

# Estrumate<sup>®</sup> Receptal<sup>®</sup> Metricure<sup>®</sup>



When it comes to cattle fertility  
timing is everything

Intervet/Schering-Plough Animal Health  
Cattle Fertility Range





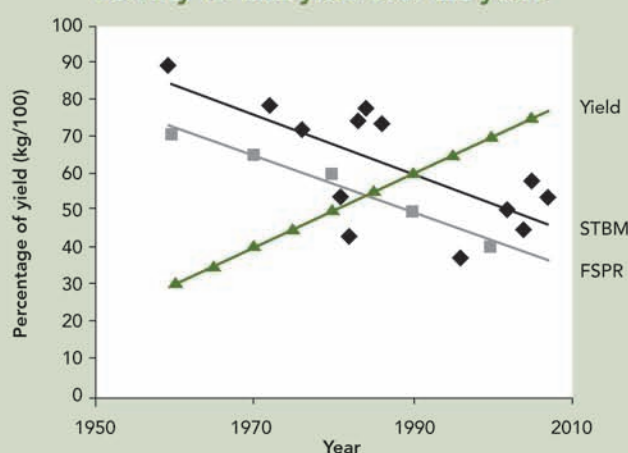
# Effective fertility management ...it's all about time

Poor fertility remains one of the top three causes of financial loss on a dairy unit. What's more, the trend towards longer calving intervals and the problems producers face getting cows successfully in calf show no sign of reversing. If anything, the situation is getting worse.

Larger herds with fewer man hours per cow plus the modern Holstein expressing heat for such a short period of time will only serve to increase the challenge for farm staff. Taking control of fertility and working with herd managers to make best use of the various products and programmes available can deliver clear benefits to herds with the result of improving the bottom line.



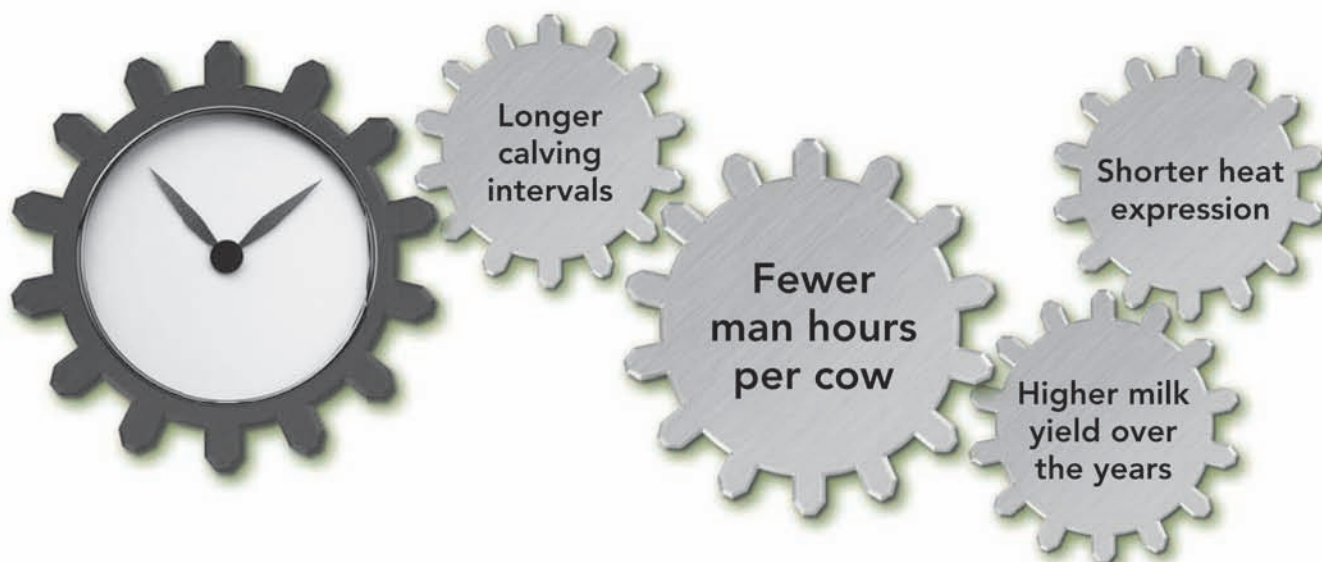
**Fertility vs. milk yield over the years**



**Figure 1**

Percentage of animals standing-to-be-mounted (STBM; ◆), first-service-pregnancy-rate (FSPR; ■) and average milk yield (▲) in Holstein Friesian dairy cows reported over the last 50 years.<sup>1</sup>

- ◆ STBM (standing-to-be-mounted)
- FSPR (first-service-pregnancy-rate)
- ▲ Average milk yield





# Metricure®

Metricure is **the only licensed intra-uterine antibiotic suspension** specifically formulated to treat subacute and chronic endometritis. Metricure contains 500mg cephapirin as cephapirin benzathine per 19 g syringe, a cephalosporin antibiotic with high activity against *A. pyogenes* and the anerobes *F. necrophorum* and *Prevotella spp.* The MIC<sub>90</sub> values for cephapirin against these very important uterine pathogens have been found to be considerably lower than those for oxytetracycline, an antibiotic previously licensed to treat endometritis.<sup>2</sup>



Available in ready-to-use syringes with catheters for administration

## Cure rate for *A. pyogenes* at 14 days post treatment<sup>3</sup>

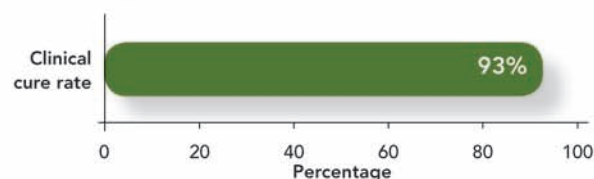


Figure 2

A single treatment of Metricure has been shown to give high clinical and bacteriological cure rates for *A. pyogenes* at 14 days after calving.

## The significance of endometritis

As figure 3 shows, virtually all cows suffer from bacterial contamination of the uterus after calving, but normally this is eliminated over time. Unfortunately, in some cows this does not occur as smoothly or rapidly as it should, and in these cases the cow often develops endometritis.

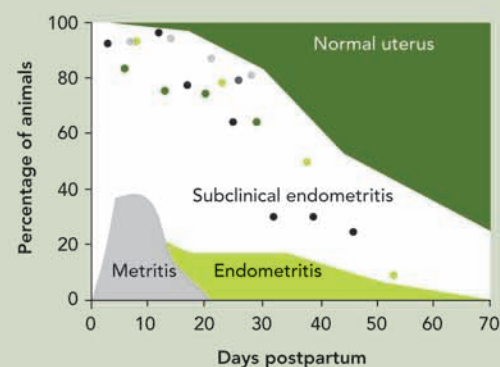


Figure 3

The incidence of uterine bacterial infection and disease in postpartum dairy cattle. Bacteria isolated from the uterus during the postpartum period; each marker (circle) indicates the percentage of animals with bacteria isolated from the uterine lumen. The shaded areas represent estimates of the proportion of animals with metritis (grey), clinical endometritis (light green), or a normal uterus (dark green), the remainder of animals have subclinical endometritis.<sup>4</sup>

## Key Metricure features:

- Specifically designed for the anaerobic intra-uterine environment
- Broad spectrum antibiotic
- Bactericidal against gram positive and gram negative bacteria
- Penicillinase resistant
- Non irritant formulation
- Rapid and prolonged antibiotic levels achieved
- Can be used one day after AI
- Nil milk withdrawal – 24h meat withdrawal
- ready-to-use syringes in a box with catheters for administration

## The use of Estrumate™ to treat endometritis

The use of prostaglandin F2 $\alpha$ , e.g. Estrumate, can be considered as an adjunct to antibiotic therapy in cases of endometritis where a functional corpus luteum (CL) is present. Furthermore, pregnancy rates were actually reduced when cows without a palpable CL were treated with PgF2 $\alpha$ .<sup>5</sup>





# Receptal®

Receptal contains 0,004mg/ml buserelin which is equivalent to the natural analogue of GnRH and causes simultaneous release of luteinising hormone (LH) and follicle stimulating hormone (FSH).

Buserelin is characterised by a very high potency measured by the ability to stimulate the release of LH from the pituitary gland. The potency of buserelin is 50 times higher than that of gonadorelin.<sup>6</sup> Practically all uses of Receptal are based on its ability to support the final development and induce ovulation of the receptive follicle; therefore its high potency is beneficial.



Available in 10ml (5x10ml) glass vials

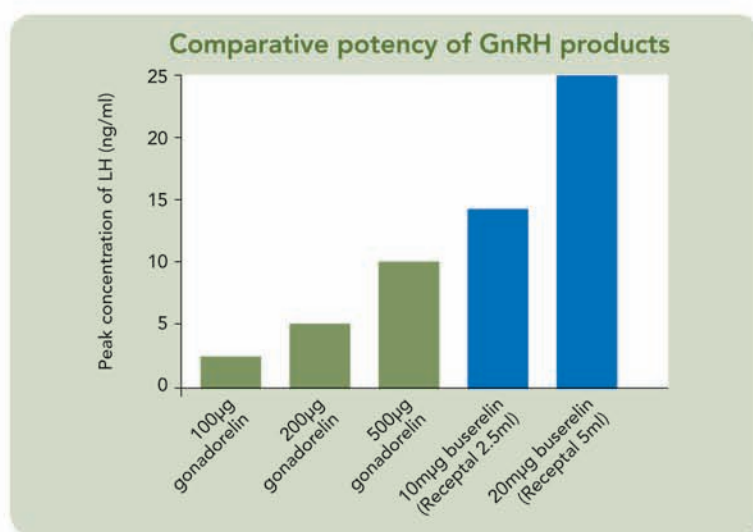
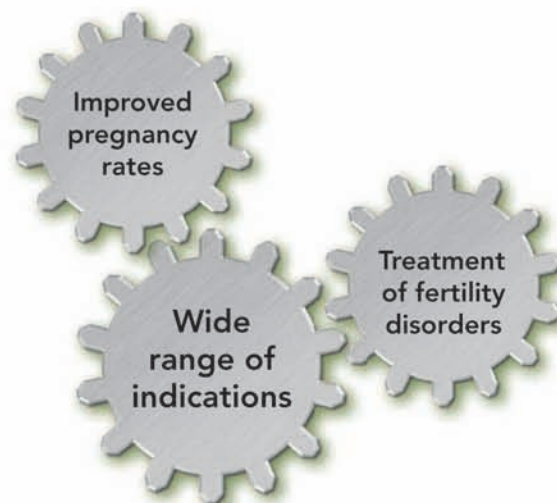


Figure 4  
Graph from reference 6



Receptal is the market leading GnRH<sup>7</sup> and has the widest range of licensed indications for the treatment of infertility of ovarian origin and improvement of pregnancy rates in cows, with a nil milk and meat withhold.

- **Follicular cysts:**  
Recommended dose: 5.0ml/animal  
Receptal can be used to treat follicular cysts without the need to manually express the cyst.
- **Acycilia (true anoestrus):**  
Recommended dose: 5.0ml/animal  
Determination of acyclicity can be made either by sequential rectal examinations or by milk progesterone assays. Oestrus should occur 8-22 days after treatment.
- **Delayed ovulation:**  
Recommended dose: 2.5ml/animal  
This condition can be treated at the time of AI or up to 6-8 hours beforehand. Ovulation is usually induced within 24 hours of treatment.

- **Improvement of pregnancy rates in dairy cows before and at AI:**  
Recommended dose: 2.5ml/animal  
Receptal can be used in multiple ways to improve pregnancy rates in dairy cows; either at the time of AI or up to 8 hours before AI in order to ensure ovulation occurs at the correct time.
- **Improvement of pregnancy rates in dairy cows after AI:**  
Recommended dose: 2.5ml/animal  
Early embryonic mortality can account for 20-45% of total pregnancy failures.<sup>8</sup> Improvement of pregnancy rates may be achieved by a single injection 11-12 days after AI to prevent luteolysis and consequent embryo mortality.
- **Controlled breeding in cattle**  
Recommended dose: 2.5ml/animal  
E.g. as part of the Intercept™ Programme in conjunction with Estrumate.

Receptal also has indications for use in mares, rabbits and rainbow trout.



# Estrumate™

Estrumate contains 250µg/ml cloprostenol, a synthetic prostaglandin analogue structurally related to prostaglandin F2α (PGF2α), for use in cattle.

Cloprostenol, the active ingredient of Estrumate, is characterised by a medium duration of half life (approximately 97 minutes) in comparison to a few minutes, in the case of natural prostaglandins and some other synthetic analogues, e.g. dinoprost. The prolonged half life and resulting more efficient and longer binding of prostaglandin receptors is a direct result of the structure of the cloprostenol molecule and slower elimination time compared to natural analogues. Natural analogues are almost completely degraded after one or two passages through the liver and/or lungs.<sup>10</sup>

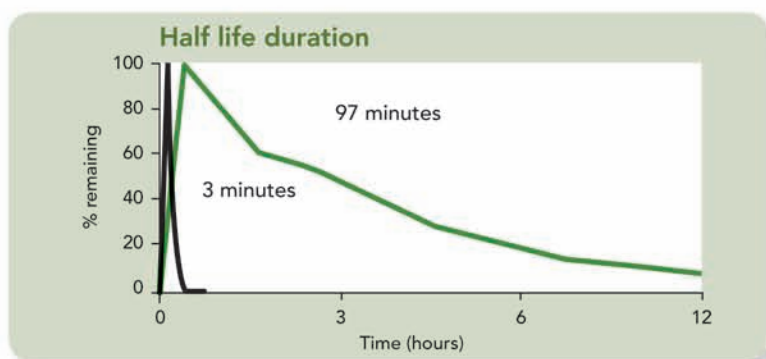


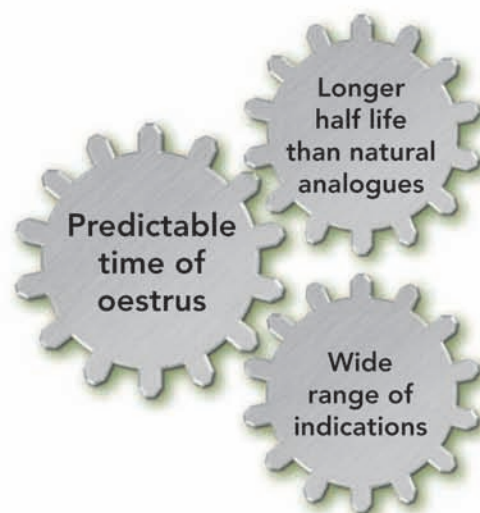
Figure 5  
Graph adapted from reference 10

— Estrumate  
— Dinoprost

The overall result is a rapid decrease of progesterone concentrations in the circulatory system which promotes the onset of oestrus with well-expressed behavioural signs at a highly predictable time.

In addition, all the indications of Estrumate in cattle require a convenient 2ml dose, compared to a 5ml dose when using most natural analogues. Estrumate is the market leading prostaglandin<sup>7</sup> and has a wide range of licensed indications in cattle fertility management, with a nil milk and 24 hour meat withhold:

- **Non-detected oestrus:** Following the diagnosis of a corpus luteum by rectal palpation, use of Estrumate should result in oestrus within the following 6 days.
- **Induction of parturition:** Estrumate can be used at the predicted calving date where extended gestations can result in dystocia.
- **Termination of a normal pregnancy:** From 7-100 days and then again after 150 days where mis-mating has occurred.
- **Termination of an abnormal pregnancy:** Such as a mummified foetus or hydrops of the foetal membranes.



- **Chronic endometritis or pyometra:** Where a functional corpus luteum (CL) is found, these cases can be successfully treated with a single dose of Estrumate. See the Metricure section for more information.
- **Luteal cysts:** Estrumate has been shown to correct this condition and bring about a return to cyclicity.
- **Controlled breeding in cattle:** With or without Receptal. Various protocols can be used with Estrumate, for example, the Intercept™ Programme as described on the next page.

Estrumate also has indications for use in mares.







# The Intercept™ Programme

A wide range of controlled breeding programmes has been developed over the years to synchronise oestrus as individual cow or herd management tools. They all have the aim of improving submission rates and reducing the calving to conception interval.

## Why Intercept™?

In order to shorten the ovulation window as required when using fixed time AI in cattle, Receptal is often used alongside Estrumate. This programme, in which both Estrumate and Receptal join forces, is called the Intercept programme. Receptal differentiates the Intercept Programme from any other synchrony protocol and Buserelin was found to be up to 50 times more potent than other GnRH analogues in an independent trial.<sup>6</sup>

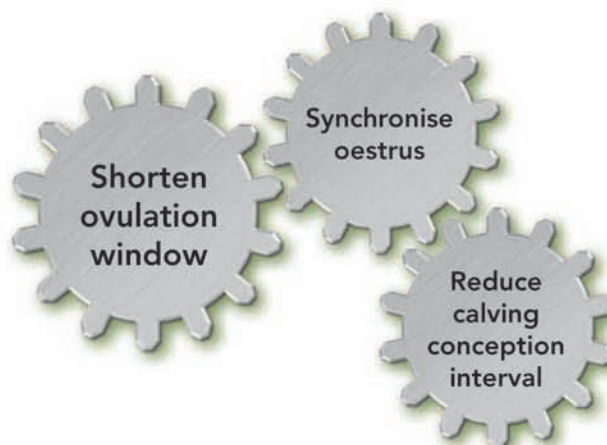
## What are the benefits of Intercept?<sup>11</sup>

- Reduces the impact of poor heat detection
- Synchronises oestrus and ovulation
- Gives 100% submission rates
- Improves the annual pregnancy rates
- Shortens the calving to conception interval
- Improves the herd Calving Index

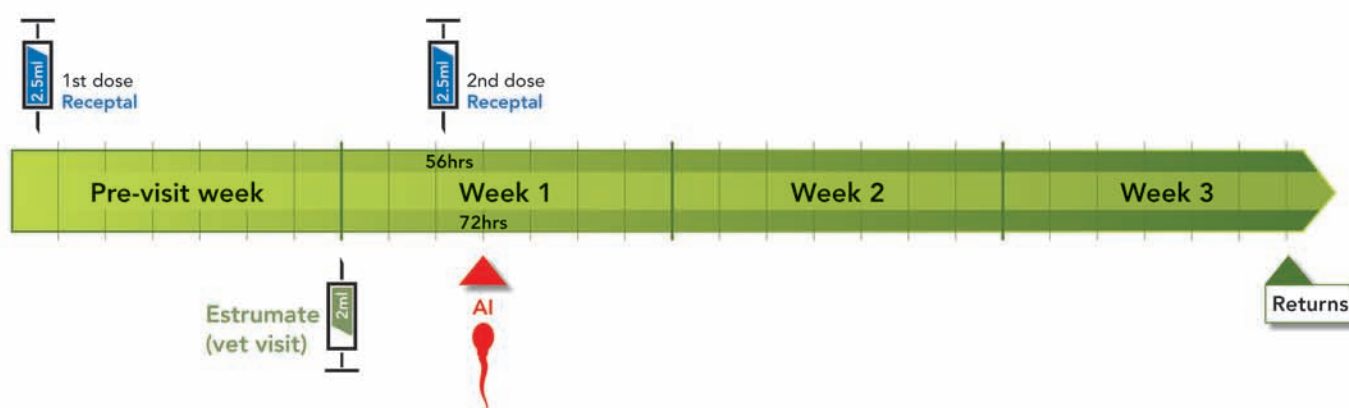
## How it works:

In a major UK study, the single factor most influencing cost benefit was the administration of the second dose of Receptal in the Intercept Programme.<sup>12</sup> The first dose of Receptal results in the luteinisation of large follicles, therefore 80–90% of cows will be in the luteal phase when Estrumate is administered, ensuring rapid removal of the CL.

The second dose of Receptal tightens up the spread of ovulation, permitting fixed time insemination. The Intercept Programme allows predictable service timing. If the animal returns after 3 weeks following the Estrumate injection, serve to the observed heat signs and give Receptal at service. Due to the specific characteristics of their cycle, the Intercept programme is not recommended for use in heifers.



## Intercept timings:



### Note:

The Intercept Programme should be used on healthy cows. Successful outcome of the programme requires an understanding of the multiple factors that influence cattle fertility. For successful treatment, animals should be cycling normally. Rectal examination before treatment should avoid the disappointment of treating non-cycling (anoestrous) or pregnant animals.

Attention should be directed to the diet and condition of the treated animals. Sudden changes in feeding levels, in feed constituents and in housing, etc. should be avoided around the time of the breeding programme, as should any other factors, such as regrouping, which could reasonably be expected to lead to stress. If AI is to be used, the quality of semen and insemination technique should be assessed beforehand.

# Other products in the range

Intervet/Schering-Plough Animal Health provides a wide range of products used for managing reproduction and treatment of various reproductive disorders in cattle and small ruminants. In addition to our leading brands Estrumate, Receptal and Metricure, the following products are also available as essential additions to your armoury:

## Chorulon®

The active ingredient of Chorulon is human Chorionic Gonadotrophin (hCG). It is used in cattle for the following indications:

- Cases of repeated failure of conception and cystic ovarian disease in cows and heifers
- Enhancement of luteal function when given 12 days after AI



## Dexafort®

The active ingredients of Dexafort are Dexamethasone Phenylpropionate and Dexamethasone Sodium Phosphate creating a long acting (7 to 10 days) corticosteroid. It is used in cattle as an anti-inflammatory and anti-allergic agent and for the following indications:

- For the treatment of primary ketosis (acetonemia) in cattle
- For the induction of parturition; Dexafort may be used to induce parturition in cattle in the last trimester and before day 260 of pregnancy



## Dexadreson®

The active ingredient of Dexadreson is Dexamethasone (as Dexamethasone Sodium Phosphate), creating a short acting (48h) corticosteroid. It is used in cattle as an anti-inflammatory and anti-allergic agent and for the following indications:

- For the treatment of primary ketosis (acetonemia) in cattle
- For the induction of parturition to avoid foetal oversize and mammary oedema in cattle. Dexadreson may be used to induce parturition in cattle after day 260 of pregnancy



## PMSG Intervet® 5000 IU (NI) Folligon PMSG 5000 IU (ROI)

Folligon/PMSG contains 5000 IU serum gonadotrophin per vial and can be substituted for both LH and FSH, stimulating development of the ovarian follicle. Indications for use in cattle are:

- In conjunction with progestagen treatment when used in protocols to synchronise non-cycling cattle
- As part of embryo transfer programmes to stimulate super ovulation
- In sheep PMSG Intervet is used in conjunction with Chronogest® CR containing 20mg flugestone acetate per sponge for synchronisation







**Intervet/Schering-Plough Animal Health provides a wide range of products used for managing reproduction and treatment of various reproductive disorders in cattle and small ruminants. More information and tailored advice are available from your partner in reproduction.**

#### References:

1. Dobson, H. *et al* (2008) *Animal* pp 1104-1111.
2. Sheldon, IM *et al* (2004) *Vet Record* 155, 383-387.
3. Dohmen, MJW *et al* (1994) *Proc 6th International Congress of EAVPT, Edinburgh*, p.107.
4. Sheldon, M *et al* (2009) *Biology of Reproduction* 81 pp 1025-1032.
5. LeBlanc, S (2003) *Cattle Practice* 11, 255-261.
6. Chenault, JR (1990) *Theriogenology* Vol. 34 no.1.
7. GFK sales data, January 2010.
8. Humblot *et al*, 2001.
9. Penny C D *et al*. *Cattle Practice* 2002 Vol 10 part 1.
10. EMEA, April 1997, June 1997; Berardinelli JG., *Theriogenology* 1989;32:301-314.
11. Malwinney, I and Biggadike, H (1998) *Cattle Practice* 6 (1) 29-31.
12. Watson C, *Vet Times* Oct (2004).

**Estrumate® NI:** POM-V **ROI:** POM

Contraindications, warnings, etc.: On rare occasions severe life-threatening local bacterial infections may occur associated with clostridial proliferation. It is important to keep treated animals under observation and, if local infection occurs, aggressive antibiotic therapy is a matter of urgency. Overdose in cattle: at x5 to x10 overdose the most frequent side affect is increased rectal temperature. This is usually transient, however, and not detrimental to the animal. Limited salivation may also be observed in some animals. Cattle should not be slaughtered for human consumption within 24 hours after administering the product. It is unnecessary to discard milk from treated cattle. Do not use in horses intended for human consumption. Operator warnings: Prostaglandins of the F2 type can be absorbed through the skin and may cause bronchospasm or miscarriage. Care should be taken when handling the product to AVOID SELF INJECTION OR SKIN CONTACT. Women of child-bearing age, asthmatics and persons with bronchial or other respiratory problems should avoid contact with, or wear disposable plastic gloves when administering the product. The possible incidence of bronchospasm with Estrumate is unknown. Should shortness of breath result from accidental inhalation or injection, seek urgent medical advice and show the doctor this warning. Accidental spillage on the skin should be washed off immediately with soap and water. For animal treatment only. Keep out of the reach of children. Protect from light. Following withdrawal of the first dose, use the product within 56 days.

**Metricure® NI:** POM-V **ROI:** POM

Contraindications, warnings, etc.: Not to be administered to animals known to be allergic to cephalosporins or penicillins. The product is not indicated for use during pregnancy but can be used during lactation. Not to be used concurrently with other intra-uterine antibiotic preparations. Withdrawal periods: Meat – 48 hours after last treatment, Milk – zero hours. Operator warnings: Penicillins and cephalosporins may cause sensitisation (allergy) following injection, inhalation, ingestion or skin contact. Sensitivity to penicillin may lead to cross sensitivity to cephalosporins and vice versa. Allergic reactions to these substances are

occasionally serious. Do not handle this product if you know you are sensitised, or if you have been advised not to work with such preparations. Handle this product with great care to avoid exposure, taking all recommended precautions. Wear disposable polyethylene gloves. If you develop symptoms following exposure, such as a skin rash, you should seek medical advice and show the doctor this warning. Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and require urgent medical attention. Wash hands after use. For animal treatment only. Keep out of the reach and sight of children. Do not store above 25°C. Syringes are for single use only.

**Receptal® NI:** POM-V **ROI:** POM

Contraindications, warnings, etc.: Pregnancy rates to first insemination after use of the 'Intercept' fixed time insemination programme in cows may be reduced by some 12% in herds with pregnancy rates to first service above 50% and in first parity animals (heifers). Highest pregnancy rates are achieved by servicing cows between 61 to 70 days after calving. Withdrawal periods: Cattle, horses and rabbits: meat – zero days. Cattle: milk – zero hours. Not to be used in trout intended for human consumption. For animal treatment only. Keep out of the reach of children. Do not store above 25°C. Protect from light. Following withdrawal of the first dose, use the product within 24 hours and store at +2°C to +8°C. Discard unused material.

**Chorulon® Dexafort® Dexadreson® Chronogest CR®**

**NI:** POM-V **ROI:** POM

**PMSG Intervet® 5000 IU: NI:** POM-V

**Folligon® PMSG 5000 IU ROI:** POM

#### Further information is available on request from:

Intervet / Schering-Plough Animal Health. Boghall Road, Bray, Co. Wicklow, Ireland. Tel: (00353)-(0)1-2050900, Fax: (00353)-(0)1-2050924  
www.partners-in-reproduction.com

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