administer PMSG. The dosage of Folligon (PMSG) depends on age, breed, season, post-partum interval, management, etc. **Note:** Cows and heifers can be inseminated without oestrus detection. If two AI’s are performed the timing of AI is 48 and 72 hours after implant removal. **Contraindications:** Crestar is not a therapeutic and therefore is to be applied in healthy animals only. Heifers to be treated should have reached at least 65-70% of the adult weight and the age should be 15-20 months, depending on breed. Cows should not be treated within 45 days after the last calving. **Withdrawal period:** Milk: nil, Meat: 2 days after removal of implant. **Storage conditions:** Store in a dry place at room temperature (15-25° C). Protect from light.

**Estrumate®**
**Description:** Estrumate is a clear colourless aqueous solution containing: 0.263mg/ml of racemic cloprostenol sodium, equivalent of 0.250mg/ml of racemic cloprostenol. Cloprostenol is a synthetic prostaglandin F2a analogue. **Indications for use:** Cattle: Treatment of reproductive pathologies (subestrus, pyometra, luteal cysts and corpus luteum persistent), improved management of reproduction (i.e. synchronization of oestrus and ovulation combined in some cases with fixed time artificial insemination, induction of calving). **Dosage and Administration:** The dose of 2ml/animal is applied intramuscularly in cows and heifers. **Withdrawal times:** Milk, meat – nil. **Contra-indications:** Animals with spastic disorders of the gastro-intestinal tract and/or the respiratory system. Not to be used in pregnant animals, unless abortion or induction of calving is required. **Undesirable effects:** Use for Induction of parturition or abortion in cattle is accompanied by an increased incidence of retained foetal membranes. **Storage conditions:** Store at temperatures below 20ºC, protected from light. **Special precautions to be taken by the person administering the veterinary medicinal product to animals:** Women of child bearing age, asthmatics and persons with bronchial or other respiratory problems should handle the product with care, as cloprostenol is readily absorbed through the skin and may cause abortion or bronchial spasm. In case of accidental self-injection, seek medical advice immediately and show the package insert or the label to the physician. Accidental spillage on the skin should be washed immediately with soap and water. **Presentation:** 2ml, 20ml and 50ml colourless, glass vials, closed with a rubber stopper.
Dexadreson®
Description: Dexadreson contains dexamethasone as the disodium phosphate ester in a clear solution of 2 mg dexamethasone per ml. Dexamethasone is a very potent corticosteroid (activity at least 30 times greater than cortisone). Sodium retention and potassium loss are almost negligible at the recommended dosage. **Indications:** Dexadreson can be used therapeutically for its anti-inflammatory, anti-allergic, anti-shock and glucoenogenic action and for induction of parturition in ruminants. Administration by intravenous, intramuscular or intra-articular injection. Repeated treatment is possible after 24-48 hours. When treatment is prolonged, withdrawal should be gradual and ACTH stimulation of the adrenal is advisable. All injections into joints should be preceded by the removal of a volume of synovial fluid equal to that of the intended injection. Dosage: cattle, horses and pigs: 0.06mg/kg, dogs and cats: 0.1mg/kg. In cases of shock Dexadreson can be administered intravenously, thus ensuring a very rapid action. In such cases the intravenous dosage should be at least 10 times the clinically advised systemic (i.m.) dose. **Contraindications:** The normal conditions for which potent glucocorticosteroids are contraindicated apply to Dexadreson. Diabetes mellitus, osteoporosis, renal diseases and cardiac congestion are all indications for avoiding corticosteroid therapy. Infectious diseases should not be treated unless suitable anti-infective therapy is given at the same time (anti-sera, antibiotics, etc.). Due to their immunosuppressive activity, corticosteroids can lead to a reduced response to vaccine. Therefore it is recommended that Dexadreson is not used in combination with vaccines. Unless abortion or early parturition is required, the use of Dexadreson during late pregnancy is contraindicated. A reduced viability of the offspring, or increased incidence of retained placenta and foetal abnormalities have been associated with the induction of parturition with corticosteroids. Subsequent fertility is usually not adversely affected. In cases of laminitis in horses Dexadreson should only be used very early in the disease process. In order to obtain a rapid response in very acute hypersensitivity reactions and anaphylactic conditions, it may be necessary to administer antihistamines and/or adrenaline together with the corticosteroid. In cases of shock treatment, intravenous fluids should be given to maintain circulating blood volume, and the acid base balance should be controlled. **Withholding period:** Milk: nil. Meat: 2 days. **Storage conditions:** Store at room temperature (15-25°C). Protect from light. Presentation: Vials of 50 ml

