

Fact Sheet Compiled by: Veronica Cowl Last Updated: April 2022 Fact Sheet Reviewed by: EAZA RMG We would like to encourage all institutions using contraception in their animals to assess the health of their animals during and after contraception. This can be done through behavioural and endocrine monitoring, as well as through reproductive tract exams. Please contact the EAZA RMG for advice. **GnRH** vaccine Contraceptive methods **Contraceptive Product:** GnRH protein conjugate **Commercial Name:** Improvac[®] Regu-mate[®] Equine 2.2 Available through veterinary drug distributors mate[®] Porcine 0.4% w/v Product Availability: through veterir Current knowledge: widely available throughout The EAZA RMG recommer **Restrictions and/or permit** European countries. The EAZA RMG recommends: required by Importing Country: local licer always check with your local licencing authority Production of anti-GnRH antibodies by the immune system, neutralising endogenous GnRH activity. This Interference with ferti results in a reduction of FSH and LH production by the mucus, interrupting gar Mechanism of action: anterior pituitary and, ultimately, in a reduction of implantation, inhibitio ovarian follicular development and /or inhibition of testosterone secretion from the testes and spermatogenesis. Administered or Gloves must be worn w Insertion/Placement: Intramuscular or subcutaneous. (absorption through the s menstrual cycle and p Females Two injections of 400µg are given 35 days apart and boosters are usually administered every 6-7 months, 0.044 DOSE although duration can vary between species and individuals. Latency to effectiveness can be up to 8 weeks so separation of the sexes is recommended if possible. In a group of 57 mares, 50% were anoestrus after the Usually 1-3 days of treatm Latency to effectiveness: primary vaccination and 100% after the booster sexes should be used for 7 vaccination, the interval from treatment to anoestrus was 2-3 weeks. If contraceptive suppression is successful then oestrus Ovulation and cycling Oestrus cycles during should also be suppressed fully; highly successful at contracepted individuals (contraceptive treatment: inducing anoestrus in domestic horses suppression Progestagens are not reco because of the possibilit Not recommended Use during pregnancy: birth, Unknown Use during lactation: Considered sa The use of synthetic pro Unknown juveniles has not been ful Use in prepubertals or juveniles: effects on fe If used should be done at least 6 weeks prior to the Treatment should begin a breeding season. Effective in the horse. Use on the Use in seasonal breeders: anticipated onset of onset of the breeding season before cycling starts. Unknown for most of species. Improvac[®] generates Duration may not be mo short lived antibodies in the domestic pig (after 7-8 administered daily. Clea weeks following second injection antibodies start to Duration system can occur in a f decline). Mares are suppressed for a full season after

> Reversibility is unknown for most species. It is presumed to be reversible when used in the short term due to short lived antibodies. The longer it is used, the longer the time required for reversal. Long term effects on fertility are unknown and therefore The EAZA RMG recommends caution when using for an extended period of time.

Reversibility

the first booster.

Species name: Kulan (Equus hemionus kulan)

	Progestagen (oral)	contraception. This can be done through behavioural and PZP vaccine	Progestagen (injection)	GnRH vaccine	GnRH agonist (implant)	GnRH agonist (injection)	Surgical/Permanent
	Altrenogest	proligestrone PZP vaccine main components are antigens derived from porcine zona pellucida glycoproteins and an adjuvant to stimulate the immune response (Freund's modified complete adjuvant for primary vaccination and Freund's incomplete adjuvant for boosters).	medroxyprogesterone acetate	GnRH protein conjugate	Deslorelin acetate	Luprolide acetate	N/A
	Regu-mate [®]	Porcine Zona Pellucida	Depo-Provera [®] , Depo-Progevera [®]	GonaCon [™]	Suprelorin ®	Lupron [®]	Castration/Vasectomy
	Regu-mate® Equine 2.2ml/mg oral solution and Regu- mate® Porcine 0.4% w/v oral solution widely available through veterinary drug distributors.	Not commercially available in Europe. Can be imported from the USA. Not available for use in the UK. Please contact www.sccpzp.org for licensing information.	Manufactured by Pfizer, Widely available throughout	Not commercially available in Europe. Can be imported from the USA. