



# GLEPRISTONE

## CLINICAL USE

2.5MHZ-M  
21 FEB  
16:17:06  
PROC 1/3/C/C/A  
YUMA REG MED CTR  
HP 1000

05663:22  
50MM/S  
XMIT:A  
129BPM  
24CM  
6HZ

### Clinical cases collection

(DOGS, CATS,  
AND EXOTIC ANIMALS)



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# Preface



Aglepristone is an antihormone with antiprogestosterone activity specifically developed for veterinary use. It is a product of French research as it is the result of studies on antihormones carried out by Roussel Uclaf in 1980-1990. For the veterinary pharmacopeia, this period was marked by the ban on administering synthetic oestrogenic derivatives in domesticated animals, derivatives which were frequently used to stop unwanted pregnancy in bitches. It is therefore for this indication that, from 1992, the first clinical trials relating to aglepristone were carried out. These trials have been particularly conclusive and led, in 1996, to the marketing authorization of aglepristone, which has been commercialised by VIRBAC laboratories since 1998.

Currently, the marketing authorization only provides for one indication: pregnancy termination in bitches. However, the interest which the veterinary world has shown in this new molecule, as well as the efficacy and safety (proven by almost 15 years of hindsight in pharmacovigilance) of aglepristone, have led a certain number of researchers to publish conclusive results on the termination of pregnancy in other species (queens, rabbits etc). Similarly, other indications have been trialed, mainly in domestic carnivores, such as the treatment of uterine infections, triggering birth in at-risk parturition, the treatment of fibroadenomatosis in queens.

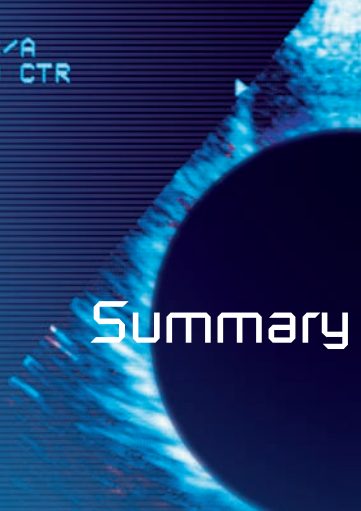
Already well established as an essential molecule in the management of reproduction, aglepristone also has potential indications in other areas, which remain to be specified by controlled and validated clinical trials.

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\* Case realised in collaboration with Dr Xavier Lévy

\*\* Bibliographical synthesis by Dr Gogny

\*\*\* Bibliographical synthesis by Dr Navarro



## LEGAL USE OF AGLEPRISTONE: ABORTION IN BITCHES

### Aglepristone – an antiprogesterone-acting molecule.

In our domestic carnivores, progesterone is the hormone which ensures that pregnancy is maintained. Its production is carried out uniquely by the ovaries at the level of the *corpus luteum* and in its absence, abortion is unavoidable.

When an “abortion of convenience” is indicated, aglepristone, as an antiprogesterone, is therefore logically placed as a molecule perfectly reserved for this use. At the uterine and mammary level, the molecule binds to the progesterone receptors with far higher affinity (three times more than progesterone in bitches and 9 times more in queens), while antagonising their effects.

	Relative binding affinity to progesterone receptors	
	Dog	Cat
Progesterone	100%	100%
Aglepristone	312%	926%

Therefore, when aglepristone is administered, it mimics an absence of progesterone at the level of uterine endometrium. As the metabolism of this is disturbed, it leads to embryonic mortality and resorption, and even expulsion of the foetuses in some cases.

## Use of aglepristone – when and how?

In the clinic, we use to face with two types of situation:

- The bitch which was mated recently (as a general rule, a few days earlier), is brought for a consultation to induce an abortion.
- The bitch in which pregnancy has been established during an ultrasonographic examination and for which the pregnancy is either unwanted or inadvisable.

### Medical reasons justifying an abortion of convenience

- Single pup syndrome in large breeds (increased risk of dystocia)
- Diabete
- Pregnancy toxemia
- Animal suffering from renal failure
- Animal suffering from heart failure

The first fundamental step is to define the stage of pregnancy: at the beginning (0-22 days, or before a diagnosis can be surely settle), in the middle (22 to 45 days of pregnancy) or at the end of pregnancy (more than 45 days). Why? Because aglepristone is indicated before 45 days of pregnancy. Further, beyond this stage, the foetuses will be expelled, a phenomenon which may be taken badly by the owners: it is therefore recommended that the animal be hospitalised for the time of the abortion. In addition, aglepristone alone is sometimes not enough and the addition of prostaglandin injections prove to be necessary to guarantee a result (see clinical case no. 1).

The highest level of efficacy is seen with two injections of 10 mg/kg (0.33 ml/kg), 24 hours apart. The abortion will then be effective in more than 95% of cases at the beginning and middle stages of pregnancy and, in all cases, this will be achieved in the following 1-7 days with a median period of 4 days. When injecting large volumes, local reactions have sometimes been reported at the injection site, reactions are often combined with a decrease in efficacy. It is therefore recommended not to inject more than 5 ml per injection site and to perform a massage to facilitate the absorption of the product.

In the directions for use, it was previously recommended to carry out injections on the inside of the thigh. This method has been recently modified: the subcutaneous route on the neck must now be used.

### Abortion with aglepristone: what to expect.

When abortion is induced at the beginning of pregnancy, translucent vulvar discharge can be observed in 8 - 12% of females, but in the majority of cases, no external appearance will be detectable. In the middle of pregnancy, medical abortion will end in embryonic resorption. 33% of bitches treated in this way then present brownish discharge 72 - 96 hours after treatment. When these are present, no adjuvant antibiotherapy is needed however.

Transient symptoms corresponding to a physiological phenomenon mimicking birth (hypothermia, beating or temporary anorexia) can also appear during the abortion.

No change in the biochemical and haematological parameters has been observed following the use of the product.

Consequences on reproductive function are minimal. An early return to the heat cycle can be seen, from 1 to 3 months after treatment was initiated, and can be connected to a central effect of the aglepristone at the hypothalamo-hypophyseal level. Fertility is preserved (86.2% of bitches treated in this way are fertile after the first oestrus and 100% after the second). No fertility problems have been reported after using this product.

## How to avoid failure?

The success of the treatment must be systematically verified by an ultrasonographic examination:

- In the 20 days after the bitch be mated
- 10 days after the injection when pregnancy has been confirmed

In all cases, if abortion has not been achieved, it is possible to readminister a second treatment up to 45 days.

When abortion has not been achieved, particularly in the middle of pregnancy, it is not rare that the uterine light appears dilated following resorption. Be careful because these images can sometimes be incorrectly interpreted as a developing pyometra.

**Aglepristone is today a standard treatment for the abortion of convenience over Europe. Its easy usage and high level of efficacy, combined with good safety, make it a treatment of choice which should be recommended in the vet practice.**

## MEMORANDUM

### → FOLLOW STRICTLY THE PROTOCOL:

- Wait for the end of the heat cycle
- Weigh the bitch.
- Inject 0.33 ml/kg exactly (do not round down)
- Only perform the injection subcutaneously in the neck
- Do not inject more than 5 ml per injection site.
- Perform a massage in the injection area to aid absorption of the product.
- Perform the second injection strictly 24 hours later.

### → COMMUNICATE WITH THE OWNER:

- Transmit the data: abortion can be carried out between D0 and D45 of pregnancy with an over 95% success rate.
- Warn of the possibility of failure: an ultrasonographic examination 10 days after the protocol is essential.
- Also warn that the oestrus cycle may return sooner.

## KEY POINTS

**Aglepristone blocks the progesterone action without changing the hormonal profile**

**Aglepristone exerts an excellent efficacy in the abortion protocol**

**Communication with the owner is essential**



## PRACTICAL SITUATIONS

In a large number of affections encountered in reproduction, there is frequently a temptation to use surgery. Aglepristone can be an interesting alternative when the owner refuses the surgical option, or when the owner wants to conserve the reproductive capacities of the female, or when general anesthetic is contraindicated or even when surgery is a risky or difficult option.







## THE BITCH

**Two major types of affections can be managed with aglepristone in bitches:**

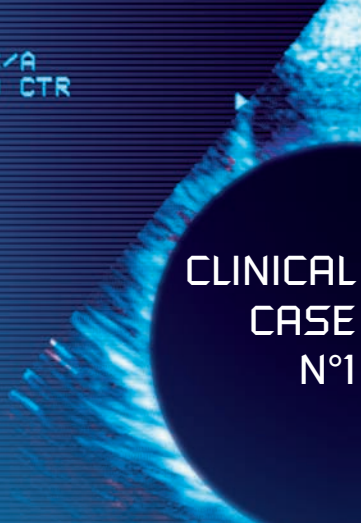
1 - Misalliances: the goal is therefore to induce a medical abortion, which is the molecule's indication. But sometimes, in the daily practice, things do not always happened as planned:

- What should you do when you are faced with a failure of the abortion protocol?
- What should you do when the owner brings his/her bitch at a very late stage, after 45 days?

2 - Uterine pathologies: if surgical treatment is the treatment of choice, various situations can lead to a move to a medical alternative

**Aglepristone is also an interesting molecule for optimising reproduction and for helping manage Caesarean sections or to trigger birth (off-label).**





# How to manage a failure of the abortion protocol?

*Relevance of aglepristone – cloprostenol combination*

**A two-year-old Sharpei bitch was presented for translucent, serous vulvar discharge, which started in the morning. An accidental mating occurred a month and a half ago.**

## CLINICAL EXAMINATION

**Clinical examination:** good general health, slight mammary hypertrophy.

**Abdominal palpation:** tight abdomen and uterus hypertrophy.

**Abdominal ultrasonographic examination:** on-going pregnancy (photo 1): foetal movements and heartbeats of four foetuses  
→ pregnancy estimated at four weeks.



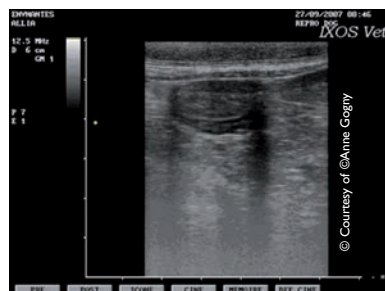
*Photo 1 : The foetuses are visualised with abdominal ultrasonographic examination, carried out at approximately four weeks of pregnancy.*

## TREATMENT

The owner wants to put an end to pregnancy, but would like the bitch to be able to reproduce at a later stage.

**Protocol:**

**Aglepristone injected subcutaneously at the dose rate of 10 mg/kg (0.33 ml/kg), twice at D0 and D1.**



*Photo 2 : Ultrasonographic examination carried out one week after the first injection shows two dead foetuses.*

## EVOLUTION

**At D8:** exhaustion, dysorexia, licking of the vulva, tumefaction and non-odorous brownish discharge in the vulva.

Ultrasonographic examination: two dead foetuses (photo 2).

Diagnosis: Failure to pregnancy termination and foetal retention

Treatment	Dose and route	Objective
Aglepristone	10 mg/kg SC	Pregnancy termination
Cloprostenol	1 µg/kg/h SC, 10 injections/day for 3 days	Contractions and uterine evacuation
Metoclopramide	IV, BID	Limit the side effects of prostaglandins
Amoxicillin	10 mg/kg per os, BID for 7 days	Prevent septicaemia
NaCl 0,9%	60 ml/kg/jour IV	Daily water intake

#### Hospitalisation for 3 days:

- mild agitation
- no vomiting or signs of discomfort
- brownish vulvar discharge for 3 days
- from 2nd day, products no longer visible on ultrasonographic examination

**At D21 :** good general health, mammary involution, ultrasound image of uterine involution

**At D90:** good general health. Heat signs appeared two months after the end of the abortion treatment, i.e. four months after the previous oestrous cycle.

## COMMENTS

Embryonic resorption or foetal expulsion took place in the four to seven days following the second injection of aglepristone. A brown-coloured mucous discharge was observed 24 hours before the expulsion of the products and lasted for three to five days.

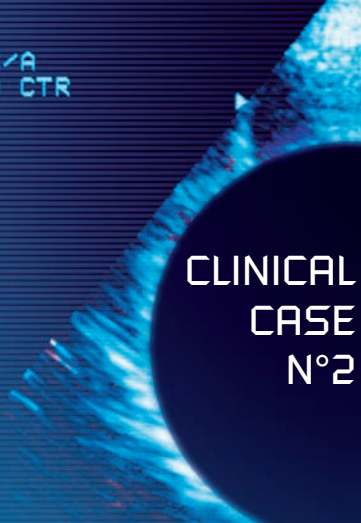
Used between the 26<sup>th</sup> and 45<sup>th</sup> day of pregnancy, aglepristone is effective in 95% of cases [Fiéni, 2001]. Failures are therefore possible. When only a partial abortion is achieved and the products are dead, combining prostaglandins with antiprogesterone enables a complete evacuation of the uterus. However, this protocol has not been tested in a controlled study [Fiéni, 2006]. Further, prostaglandins have major side effects (tachycardia, bronchoconstriction, digestive problems etc) and cannot be used in animals with cardiorespiratory problems.

In the bitch studied, the initial injections of aglepristone terminated pregnancy, but did not lead to the expulsion of the products. Cloprostenol allowed completing the uterine evacuation within three days with side effects limited by the use of a low dose (1 µg/kg).

After the abortion, the interoestrus phase was shortened by two months. This phenomenon is described without clarification of its physiological support [Fiéni, 2001, Galac, 2000].

## CONCLUSION

When induced abortion is indicated in bitches, aglepristone is very effective. However, after the 26<sup>th</sup> day of pregnancy, a 5% failure rate is possible. That is why it is essential to perform a follow-up by ultrasonography in order to check that the abortion is complete. In the event of failure, the combination of aglepristone-cloprostenol at a low dose can help to complete the uterine evacuation. This solution makes it possible to preserve the bitch's breeding potential.



# Can you abort after 45 days of pregnancy?

(off-label)

*Late abortion in bitches*

**A 4-year-old German shepherd bitch was presented for a suspicion of presumed pregnancy for six weeks. The owner does not want to neuter the bitch.**

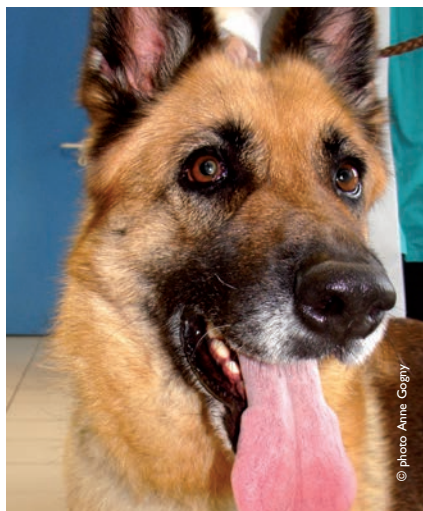


Photo 1 : A German shepherd bitch is presented for a suspicion of pregnancy.

## CLINICAL EXAMINATION

**Clinical examination:** thinness in the lumbar region, voluminous abdomen and slight mammary hypertrophy (photo 1).

**Abdominal palpation:** Presence of foetus.

**Ultrasonographic examination:** visualisation of 4 living foetuses → birth estimated at D13 or D14 (photos 2 and 3).

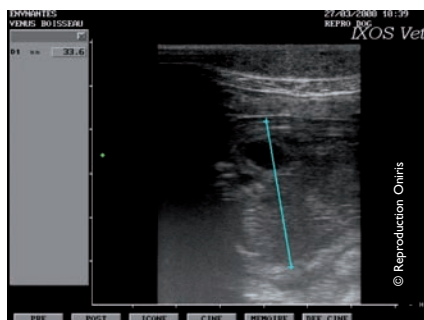


Photo 2 : At ultrasonographic examination, the foetuses are visible. The visible structures (femur, metatarsus etc) imply advanced pregnancy.

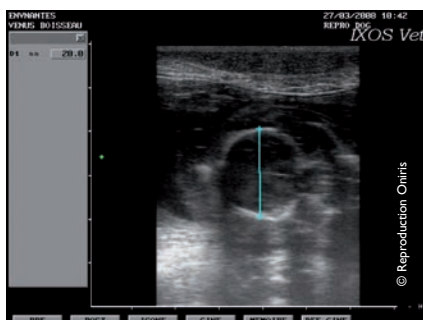


Photo 3 : The measurement of the cranial biparietal diameter is performed on a perpendicular section at the cerebral lobes.

## TREATMENT AND EVOLUTION

**Injection of 10 mg/kg of aglepristone SC (i.e. 0.33 ml/kg) on D0 and D1 (off-label).**

**Hospitalisation:** the objective was to follow the abortion procedure.

**D2:** start of the abortion

**D3:** end of the abortion (five runs).

**D4:** ultrasonographic examination: empty uterus (photo 4).

**D15:** bitch in good general health.



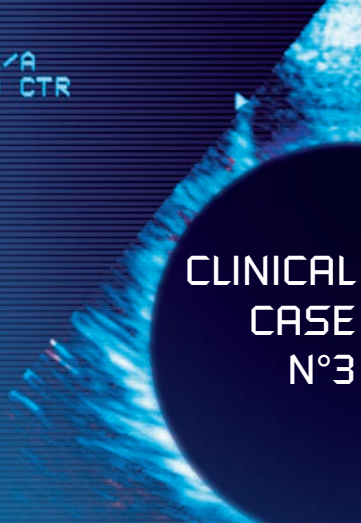
*Photo 4: The measurement of the abdominal diameter is carried out on the stomach protrusion.*

## COMMENTS

Aglepristone has an effect for the whole pregnancy period in bitches, even if it only has market authorisation for pregnancy termination up to 45 days. Its efficacy is good, but after D26, treatment failures have been described [Gogny, 2004; Fiéni, 2001a, Fiéni, 1996; Fiéni, 2001b]. Further, when pregnancy is very advanced, the birth of live and viable products is possible. In this case, hospitalising the bitch allows to verify that the abortion did take place, that the products have all been expelled and to move to the euthanasia of the pups which are born alive.

The relevance of a late abortion is justified when the bitch is intended for reproduction and the on-going pregnancy is the result of a misalliance or when maintaining pregnancy is too risky for the animal (very young, large-breed bitch or a very elderly bitch, risk of eclampsia, past history of pelvic fracture, diaphragmatic or inguinal hernia, brachycephalic breed, distortion between the size of the male and the female, prospect of Caesarean section in bitches where intervention is risky etc). In this event, abortion between the 45<sup>th</sup> and 50<sup>th</sup> day allows avoiding the last phase of pregnancy – which leads to the most important changes in the bitch – and the euthanasia of the viable pups born full term can be avoided. It also allows to avoid any intervention on the genital organs at a stage where the risk is higher because of physiological changes resulting from pregnancy, as much from the point of view of the anesthetic (anaemia, effects on the metabolism of glucose, volemic changes, arterial hypertension etc) as from the surgical or post-operative perspective (increase in uterine volume, immunodepression etc). The absence of surgery also means that the female's reproductive potential can be best protected.

On the other hand, late abortion can be useless when neutering is desired at a later stage, especially in a large-sized dog in which the injection represents a high cost. Moreover, beyond the 55<sup>th</sup> day, when pregnancy termination is justified by a foeto-maternal disproportion, the risk of Caesarean section becomes equivalent to that of a full-term birth and the benefit brought by the abortion is limited. The treatment choice should therefore be evaluated case by case, depending on the health of the bitch, its reproductive future, and the stage of pregnancy and the result of the risk-benefit balance. In a financial point of view, when sterilisation is planned at a later stage, it is sensible to check whether the cost of the abortion added to that of the ovariectomy is lower than that of an Ovariohysterectomy.



## CLINICAL CASE N°3

# Can pyometra be prevented? (off-label)

*Treatment of early cystic glandular hyperplasia in a bitch suffering from heart failure*

**A 8.5-year-old Arab greyhound bitch (sloughi) weighing 17,8 kg, was presented for a cough and heart murmur, which appeared a year earlier (photo 1). The last heat cycle occurred four months ago and, since then, frequent licking of the vulva was observed.**



© Aurélie Bourguet

*Photo 1 : An 8.5-year-old sloughi greyhound bitch is brought to consultation because of a chronic cough and a cardiac murmur detected one year earlier. Courtesy of Aurélie Bourguet*

## CLINICAL EXAMINATION

**Clinical examination:** thin animal.

**Cardiorespiratory examination:** holosystolic murmur on the left part, grade 4/6; short, dry cough with no respiratory auscultation disorders.

**Abdominal palpation:** hypertrophied uterine horns.

**Cardiac ultrasonographic examination:** Major mitral reflux associated with minimal tricuspid reflux, diminished cardiac contractility with preservation of the thickness of the cavity walls and no dilation of the cardiac cavities.

**Abdominal ultrasonographic examination:** uterine dilatation (light diameter: 5 - 7 mm (photo 2)), some parietal cysts.

**Biochemical profile (to investigate the animal's thinness):**

Alkaline phosphatase measurement, ALAT, cholesterol, GGT, potassium, bile acids, albumin and total proteins: within usual values (excludes digestive problems).



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*Photo 2 : At the abdominal ultrasonographic examination, the uterus appeared slightly dilated. The diameter of the light of the uterine horns is 5 - 7 mm. Some parietal cysts are also visible. Courtesy of CHV ENVN*

## TREATMENT

**Cardiac failure:** follow-up of the development of the cough and general health of the animal.

**Glandular cystic hyperplasia:** injections of 10 mg/kg of aglepristone SC (i.e. 0.33 ml/kg, off-label), at D0 and D1.

## EVOLUTION

**At D90:** good general health, vulvar licking has stopped.

**At D135:** at ultrasonographic examination, minimal parietal hyperplasia of the proximal section of the left uterine horn, no liquid content, cysts absent, body of uterus and right uterine horn look normal (photo 3).



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*Photo 3 : Abdominal ultrasonographic examination check-up carried out 4.5 months after treatment shows improvement: although the left uterine horn still has slight parietal hyperplasia, the body of the uterus and the right uterine horn look normal.*

## COMMENTS

The elements currently known on the pathogenesis of glandular cystic hyperplasia implicate the progesterone's action, which favours endometrial glandular secretion and that of oestrogens, which potentiates the progesterone action by increasing the endometrial response to the latter. An increase in the number of receptors to oestrogens and to the progesterone has also been noted. [Fransson, 2003].

In addition, progesterone inhibits uterine contractions, which, added to the endometrial hypersecretion, encourages the development of bacteria in the uterine light. Glandular cystic hyperplasia is therefore a favourable ground for the appearance of pyometra, an affection which concerns 23 - 24% of unsterilised bitches.

Regarding the bitch studied, glandular cystic hyperplasia was luckily discovered. Nevertheless, this animal presents several factors which promoted its development: its age (8.5), its status (nullipara) and the stage of its oestral cycle (4 months after the last cycle) (table).

Risk factors for appearance of pyometra in bitches
Nullipara
Over 8 years old
Treatments with progestogens or oestrogens
Termination of heat cycle with progestogens
Breed predisposition

The treatment of early glandular cystic hyperplasia seems to be relevant as it can prevent the secondary development of pyometra.

## CONCLUSION

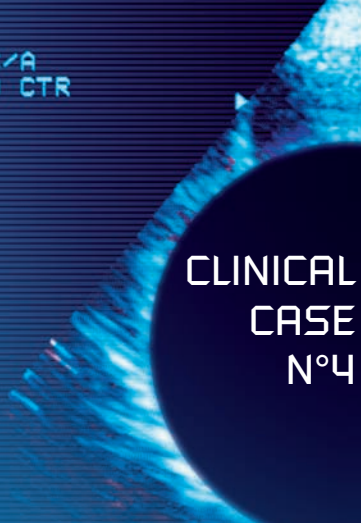
To treat pyometra while maintaining the animal's reproductive function, it is possible to use aglepristone, in combination or not with prostaglandins [Fiéni, 2006a].

For glandular cystic hyperplasia, it is possible to use aglepristone to stop the endometrial development induced by progesterone. At the moment, no controlled study has been carried out on a large scale to evaluate the efficacy of this treatment, but in the case of the bitch studied, progress showed that an improvement had been brought about.

## Thanks

The author would like to thank the ENVN (French National Veterinary School of Nantes) technical imaging floor for the ultrasound images and Miss Aurélie Bourguet for the photo of her animal.





# What should be done on a dog with pyometra and which has an anesthetic risk? (off-label)

*Treatment with aglepristone of pyometra in an elderly bitch with pulmonary metastases*

**A poodle bitch of 11.5 years old, intact, was presented at the consultation for purulent and haemorrhagic vulvar discharge, which had occurred for three days (photo 1). The last heat cycle started 6 weeks before.**

## CLINICAL EXAMINATION

**Clinical examination:** good general health, advanced periodontal disease, respiratory rattling and whistling, present since the animal was 7 years old. Numerous nodules of 0.5 - 2 cm in diameter on both mammary glands, and a cutaneous nodule of 2.5 cm in diameter in the cervical area were observed.

**Abdominal palpation:** Hypertrophied uterus.

**Abdominal ultrasonographic examination:** uterine hyperplasia containing liquid and debris in suspension in the light of the uterine horns.

**Pulmonary radiography:** contained nodular image with tissue opacity, of 7 mm in diameter, on the chondrocostal junctions of the 4<sup>th</sup> intercostal space, and diffuse, generalised interstitial opacification of the pulmonary parenchyma → strong suspicion of pulmonary metastases.

**Blood test:** slight increase in alkaline phosphatases.



*Photo 1 : A poodle bitch of 11.5 years old is presented at consultation for purulent, haemorrhagic vulvar discharge, which have been present for three days.*

## DIAGNOSIS

Open cervix pyometra and mammary tumours combined with pulmonary metastases.



## TREATMENT

### Surgical treatment:

Inconceivable due to the anesthetic risks connected to the health of the lung.

### Medical treatment:

- Hospitalisation for three days
- SC amoxicillin injection, once a day for three days, then per os for 10 days.

### Protocol:

**SC injection of 10 mg/kg of aglepristone (i.e. 0.33 ml/kg, off-label) on D0, D1, D8 and D15.**

## EVOLUTION

**D2:** more intense purulent and haemorrhagic vulvar discharge observed.

**D3:** disappearance of vulvar discharge. At the ultrasonographic examination, a significant improvement with reduction in diameter of the uterine light and absence of liquid content was observed.

**D8:** the owner does not come to the appointment for the third injection of aglepristone.

**D15:** the 3<sup>rd</sup> injection of aglepristone and an ultrasonographic examination is performed: reduction in size of the uterus and the thickness of the uterine wall (photo 2).

**D28:** ultrasonographic examination planned, phone call from the owner informing of the good health of the bitch and the absence of vulvar discharge.



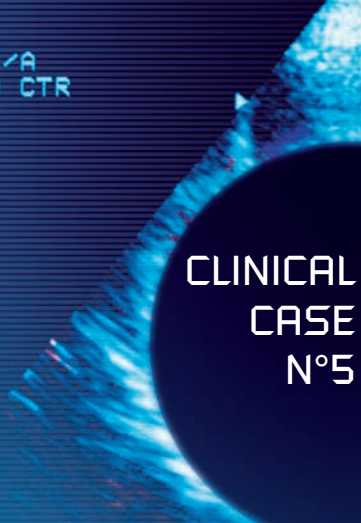
Photo 2: Ultrasonographic examination check-up performed on D15 shows a reduction in the size of the uterus, with a diameter of only 1 cm now, and in the thickness of the uterine wall. The uterine light is still visible however.

## COMMENTS

Taking into account the pulmonary lesions, any surgery was recommended in this bitch. The medical treatment, based on aglepristone has enabled to cure the pyometra but without enabling full restoration of the uterine wall. Recurrence is therefore possible, although it is probable, taking into consideration the bitch's health that the cancer develops more quickly than a possible recurrence of the uterine infection.

The combination of prostaglandins with aglepristone would have enabled to improve uterine evacuation. However, these molecules have side effects, particularly tachycardia and bronchoconstriction, which are incompatible with the health of the bitch studied.

In the management of pyometra, aglepristone is a good alternative to Ovariohysterectomy when the bitch is not in sufficient health to cope with the anesthetic risk which goes with surgical treatment.



# How to facilitate surgery of pyometra? (off-label)

*Treatment of pyometra:*

*prepare ovariohysterectomy with aglepristone*

**An intact, mixed-breed bitch, 8 years old and weighing 12 kg, was presented for weight loss and increase in drinking intake for five days (estimated at 3 litres of water per day).**

**A prevention treatment of heat cycle with medroxyprogesterone acetate was given between 2 and 4 years.**

**The heat occurred a month and half ago.**

## CLINICAL EXAMINATION

**Clinical examination:** : T = 39.5°C, slight amyotrophy of the hindquarters

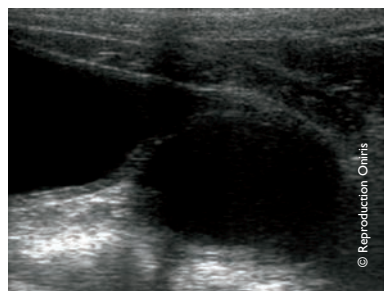
**Abdominal palpation:** uterine hypertrophy

**Urinary analysis:**

- Urinary density = 1.006, which confirms polyuropolydipsia
- Urine dipstick test: leukocyturia, proteinuria and haemoglobinuria
- Heller's test: albuminuria
- Examination of the urinary precipitate: numerous bacillae

**Abdominal ultrasonographic examination:** bilateral dilation of the urinary horns, filled with liquid from the body of the uterus to the caudal kidney region, with a diameter of 3.5 cm, which confirms the presence of pyometra (photo 1).

**Biochemical blood parameters:** slight increase in alkaline phosphatases (267 IU/l, usual values between 0 et 200 IU/l) and slight increase in total proteins (84 g/l, usual values from 55 to 80 g/l).



*Photo 1 : At ultrasonographic examination, a tubular structure of 3.5 cm, corresponding to the uterus, can be seen in a ventral position to the bladder.*

## TREATMENT

→ Long-term treatment: ovariohysterectomy

→ Preparatory treatment: taking into account the degree of uterine distension, it seems appropriate to trigger the evacuation of the uterus before intervention with: **2 injections SC of 10 mg/kg of aglepristone (i.e. 0.33 ml/kg, off-label) at D0 and at D1.**

→ Amoxicillin, 10 mg/kg, per os from D0 to D5 to prevent possible septicaemia.

→ Hospitalisation to monitor uterine evacuation.

## EVOLUTION

- D2:** Massive purulent vaginal discharge, reduction of the uterine volume on ultrasonographic examination (photo 2).
- D4:** ovariohysterectomy: easy intervention without complications on a uterus, which is almost normal in size.
- D14:** good general health, quantity of water drunk within usual values and normal urine analysis.

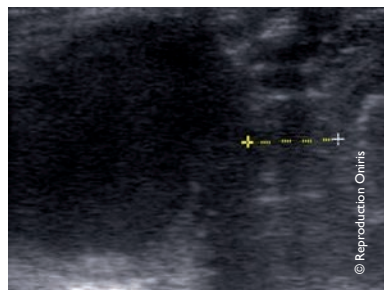


Photo 2: Three days after treatment with aglepristone, the uterus is less dilated and its contents are more echogenic.

## COMMENTS

In the management of pyometra, the recommended treatment in the first instance is ovariohysterectomy, except in cases where the animal is not in good health enough to cope with the anesthetic or if it is a breeding animal.

However, when the volume of the uterus is large, especially in closed pyometra, it can seem important to trigger uterine evacuation before intervention, in order to:

1. Diminish the risk of uterine rupture;
2. Limit the risk of a vacuo shock related to the sudden exeresis of the uterus (photo 3);
3. Improve the comfort of the surgeon's work.

This can be performed with aglepristone which, administered at a dose of 10 mg/kg SC on the neck causes vaginal discharge 4 - 38 hours after the 1<sup>st</sup> injection in closed pyometra [Fiéni, 2006a].

This preliminary treatment has an additional interest: it stops the evolution of pyometra, which means that treatments designed to restore the animal's renal function can be carried out, and to contain any possible start of septicaemia, before intervention. These measures have the advantage of limiting the perianesthetic risk, which goes from 1.33% for an ASA III class animal (systemic complaint with reduced general repercussions) to 0.05% for an ASA II class animal (systemic complaint with minor general repercussions) [Brodgelt, 2009].

**In the case of the bitch presented here, treatment with aglepristone has made it possible to evacuate the uterus and tackle surgical intervention in more favourable conditions.**

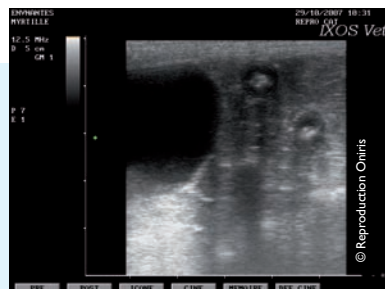
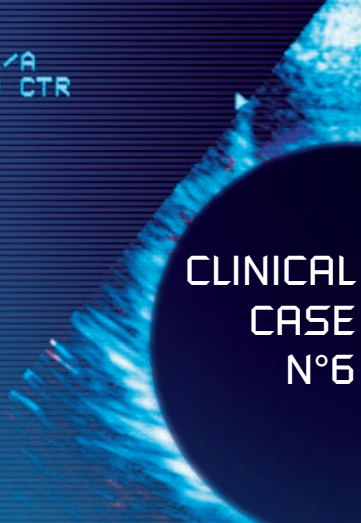


Photo 3: In pyometra in bitches, the volume of the uterus can increase. Ovariohysterectomy is therefore related to a risk of uterine rupture and/or a vacuo shock, which increases the risk of perioperative mortality. Preliminary evacuation makes it possible to move to intervention in more favourable conditions.



# Can birth be triggered in bitches\*? (off-label)

Litterature synthesis

**Some pathological situations (pregnancy toxemia, pre-partum eclampsia, risk of dystocia or abnormally increased pregnancy length) can necessitate medical induction of parturition.**



Photo 1 : Labrador bitch with its litter (Catherine Picot © VIRBAC - DR)

## PROTOCOL

### Determination of the date of birth:

- Using to the ovulation date: determined when the progesterone rate reaches 6 ng/ml or by ovarian ultrasonographic examination
- By determination of the LH peak

### Protocol:

Birth is induced between 59 and 61 days post ovulation (60 days post LH peak):

**Aglepristone 15 mg/kg (0.5 ml/kg, off-label) SC**

**24 hours later, oxytocin, 0.15 UI/kg every 2 hours until expulsion of the last pup.**

## RESULTS

**Time before the birth of the first pup:** on average 25.9 hours after the aglepristone injection. Breed variations are observed: small bitches (< 10 kg) start give birth earlier (sometimes before the first injection of oxytocin) than bitches of large breed, Beagle bitches give birth on average 30 hours after the first injection.

**Average duration of birth:** 9.5 hours (no difference with a physiological birth). The duration is shortened for small dogs (3.8 hours) compared to the Beagle (5.9 hours), and large breeds (30 – 40 kg) (11.2 hours) and giant breeds (> 40kg) (14 hours).

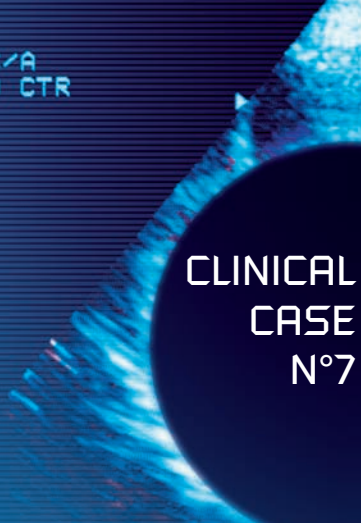
**Interval between 2 pups:** a little less than 2 hours (higher than for a natural birth).

The size of the litters and the survival rate of the pups are similar to those obtained during a natural birth. One litter of small-breed pups probably died because of prematurity.

## CONCLUSION

The protocol combining aglepristone and oxytocin is effective and safe to trigger birth in bitches if the start date of pregnancy is accurately known, otherwise there is a risk of prematurity.

\* According to the studies published by Fontbonne in 2009 and Fiéni in 2009.



# How to plan a caesarean section\*? (off-label)

Literature synthesis

**A planned Caesarean section gives the owner and veterinarian more peace of mind than one which is carried out as an emergency. This type of Caesarean section cannot be offered for all bitches.**

## PROTOCOL

Selection criteria for bitches:

Epidemiological criteria	Elderly primiparous bitch	Litter < 3 pups or > 8 pups	Brachycephalic breed
"Physical" criteria	Dystocia during a previous pregnancy	Bitch's lineage known to have dystocia (e.g. uterine atony)	Vaginal anomaly preventing natural birth (bridle, stenosis)
"Emergency" criteria	End-of-pregnancy metabolic disorder (eclampsia, hypocalcaemia)	Absence of veterinary emergency within 1 hour	

**The planned date of birth must be accurately known:**

- Determination of ovulation (see: clinical case n°6)
- Highlight the drop in progesterone (< 2 ng/ml) before birth

**Caesarean section is programmed between 59 and 60 days post-ovulation with the following protocol:**

**Aglepristone 15 mg/kg (0.5 ml/kg, off-label) SC**

**Caesarean section 20 hours after** (pre-medication: metoclopramide, cephalexin and oxygen mask; induction: propofol; maintenance: isoflurane).

**Post surgery:** bitch: NSAID, oxytocin and cephalexin injections; pups: put in paediatric incubator until complete awakening of the mother.

## RESULTS

89% of bitches produce milk from the end of surgery, the others start lactation the next day (pups are fed with substitution milk while waiting).

The pups death-rate (in the first 15 days of life) is low (2.6%) compared to rate reported for Caesarean sections carried out as an emergency (13 to 30%).

## CONCLUSION

The use of this protocol to carry out a Caesarean section one to two days before the planned date of the term is safe for bitches and for pups if the date ovulation has been determined accurately. This protocol can allow you to programme the Caesarean section and therefore best organise the procedure (presence of qualified staff, preparation of resuscitation equipment etc) so that you have all the chances of survival on your side.

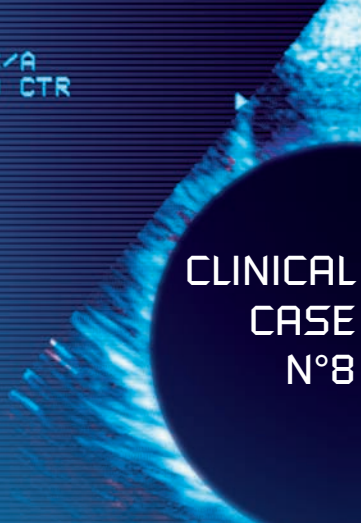
\* According to Levy's publications of 2008 and 2009.



## THE QUEEN (off-label)

**Aglepristone acts by competitively inhibiting the effects of the progesterone and this was the case everywhere where progesterone receptors are to be found. In cats, different situations can therefore be treated using aglepristone (off-label): misalliances, uterine complaints or certain mammary complaints such as mastosis or fibroadenomatosis.**





## CLINICAL CASE N°8

# Abortion: how to terminate pregnancy in queens? (off-label)

*Late abortion in a queen using aglepristone*

**1-year-old Russian blue queen presented for a supposed pregnancy. Animal intended for reproduction, but has not produced any litter yet.**



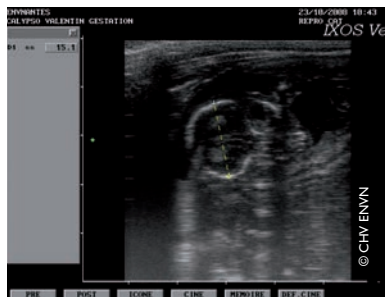
*Photo 1 : Queen, in good general health, displays abdominal distension and pinkened areolae around the teats.*

## CLINICAL EXAMINATION

**Clinical examination:** good general health (photo 1), distended abdomen and pinkened areola on the area surrounding the nipples.

**Abdominal palpation:** indurated structures in the abdominal area.

**Abdominal ultrasonographic examination:** visualisation of 3 foetuses (photo 2) with foetal movement and heartbeats. Date of birth estimated 25 days later.



*Photo 2 : Three foetuses can be seen by ultrasonographic examination.*

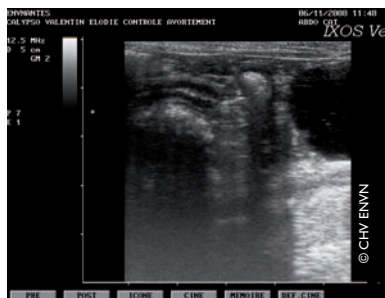
## TREATMENT

**Protocol:**  
**SC injection of 15 mg/kg of aglepristone**  
**(i.e. 0.5 ml/kg, off-label specie) at D0 and D1.**  
The owner refuses hospitalisation of the animal.

## DEVELOPMENT

**D3:** Expulsion of three foetuses in a few hours.

**D10:** on ultrasonographic examination, empty uterus on the way to involution (photo 3). As there are no milky secretions on the day of the check-up ultrasonographic examination, antiprolactins are not prescribed.



*Photo 3 : Ten days after treatment with aglepristone, ultrasound shows an empty uterus on the way to involution. Abortion began three days after the first aglepristone injection and ended a few hours later.*



Aglepristone is approved for inducing abortion up to 45 days of pregnancy in bitches, but not in queens. In cats, aglepristone triggers abortion in 88.5% of cases, when administered between D29 and D37 at the rate of 15 mg/kg SC twice at a 24-hour interval [Fiéni et al, 2006]. An equivalent efficacy, of 87%, was obtained in another study [Georgiev, 2006]. 72% of queens abort in the four days after the first injection, the others in eight days.

The birth of live products is possible if pregnancy is advanced. Hospitalising the cat allows the vet to euthanize, as soon as they are born, the live kittens and save owners from seeing live foetuses at a more or less advanced stage of development.

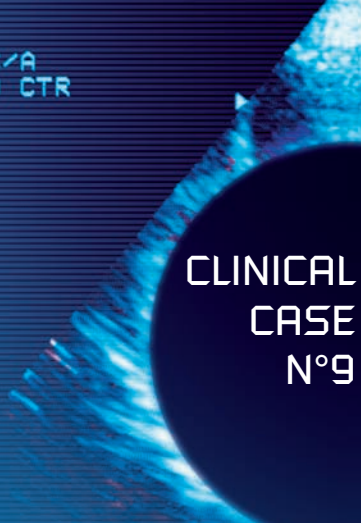
Aglepristone displays low toxicity, with injection pain in 10% of cats and inflammation at the injection site which affects 1.8% of cats. This reaction calms down within 24 hours [Fiéni et al, 2006].

The usefulness of a late abortion can be discussed and one can consider letting the pregnancy go to term. However, the final third of pregnancy is characterised by marked hormonal and blood changes with major repercussions (anaemia, neutrophilia, weight gain, metabolic changes etc). As such, pregnancy constitutes a demanding event for the body and it does not seem useful to prolong it when reproduction is not wanted. There is also the issue of euthanizing the kittens, a prospect which is appreciated by owner-breeders to a greater or lesser extent.

As a competitive progesterone antagonist, aglepristone triggers abortion during the entire pregnancy period in queens [Gogny, 2004]. Failures are nevertheless possible, as in bitches, especially when pregnancy is very advanced. This is why it is advisable to carry out an ultrasound evaluation of the abortion 8 to 10 days after the injections, and to repeat an injection of aglepristone if the foetuses are still present.

After an abortion triggered by aglepristone, the later fertility of the cat is unchanged, an essential condition in the case studied as the animal was intended for reproduction [Fiéni et al., 2006].





# Pyometra:

## Can pyometra be medically treated on the queen? (off-label)

*Treatment of pyometra in a queen in bad general condition with aglepristone*

**A 7-year-old queen, sterilised, presented at consultation for purulent vulvar discharge since a few days (photo 1).**

### CLINICAL EXAMINATION

**Clinical examination:** exhaustion, 7% dehydration, polydipsia, purulent vulvar discharge, vulvar congestion and oedema

**Abdominal palpation:** uterine hypertrophy

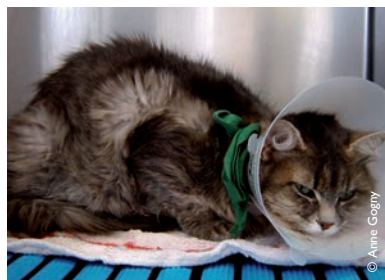
**Abdominal ultrasonographic examination:** thickening of the uterine wall evocative of a cystic glandular hyperplasia, presence of liquid in the uterine light (photo 2).

**Analysis of urine collected by cystocentesis:**

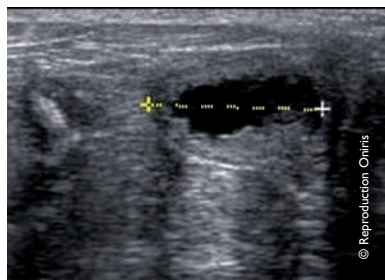
- Density: 1.010 (confirms polyurodipsia)
- Bandage: pH = 5, leukocyturia, proteinuria, haematuria
- Heller's test: positive
- Residue: Presence of bacteria

**Biochemical analysis and blood formula count:**

values within usual values, except urea: 1.9 g/l, creatinine: 40 mg/l, total proteins: 78 g/l.



*Photo 1 : The queen presents with 7% dehydration and purulent vulvar for discharge for several days.*



*Photo 2 : On abdominal ultrasonographic examination, the uterine wall has thickened and there is liquid present in the light of the uterus.*

### DIAGNOSIS

Pyometra connected with chronic renal failure and with cystitis, with significant impact on general health.

Further, a residual portion of ovary is probably the reason for the uterine complaint.

## TREATMENTS

Goals	Benchmark solution	Alternative solution	Development
Suppress progesterone source	Exeresis of the residual ovarian part <i>but anaesthesia to be postponed because of the animal's health</i>	SC Injections of 15 mg/kg of aglepristone (i.e. 0.5 ml/kg, off-label specie) at D0, D1, D8 and D15	• Light vaginal discharge on D2
Stop the progression of pyometra	Hysterectomy <i>but anaesthesia to be postponed because of the animal's health</i>		
Animal rehydration and renal function restoration	• Perfusion of NaCl 0.9% • High-energy food • Monitoring of biochemical parameters and electrolytogram		• Ovariohysterectomy at D3 after restoring the animal's general condition and biochemical parameters and histological analysis of the removed ovarian tissue
Treat cystitis	• Antibiotherapy (marbofloxacin)		• Check-up on D13: disappearance of clinical signs and good general condition of the animal

## COMMENTS

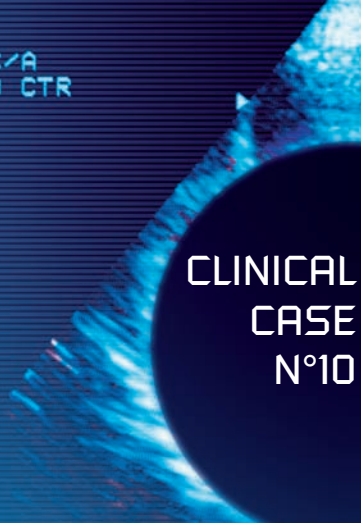
Ovariohysterectomy is the standard treatment solution for pyometra. However, when the risk link with the intervention is high because of the animal bad condition, it is preferable to abandon it. In the queen, two medical treatments are therefore possible:

1. Prostaglandins, used for their uterokinetic properties, in order to cause uterine evacuation [Davidson, 1992] ;
2. Aglepristone, which antagonises the action of progesterone involved in the development of pyometra.

Aglepristone is the molecule which offers the most interesting risk-benefit ratio with good efficacy and minimal side effects [Nak, 2009].

However, the use of prostaglandins, which cause contraction of the smooth muscles, was excluded here: the vasoconstriction created would have made the renal hypoperfusion worse and the induced digestive problems (vomiting, diarrhoea) would have accentuated the animal's loss of water. This treatment would probably have led to the cat's death.

In the case presented here, aglepristone allowed to limit the progression of pyometra for the entire essential resuscitation phase prior to surgical intervention.



# Mastosis: Which medical approach should be followed for mastosis in the queen? (off-label)

*The principles of the treatment decision in treating feline mastosis: discussion around an example*

**Intact 5-year-old cat presenting with a mammary mass, which appeared two weeks earlier.**

**Prevention of heat cycle by megestrol acetate since the age of 6 months.**

## CLINICAL EXAMINATION

Smooth mass of liquid consistency, 5 cm in diameter, on the left thoracic teat (photo 1).

## DIAGNOSIS

Mastosis

## TREATMENTS

Goal	Application	Result and progress
<b>Eliminate the source of progesterone</b>	Stop administration of progestogens	
<b>Maintain control of reproduction</b>	Ovariectomy	Laparotomy reveals glandular cystic hyperplasia of the uterus and an ovariectomy is performed.
<b>Induce regression of the mammary mass</b>	<b>SC injections of 15 mg/kg of aglepristone (i.e. 0.5 ml/kg, off-label specie) on D0, D1, D8, D15 and D21.</b>	D8: no change in size or consistency of the mass D15: diameter of the mass = 2.5 cm (photo 2). D21: diameter of the mass = 1 cm D28: mass is not palpable



Photo 1 : On clinical examination, a smooth mass of liquid consistency and of 5 cm in diameter is present on the M2 left thoracic teat.

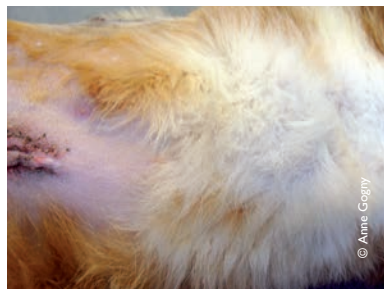


Photo 2 : Treatment starts to become effective two weeks after the first injection, complete recovery is obtained in four weeks.

Mastosis is a mammary lesion characterised by the formation of a liquid pocket, possibly compartmentalised, neither inflammatory nor painful. Like fibroadenomatosis, its pathogenesis involves progesterone and mastosis can have iatrogenic origins [Lévy, 2007].

### **Remove the ovaries or not?**

Exeresis of the ovaries eliminates the source of progesterone and sometimes enables regression of the feline mastosis lesions. However, this is not systematic: a local hormonal action would contribute to maintaining the lesions [Mol et al., 1996]. This justifies the use of aglepristone in parallel with the ovariectomy [Gorlinger et al, 2002]. Weekly treatment should be continued until complete regression of the mammary lesions. Recovery takes place more frequently at 4-5 weeks, but can need up to 11 weeks [Lévy, 2007 ; Meisl et al, 2003].

Ovariectomy has no therapeutic effect when mastosis is related to the administration of progestogens, especially if these were administered as a delayed-action form (e.g. all injectable forms). Medical treatment is then the only treatment indicated in first line. When injectable progestogens (half-life around 3 weeks) have been administered, at least 6 weeks of treatment should be anticipated. Here, the cat had received megestrol acetate per os (half-life of around 8 hours) and four weeks of treatment were sufficient.

### **Remove the mammary mass or not?**

Mastoses recur rarely after medical treatment. The mastectomy, deteriorating surgery, is therefore useless in first line. Nevertheless, when the volume of lesions is large or the mammary tissue is ulcerated, it should be carried out straight away. Histological analysis is essential to confirm that it was a non-tumoral lesion.

Here, recourse to medical treatment has permitted to limit complications connected to a mastectomy and ovariectomy together: pain, higher risk of infection and of perianesthetic risk increased by the extension of the operating time.

