EAZA RMG
EAZA Reproductive Management Group

Animal name: Margay (*Leopardus wiedii*)

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We would recommend assessing any contraceptive bout with behavioural and hormone monitoring. For more information on this, please contact contraception@chesterzoo.org

Contraceptive methods	GnRH agonist (implant)	GnRH agonist (injection)	GnRH vaccine (injection)	Progestogen (implants)	Progestogen (Oral)	Progestogen (injection)	Surgical/Permanent
Contraceptive Product:	Deslorelin acetate	Leuprolide acetate	GnRH protein conjugate	Etonogestrel 68 mg	Megestrol acetate	Medroxyprogesterone acetate	
Commercial Name:	Suprelorin ®	Lupron ®	Improvac®	Implanon® Nexplanon®	Ovarid®	Depo-Provera®, Depo-Progevera®	
Product Availability:	4.7mg ('Suprelorin 6') and 9.4 mg ('Suprelorin 12') widely available through veterinary drug distributors in the EU.	Leuprolide acetate licenced for human use	Available through veterinary drug distributors.	Manufactured by Bayer Schering Pharma AG. Available through human drug distributors	Manufactured by Virbac, available through veterinary distributors	Manufactured by Pfizer. Widely available throughout Europe through human drug distributors.	N/A
Restrictions and/or permit required by Importing Country:	The EAZA RMG recommends: always check with your local licencing authority	**Data deficient**	Current knowledge: widely available throughout European countries. The EAZA RMG recommends: always check with your local licencing authority	The EAZA RMG recommends: always check with your local licencing authority	The EAZA RMG recommends: always check with your local licencing authority	The EAZA RMG recommends: always check with your local licencing authority	N/A
Mechanism of action:	GnRH agonist suppress the reproductive endocrine system, preventing production of pituitary and gonadal hormones. As an agonist of the GnRH initially stimulates the reproductive system - which can result in oestrus and ovulation in females or temporary enhancement of testosterone and spermatogenesis in males- therefore additional contraception needed during this time. Please see below and refer to Deslorelin datasheet for detailed information	GnRH agonist suppress the reproductive endocrine system, preventing production of pituitary and gonadal hormones	Production of anti-GnRH antibodies by the immune system, neutralising endogenous GnRH activity. This results in a reduction of FSH and LH production by the anterior pituitary and, ultimately, in a reduction of ovarian follicular development and /or inhibition of testosterone secretion from the testes and spermatogenesis.	Interference with fertilization by thickening cervical mucus, interrupting gamete transport, disruption of implantation, inhibition of LH surge necessary for ovulation.	Anti-estrogenic activity. Interference with fertilization by thickening cervical mucus, interrupting gamete transport, disruption of implantation, inhibition of LH surge necessary for ovulation. Progestogen contraceptives are associated in felids with progressive uterine growth that can result in infertility, infections, and sometimes uterine cancer; mammary tissue stimulation can also result in cancer.	Anti-estrogenic activity. Interference with fertilization by thickening cervical mucus, interrupting gamete transport, disruption of implantation, inhibition of LH surge necessary for ovulation.	**Castration and Ovariohysterectomy/ovariectomy - recommended** Permanent contraception by surgical gonadectomy, with similar side effects to those in domestic species - weight gain, loss of secondary sex characteristics **Vasectomy - Caution** Surgical procedure in which the ductus deferens are cut, tied, cauterized, or otherwise interrupted. Generally considered irreversible though reversible techniques have been successful in certain species. Vasectomy of males will not prevent potential adverse effects to females from prolonged, cyclic exposure to endogenous steroids associated with the obligate hormonal pseudo-pregnancy that follows ovulation in most felids. Endogenous steroids and steroid contraceptives cause similar side effects.
Insertion/Placement:	Sub-cutaneous, in a place where it can be easily detected or seen for removal at a later date (I.e. Upper inner arm); refer Suprelorin fact sheet for effective method of implant placement (tunnelisation)	Injectable	Injectable intramuscular or subcutaneously	Intramuscular or subcutaneous. The EAZA RMG recommends sub-cutaneous, upper inner arm for visibility (aid for later removal)	Orally daily	Injectable intramuscular	Surgical
Females	**RECOMMENDED**	**Data deficient - product should work in a similar manner to deslorelin**	**Data deficient**	**Not recommended**	**CAUTION - see side effect below**	**CAUTION - see side effect below**	**Ovariohysterectomy/ovariectomy recommended**
Dose	GnRH agonist are considered the safest reversible contraceptives, but dosages and duration of efficacy are not well established for all species; side effects are generally similar to those associated with gonadectomy, especially the potential for weight gain unless diet is controlled. Dosages and duration of efficacy have not been well established for exotic felid species. As a guide: 1 x 4.7 mg for a **minimum** of 6 months; 1 x 9.4 mg for a **minimum** of 12 months.		**Dose is not well established in the species.** In lions, two injections of 400-600ug are given 5 weeks apart and boosters are usually administered every 4-5 months. Doses as low as 50ug have been effective at contracepting male cats[4].		2-5mg/kg daily orally for no more than for 1 oestrus period. Megestrol acetate can be used to avoid the stimulation phase associated with GnRH implant (see GnRH recommendations)	5mg/kg body weight. Duration of effect should be 3 months. Treatment should not occur for more than 2 oestrus periods. If a progestin is used, treatment should only be short term, because of the increased likelihood of side effects with prolonged exposure.	
Latency to effectiveness:	3 weeks average as GnRH agonist initially stimulates the reproductive system- please refer to Deslorelin datasheet on this website for detailed information - additional contraception is needed during this time in order to suppress the initial stimulation phase (see product data sheet. ~2mg/kg Megestrol acetate pills /Ovarid®/Megace® daily 7 days before and 8 days after has been used to suppress initial stimulation phase). Treatment **MUST** commence when the female is in anoestrus.		Latency to effectiveness can be up to 6 weeks so separation of the sexes is recommended if possible.				
Oestrus cycles during contraceptive treatment:	Initial oestrus and ovulation (during the 3 weeks of stimulation)-will occur and then no oestrus cycle. To supress the initial oestrus and ovulation with the concommitant progesterone production and the associated deleterious effects of this you MUST follow the megestrol acetate protocol mentioned above.		**Unknown**				
Use during pregnancy:			**Unknown**				
Use during lactation:	No contraindications once lactation established.		**Unknown**				

Use in prepubertals or juveniles:	**Data deficient.** Deslorelin suppresses gonadal steroids; its use may delay epiphyseal closure of the long bones, resulting in taller individuals, similar to the effects of pre-pubertal spaying and neutering in domestic cats and lions. GnRH agonist use in prepubertal domestic cats was followed by reproductive cycles after treatment ceased however, species differences may occur.		**Unknown**				
Use in seasonal breeders:	**Data deficient.** Should start at least 1 month prior the breeding season. In females, GnRH agonists can induce oestrus and ovulation even during the non-breeding season in some taxa.		**Unknown**		If a progestin is used in felids, treatment should start well **BEFORE** any signs of proestrus, since the elevated endogenous oestrogen can exacerbate side effects of the progestin.	If a progestin is used in felids, treatment should start well **BEFORE** any signs of proestrus, since the elevated endogenous oestrogen can exacerbate side effects of the progestin.	
Duration	Duration of efficacy has not been well established as a guide: 4.7 mg implants will suppress for a **MINIMUM** of 6 months; 9.4mg will be effective for a **MINIMUM** of 12months. The average duration of efficacy however is ~1 year for 4.7mg and ~2 years for 9.4mg. Individual variation occurs but durations tends to be regular for a particular individual's contraceptive bout.					Duration of efficacy, and thus latency to conception following last injection can be extremely variable and has been seen to vary from 4 weeks to 2 years in some individuals. In general, the recommended dose (2.5-5mg/kg body weight) is effective for at least 2 months in most species. Treatment should only be short term, because of the increased likelihood of side effects with prolonged exposure in felids.	
Reversibility	Deslorelin is generally considered reversible. 1/3 females in our database that had been allowed to breed following implant treatment have reversed. Time to conception was 2.5 years following the estimated date of implant expiry. It is recommended to place the implants creating a subcutaneous tunnel to avoid breakage in a place (like the inner arm) where could be easily detected later for removal to aid reversal if this is desired.		It must be taken in to consideration that younger individuals will take longer to reverse in comparison to older individuals. Improvac is not designed to be reversible, although reversibility has been demonstrated in some wild animal species. We do not have any records of reversal in this species.			**Data deficient.** We have several records of reversal in other felids, with time to conception ranging between 1 months and 3.5 years after the estimated expiry of the product	
Effects on Behaviour	Similar to those seen with gonadectomy but reversible.		Similar to surgical castration but short-acting (duration of antibody effect).				
Effects on sexual physical characteristics	Similar to gonadectomy but should be reversible. Weight gain has also been observed.		Similar to surgical castration but short-acting (duration of antibody effect).				
Males	**Data deficient**	**Data deficient but effects should be similar to deslorelin**	**Data deficient**	**Not recommended**	**Not recommended**	**Not recommended**	**Castration recommended; vasectomy not recommended**
Dose	**Data deficient.** As a guide: 1 x 4.7 mg for a **minimum** of 6 months; 1 x 9.4 mg for a **minimum** of 12 months. Product efficacy is harder to monitor in males (ensuring continued absence of sperm requires regular ejaculate examination) and the latency to effect is longer than in females. It can, however, be used to ameliorate aggression in males of some species. Keep away from females at least 2 months after implant as in vasectomy.		**Dose is not well established in the species.** In lions, two injections of 400ug are given 5 weeks apart and boosters are usually administered every 4-5 months. Doses as low as 50ug have been effective at contracepting male cats[4].				N/A
Latency to effectiveness:	Depending on the species there may be fertile sperm present in vas deferens for 6-8 weeks post treatment or even longer[2]. Testosterone decreases after 3-4 weeks but sperm can stay fertile for many weeks after. In cheetah, treatment with either 1x6mg or 1x12mg deslorelin resulted in untraceable blood testosterone concentrations 45 days after initial treatment, but semen samples still had high concentrations of spermatozoa. By 3 months, most males (N=6 cheetah) were azoospermic or were close to azoospermic[3].		Latency to effectiveness can be up to 6 weeks so separation of the sexes is recommended if possible.				
Use in prepubertals or juveniles:	**Data deficient** in this group, see product information sheet. Deslorelin suppresses gonadal steroids, its use may delay epiphyseal closure of the long bones, resulting in taller individuals, similar to the effects of pre-pubertal spaying and neutering in domestic cats. GnRH agonist use in prepubertal domestic cats was followed by reproductive cycles after treatment ceased. However, species differences may occur. There appear not be any such problems in cheetahs.		**Data deficient**				
Use in seasonal breeders:	**Data deficient.** In males, GnRH agonists can transiently stimulate testosterone production even during the non-breeding season. Treatment should begin more than two months prior to the anticipated breeding season to prevent initiation of spermatogenesis, because it appears that suppression of sperm production is more easily accomplished before it has commenced.		**Unknown** but if used should be done at least 6 weeks prior to the breeding season. Effective in the horse. Use at the onset of the breeding season before cycling starts.				

Duration and Reversibility	Duration of efficacy has not been well established as a guide: 4.7 mg implants will suppress for a **MINIMUM** of 6 months; 9.4mg will be effective for a **MINIMUM** of 12months. Deslorelin is designed to be reversible however, we do not have any records of reversal in this species. We 4 records of reversal in other felid species: one cheetah implanted with 2x 9.4mg implants showed a return of sperm 4 years after being implanted, and three domestic cats implanted with 1x 4.6mg implants, all of which showed a return of sperm towards the end of the estimated implant expiry (6 months). There are anecdotal reports that reversals cannot be demonstrated in cheetah males that have been treated for over 5 years.		**Data deficient** for this species. Ilt must be taken in to consideration that younger individuals will take longer to reverse in comparison to older individuals.				Vasectomy is generally considered irreversible however, some successful reversible techniques have been used in certain species, but no publications in exotic felids.
Effects on Behaviour	Testosterone related aggression is likely to decrease. **Data deficient** in this group, see product information sheet.		Similar to surgical castration but short-acting (duration of antibody effect). Decrease male aggression due to down regulation of testosterone synthesis.				Vasectomy does not affect male behaviour. Castration will alter male sexual behaviour and may alter aggression if related to male hormones.
Effects on sexual physical characteristics	**Data deficient** in these taxa. Likely that body size may decrease, decrease testicular size, feminisation of males. Similar to gonadectomy but reversible. In cheetahs, use for up to 10 years has not reduced body size or weight. There have been no signs of feminisation and behaviour, excepting that aggression is normal in the group situation.		Similar to surgical castration but short-acting (duration of antibody effect).				Vasectomy - no loss of secondary sex characteristics Castration - results in loss of secondary sex characteristics.
General:							
Side effects	Deslorelin first stimulates then suppresses oestrus in females. Species with induced ovulation (e.g., most felids, some mustelids, and bears) may ovulate and become pseudo-pregnant (which may also occurs in canids) when first treated; also the abundant endogenous progesterone production during the stimulation phase may induce endometrial hyperplasia. In males, initial stimulation may be accompanied by increased aggression or sexual interest. Oestrous behaviour or even copulation may occur during a transition phase near the end of the period of contraceptive efficacy. Pseudopregancy, endometrial hyperplasia and pyometra may be associated with the use of GnRH agonist as a result of high progesterone levels during the stimulation phase. A more recently developed Suprelorin®/ deslorelin protocol using Ovarid®/megestrol acetate to prevent the initial stimulation phase, followed by implant removal when reversal is desired, may be a safer contraceptive option.		Occasional swelling at the vaccination site - need to inject deep intramuscular in elephants and horses. Anecdotally, the smaller the species, the worse the injection site swelling. Necrosis in domestic dogs has been observed. The EAZA RMG recommends always reading the manufacturer's data sheet.	Risk of pseudopregancy, endometrial hyperplasia and pyometra increases with exposure to prolong circulating progestogens/progesterone and this is why the use of progestagens is dicouraged in carnivores.	Risk of pseudopregancy, endometrial hyperplasia and pyometra increases with exposure to prolong circulating progestogens/ progesterone and this is why the use of progestagens is dicouraged in carnivores	Progestogen contraceptives are associated in felids with progressive uterine growth that can result in infertility, infections, and sometimes uterine cancer; mammary tissue stimulation also can result in cancer. Risk of pseudopregancy, endometrial hyperplasia and pyometra increases with exposure to prolong circulating progestogens/ progesterone	Vasectomy of males will not prevent potential adverse effects to females from prolonged, cyclic exposure to endogenous steroids associated with the obligate hormonal pseudo-pregnancy that follows ovulation in most felids. Endogenous steroids and steroid contraceptives cause similar side effects.
Warnings	Causes initial gonadal stimulation that **MUST** be suppressed; correct administration essential - see product information sheet		It should be handled with extreme care to avoid handler accidents. The EAZA RMG recommends always reading the manufacturer's data sheet			SHOULD NOT BE USED PRIOR TO GnRH IMPLANT PLACEMENT Depo-Provera® should not be substituted for megestrol acetate, because its initial high levels and prolonged release can interfere with Suprelorin® efficacy.	Precautions - Vasectomy is not recommended for species with induced ovulation because mating will result in female pseudopregnancies with prolonged periods of progesterone elevation, which can cause pathology of uterine and mammary tissue. Endogenous progesterone and progestin contraceptives cause similar disease. In lions vasectomy commonly results in repeated mating many times without ovulation. Females get tired of being harassed and sometimes this results in fighting between sexes. As a result some collections have resorted to "switching off" females with deslorelin when they have a vasectomised male.

Reporting Requirements: In order to increase our knowledge of the efficacy of contraception methods in felidae it is recommended that all individuals on contraception be reported to the EAZA RMG

References:

1) Dematteo, KE. (2005) Contraception in carnivores. In: Wildlife Contraception: Issues, Methods, and Applications. Baltimore: Johns Hopkins Press. 105-118.
2) Bertschinger, HJ & Caldwell, P. (2016) Fertility suppression of some wildlife species in southern Africa - a review. *Reproduction in Domestic Animals* , 51(Suppl 1): 18-24
3) Bertschinger HJ, Jago, M, Nöthling, JO, Human, A. (2006) Repeated use of the GnRH analogue deslorelin to down-regulate reproduction in male cheetahs (Acinonyx jubatus). *Theriogenology* ; 66(6-7): 1762-1767.
4) Levy, JK, Miller, LA, Crawford, PC, Ritchey, JW, Ross, MK, Fagerstone, KA (2004) GnRh immunocontraception of male cats. *Theriogenology* , 62:1116-1130.