Folligon® (Chrono®-gest PMSG)
Description: Folligon contains the hormone Pregnancy Mare Serum Gonadotrophin (PMSG; Equine Chorionic Gonadotrophin - ECG) as a white freeze-dried crystalline powder together with solvent for reconstitution. **Mode of action:** The active compound of Folligon is PMSG/ECG, a complex glycoprotein. PMSG/ECG is a gonadotrophin with Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH) activities. In females, PMSG stimulates the growth and maturation of the follicles. In the male, PMSG stimulates development of the interstitial tissue of the testis and spermatogenesis. **Indications:** Folligon can be used for the management of reproduction and treatments of reproductive disorders in domestic animals: Anoestrus (oestrus induction and increase of ovarian activity leading to an increased fertility) in the cow, the rabbit, the bitch and in mink. Induction of multiple ovulation (Superovulation) in embryos/oocyte donors in the cow, the rabbit and in deer. Increase of fertility rate after prostegestagen treatment (oestrus induction and synchronisation, increase of ovarian activity) in the cow, the ewe, the goat and in deer. **Dosage:** Cattle – anoestru: 500-1000IU, oestrus management with progestogens: 300-750IU, superovulation: 3000IU; Dogs - 500IU, Sheep – 400-750IU, Goats – 400-750IU, Rabbit – 40IU, Mink – 100IU, Deer – 200IU. **Contraindications:** In rare cases, as with all protein-containing preparations, anaphylactoid-type reactions may occur shortly after administration. In such circumstances, prompt medication with adrenaline (1:1000) or glucocorticosteroids may be indicated. **Withholding period:** milk, meat – nil. **Storage conditions:** Store at 8-15°C. Protect from light. Reconstituted product should be used within 12 hours. **Presentations:** Folligon: vials of 1000 and 5000 IU together with solvent for reconstitution. Chrono-gest PMSG: vials of 400, 500, 600, 700, 5000 and 6000 IU together with solvent for reconstitution.

Intertocine®-S (Oxytocin-S)
Description: Intertocine S is a synthetic oxytocin at a concentration of 10 IU per ml. There are no vasopressor or anti-diuretic fraction impurities. **Mode of action:** Intertocine-S causes contractions of the smooth muscle of the oestrogen-sensitized uterus and mammary gland. It also stimulates uterine involution. **Indications:** Stimulation of uterine contractions, to facilitate parturition. Improvement of involution of the post-parturient uterus and thus aid the passage of retained placenta and removal of detritus. Control post-partum haemorrhage. Stimulation of milk let-down in cases of agalactia. **Dosage and administration:** Mare – 5-50IU, cow – 10-50IU, Sheep, sow goat – 5-30IU, bitch – 2-10IU, queen – 1-5IU. The product is administered by intramuscular or subcutaneous injection: repeat if necessary after 40 minutes. If a very quick effect is required, intravenous injection is possible. Therefore a quarter of the above mentioned dosage, diluted 1 in 10 with water for injection, is to be prepared. Inject slowly. By any route and especially when used during parturition, low initial dosage is recommended as repeat administration is permissible. In post-parturient animals larger doses may be employed. **Contraindications:** The use of Intertocine-S is contraindicated in any form of obstructive dystocia. When Intertocine is used as an aid to parturition, cervical dilatation must be confirmed prior to administration. Excessive doses of Intertocine-S may delay parturition by producing uncoordinated uterine contractions which interfere with the progress of the foetus, especially in multiple pregnancies. Adrenaline reduces the effect of oxytocin on the uterus or mammary gland. For this reason the animal should not be frightened when complete oxytocin effect is desired. **Withholding period:** milk, meat – nil. **Storage conditions:** Store at 2-8°C. Protect from light. **Presentations:** Vials of 10, 25 and 50 ml, containing 10 IU Oxytocin/ml.

Metricure®
Description: Each syringe of Metricure intra-uterine suspension contains 500 mg of cephapirin (as benzathine). **Mode of action:** Cephapirin - a first generation cephalosporin - is a broad spectrum antibiotic with bactericidal action against Gram-positive and Gram-negative bacteria. Cephapirin is resistant to the action of penicillinase produced by staphylococci, and is active in the anaerobic environment of the uterus. After a single treatment with Metricure, concentrations of cephapirin in the endometrium tissue above the MIC of sensitive bacteria are maintained for at least 24 hours. The suspension is well tolerated, enables good diffusion of cephapirin into the endometrium and can be infused easily. **Indications:** Subacute and chronic endometritis in cattle (> 14 days after parturition). Treatment of repeat breeder cows at the day after AI. **Dosage and administration:** The contents of the Metricure syringe are introduced into the lumen of the uterus using the disposable catheter provided with each syringe. 1. Fix the syringe to the catheter. 2. Take the cervix of the uterus into one gloved hand introduced
into the rectum. 3. Introduce the catheter through the cervix into the lumen of the uterus by gentle oscillating movements of the cervix. 4. Inject the contents of the syringe into the lumen of the uterus. One treatment with Metricure is generally sufficient for complete cure. If necessary, treatment can be repeated after 14 days. In animals that are inseminated, Metricure can be used at one day after insemination. In cases of pyometra it is advised to start treatment with an injection of prostaglandin in order to induce regression of the corpus luteum and to remove the debris from the uterine cavity before treatment with Metricure. 

**Contraindications:** Animals with known allergy to cephalosporins. **Withholding period:** Meat: 48 hours, Milk: nil. **Storage conditions:** Store at room temperature (15-25° C). **Presentation:** Box with 10 syringes plus 10 catheters and 10 gloves.

**Contraindications:** None. **Side effects:** Unknown. **Interactions:** None. **Presentation:** Vials of 2.5ml, 10 ml and 50ml.
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Intervet the experts in reproduction management

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