If the mass has a tissue density, carry out an ultrasonographic examination of the mammary tissue. If nodules are identified in addition to liquid cysts related to the mastosis, the treatment approach depends on the age of the female:

- If the cat is elderly, carry out the mastectomy in first line;
- If the cat is young, carry out an ultrasonographic examination follow-up and do not proceed to mastectomy unless the size of the nodules recedes after 6 weeks of treatment with aglepristone.

The diagnosis of feline mastosis is easy. Pay attention to the treatment decision, which may include the cat's status – reproductive or not – its capacity to cope with surgical intervention and the pain and complications connected to a related mammary exeresis. The treatment of mastosis with aglepristone has the benefit of elegance because it gives good results and has no described side effects. However, it is often long, which assumes good information and strong motivation on the part of the owner.

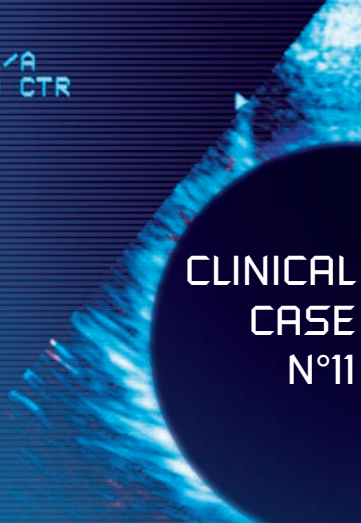


## EXOTICS ANIMALS (off-label)

**In exotics, the risks connected with surgical interventions which are generally carried out by the practitioner are greater than those incurred by the carnivores.**

**In these species, a medical alternative can prove interesting.**





## The rabbit: Is it possible to abort a rabbit\*? (off-label)

*Stop pregnancy with aglepristone in rabbits Literature synthesis*

**Rabbits are increasingly present as pets. When families adopt several individuals of different sex, it becomes necessary to control reproduction. Aglepristone makes it possible to stop unwanted pregnancy when preventative solutions have been exceeded. [Gogny, 2010].**

### TRIGGERED ABORTION PROTOCOL

The recommended protocol for stopping pregnancy in rabbits is identical to that advised for canine and feline species.

#### Period of use

According to studies, from D6 to D16 after mating (for the record: puberty takes place towards the age of 3 months and the duration of pregnancy is 32 days in female rabbits), but the usage bracket is probably longer.

#### Protocols and doses

**Two injections of aglepristone SC, at the rate of 10 mg/kg (0.33 ml/kg SC) at a 24-hour interval [Ozalp, 2008a and 2008b].**



*The rabbit is increasingly present as a pet; when families adopt individuals of different sexes, it becomes necessary to control reproduction.*

\* According to studies published by Ozalp in 2008.

## EFFECTS OF THE TREATMENT

### **Pregnancy termination**

#### **Treatment in early pregnancy (D6 and D7)**

- No pregnancy at D11 [Ozalp, 2008b]

#### **Treatment in mid-pregnancy (D15 and D16)**

- Foetal expulsion between 21 hours and 5 days after the first aglepristone injection [Ozalp, 2008a]
- Decline in food consumption during the abortion phase [Ozalp, 2008a]
- Ultrasonographic examination check-up is essential 10 days after the initial injection

### **Side effects**

#### **In early pregnancy termination**

- None [Ozalp, 2008b]

#### **In mid-pregnancy termination**

- Brownish vulvar discharge, which start on average 32 hours after the first injection [Ozalp, 2008a]
- Increase of the interoestral period in the treated animals [Ozalp, 2008a]

## INTERESTS AND LIMITS

### **Interests**

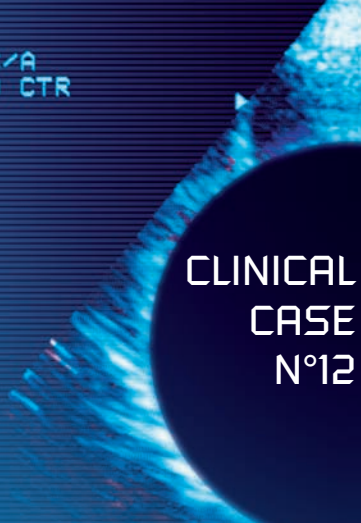
- Good efficacy (100% efficacy in the 10 rabbits treated in mid-pregnancy, 100% in the 13 rabbits treated in early pregnancy) [Ozalp, 2008a and 2008b]
- No effect on the later fertility of the rabbit [Ozalp, 2008a]
- Safety [Ozalp, 2008a and 2008b]

### **Limits**

- Side effects, efficacy rate, dose etc. are not known for the use at a later stage of pregnancy.

## CONCLUSION

The results of currently published studies show that aglepristone is an effective abortive substance in rabbits and that its side effects are limited. Nevertheless, greater samples of animals are needed to evaluate the efficacy of treatment at all stages of pregnancy.



## Guinea pig :

# Is it possible to medically treat pyometra in guinea pig\*? (off-label)

*Litterature synthesis*

**A four-year-old female guinea pig, 1.3 kg, presented at consultation for purulent bleeding present in the cage and around the vagina.**

**Animal has been apathetic and anorexic for several days.**

## CLINICAL EXAMINATION AND DIAGNOSIS

**Clinical examination:** hyperthermia ( $T = 39.6^{\circ}\text{C}$ ).

**Abdominal palpation:** no pain, presence of a mandarin-size mass with elastic consistency at the front cranial section, supple caudal palpation.

**X-ray examination:** at the centre of the abdomen, radio-opaque area consisting of a circular structure of 7 cm in diameter corresponding to the stomach and of a tubular structure suggestive of the uterus in the caudal section of the abdomen.

→ diagnosis of pyometra



Photo 1 : Guinea pig/ *Cavia porcellus*

## TREATMENT

**Surgical treatment:** refused by the owner

**Medical treatment:**

- **SC injections of 0.43 ml (i.e. 0.33 ml/kg or 10 mg/kg) of aglepristone (off-label specie) on D0, D1, and D7.**
- Antibiotic therapy (enrofloxacin 2.5%, 0.7 ml SC) and probiotics (3 times a day) all the treatment long.

Three days of hospitalisation for observation.

\* According to the publication of Von Engelhardt en 2006.



## DEVELOPMENT

2 hours after the 1<sup>st</sup> injection: observation of 2 - 3 ml of mucopurulent secretion in the cage.

**D1** : significant improvement in general condition and return of exploratory behaviour.

**D3** : observation of a large quantity of indeterminate liquid (urine or vaginal discharge) in the cage.

**D7** : no signs suggestive of uterine complaint.

## COMMENTS

The dose of 10 mg/kg of aglepristone was chosen by extrapolation of the dose used experimentally and with good results in rabbits and rats. Injections of aglepristone were well tolerated.

In the treatment of pyometra in guinea pigs, antibiotics are not systematically recommended. As in carnivores, ovariectomy is the treatment of choice, but in the present case, the owner was against it and a medical alternative was suggested. Aglepristone is routinely used in dogs and cats (off-label) to treat pyometra while retaining the female's reproductive capacities [Fiéni, 2006a]. Further, in guinea pigs, the risks related to ovariectomy are greater than those described in dogs or cats, in particular, the fitting of ties is difficult and the risk of a vacuo shock is increased.

Medical treatment of pyometra is therefore of particular interest in guinea pigs.



# TABLE 1 Use of aglepristone in Dogs

Uses	Treatment modalities	Effects observed
Abortion	<ul style="list-style-type: none"> <li>• D0 to D45</li> <li>• 10 mg/kg (0.33 ml/kg) SC 2 times at 24 h interval</li> <li>• Ultrasonographic examination check-up 10 days later</li> </ul>	<ul style="list-style-type: none"> <li>• Abortion 4 to 7 days after first injection</li> <li>• Shortening of interœstrus by 1-3 months</li> <li>• Clinical signs close to those of parturition in late abortion</li> </ul>
Treatment of pyometra (off-label)	<ul style="list-style-type: none"> <li>• 10 mg/kg (0.33 ml/kg) SC at D1, D2, D8 and D15 and possibly D28</li> <li>• Cloprostenol: 1 µg/kg SC per day from D3 to D7</li> <li>• Ultrasonographic examination check-up at D22 and/or 10 days after the last injection</li> <li>• Fluidotherapy and antibiotherapy to prevent or treat septicaemia</li> </ul>	<ul style="list-style-type: none"> <li>• In closed pyometra, opening of the cervix</li> <li>• Purulent discharge in the 4 to 38 h following first injection → improvement in general health</li> <li>• Ultrasonographic examination: reduction in diameter of the uterine light from D8</li> <li>• Efficacy rate (metritis): close to 100%</li> <li>• Efficacy rate in the treatment of pyometra:</li> <li>• Aglepristone alone: 60%</li> <li>• Combined with cloprostenol: 85%</li> <li>• Shortening of interœstrus</li> <li>• Extension of anœstrus in some bitches</li> </ul>
Induction of parturition (off-label)	<ul style="list-style-type: none"> <li>• 15 mg/kg (0.5 ml/kg) SC from D59</li> <li>• 24 h after, 0.15 UI/kg SC of oxytocin every 2 hours until all products expelled</li> </ul>	<ul style="list-style-type: none"> <li>• Expulsion of the first foetus around 30 h after the aglepristone injection: time varies depending the bitch's weight</li> <li>• No influence on duration of birth, number of pups born alive, birth weight of the pups, number of pups alive 30 days after birth</li> </ul>
Planning caesarean section (off-label)	<ul style="list-style-type: none"> <li>• 15 mg/kg (0.5 ml/kg) SC, 20 h before caesarean section</li> </ul>	<ul style="list-style-type: none"> <li>• Start of lactation from the end of surgery (89% of bitches)</li> <li>• Low mortality rate: 2.6%</li> </ul>



Treatment interests		Treatment limits	Main references
	<ul style="list-style-type: none"> <li>• Usage is possible during a wide period of pregnancy</li> <li>• Safety</li> <li>• Efficacy rate of 99% (between 0 to 25 days) and 95.7% (between 25 to 55 days)</li> <li>• No impact on further fertility</li> </ul>	<ul style="list-style-type: none"> <li>• Treatment cost</li> <li>• In late abortion, possible expulsion of live foetuses</li> </ul>	[Fiéni, 1996]
	<ul style="list-style-type: none"> <li>• Good efficacy</li> <li>• No impact on reproductive function</li> <li>• Safety</li> <li>• Alternative to ovariohysterectomy when intervention is not possible</li> <li>• In significant uterine dilation or closed pyometra, induces preliminary evacuation of the uterus which makes the surgeon's work easier and limits the risk of a vacuo shock</li> </ul>	<ul style="list-style-type: none"> <li>• Recurrence rate around 20% (recurrence mimicked by pregnancy during the next heat cycle)</li> </ul>	[Fiéni, 2006a]
	<ul style="list-style-type: none"> <li>• Good efficacy</li> <li>• Safety</li> <li>• Strictly therapeutic induction of the birth (term exceeded, risk of eclampsia etc)</li> </ul>	<ul style="list-style-type: none"> <li>• Need to know the precise date of the term</li> <li>• Risk of inducing birth at a stage where the foetuses are still immature: inducing birth for convenience is not advised</li> </ul>	[Fiéni et al., 2009]  [Fontbonne et al., 2009]
	<ul style="list-style-type: none"> <li>• Increases the chances of survival of the pups (presence of qualified staff)</li> <li>• More comfortable work for the surgeon</li> </ul>	<ul style="list-style-type: none"> <li>• Need to know the precise date of the term</li> </ul>	[Levy 2009]

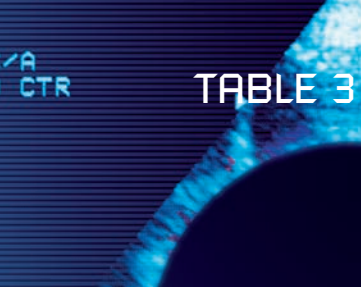


**TABLE 2** Use of aglepristone  
in cats  
(off-label)

Uses	Treatment modalities	Effects observed
Abortion (off-label)	<ul style="list-style-type: none"><li>• From D0 to D45</li><li>• 15 mg/kg (0.5 ml/kg) SC twice at 24 h interval</li><li>• Ultrasonographic examination check-up 10 days after</li></ul>	<ul style="list-style-type: none"><li>• Carried out between 25 and 35 days after mating, 88% of efficacy</li><li>• Foetal expulsion in 8 days following the first injection</li><li>• Sometimes, brownish vulvar discharge</li><li>• Sometimes, another heat cycle 8-10 days after treatment</li></ul>
Treatment of pyometra (off-label)	<ul style="list-style-type: none"><li>• 15 mg/kg (0.5 ml/kg) SC at D1, D2, D8 and D15</li><li>• Possibly in combination with cloprostenol (1 µg/kg SC per day for 3 to 5 days)</li><li>• Ultrasonographic examination check-up at D15 or 10 days after the last injection</li></ul>	<ul style="list-style-type: none"><li>• Purulent discharge in the hours following the first injection → immediate improvement in general health</li><li>• 90% of clinical efficacy at 7 days</li><li>• In 90% of cases, disappearance of the ultrasound image of the uterus in the two weeks after the first injection</li><li>• Heat cycle: 10 days to 2 months after treatment</li></ul>
Traitement of fibroadenomatosis (off-label)	<ul style="list-style-type: none"><li>• Stop any ongoing progestogen treatment</li><li>• 15 mg/kg (0.5 ml/kg) SC on D0 (day of diagnosis), D1, D8, D15, D21 and possibly D28</li></ul>	<ul style="list-style-type: none"><li>• Reduction in mammary masses in 3 to 4 weeks after the first injection</li><li>• Continue treatment until complete involution of the mammary gland</li></ul>
Treatment of mastosis (off-label)	Identical to treatment for	



Treatment interests	Treatment limits	Main references
<ul style="list-style-type: none"> <li>• Usage possible during a long period of pregnancy</li> <li>• Safety</li> <li>• Good efficacy</li> <li>• No uterine complaints described later</li> <li>• No impact on later fertility</li> </ul>	<ul style="list-style-type: none"> <li>• Expulsion of live foetuses is possible in late abortion</li> <li>• Partial or total failure is possible</li> </ul>	[Fiéni et al., 2009]
<ul style="list-style-type: none"> <li>• No impact on reproductive function</li> <li>• Safety</li> <li>• Alternative to ovariohysterectomy when surgical intervention is not possible</li> <li>• If there is marked uterine dilation or closed pyometra, induces preliminary evacuation of the uterus which makes the surgeon's work easier and limits the risk of a vacuo shock</li> </ul>	<ul style="list-style-type: none"> <li>• Doesn't treat puerperal metritis</li> <li>• Possible recurrence (recurrence rate unknown)</li> </ul>	[Nak et al., 2009]
<ul style="list-style-type: none"> <li>• Good efficacy</li> <li>• Safety</li> <li>• Makes it possible to retain the reproductive potential of the breeders</li> <li>• Before ovariectomy, reestablishes access to the linea alba (although ovariectomy via the flank is possible) and limits pre-operative stress related to inflammation and pain</li> <li>• Can improve the result of the ovariectomy, sometimes ineffective alone</li> </ul>	<ul style="list-style-type: none"> <li>• Treatment failures possible (if treatment is not long enough), which then requires exeresis of the teat (plan histological analysis to confirm the diagnosis)</li> </ul>	[Gorlinger et al., 2002]
fibroadenomatosis		No controlled study

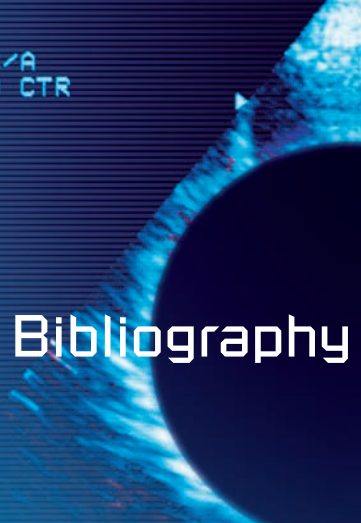


**TABLE 3** Use of aglepristone  
in exotics (off-label)

Uses	Treatment modalities	Effects observed
Abortion in rabbit (off-label)	<ul style="list-style-type: none"><li>• from D6 to D15 after mating</li><li>• 10 mg/kg (0.33 ml/kg) SC twice at 24 h interval</li><li>• Ultrasonographic examination check-up 10 days later</li></ul>	<ul style="list-style-type: none"><li>• Observation of vaginal discharge 32 hours on average after the first injection</li><li>• Increase of the intraoestral period</li><li>• 100% efficacy rate (on 10 animals)</li></ul>
Treatment of pyometra in guinea pigs	<ul style="list-style-type: none"><li>• 10 mg/kg (0.33 ml/kg) SC at D0 (day of diagnosis), D1 and D7</li></ul>	<ul style="list-style-type: none"><li>• Observation of vaginal discharge a few hours after the first injection</li><li>• Complete recovery in 8 days</li></ul>



Treatment interests	Treatment limits	Main references
<ul style="list-style-type: none"> <li>• Good efficacy</li> <li>• Safety</li> <li>• No incidence on further fertility</li> </ul>	<ul style="list-style-type: none"> <li>• Unknown</li> </ul>	[Ozalp, 2008a, Ozalp 2008b]
<ul style="list-style-type: none"> <li>• Efficacy</li> <li>• Safety</li> </ul>	<ul style="list-style-type: none"> <li>• Only one case observed to date</li> </ul>	[Von Engelhardt, 2006]



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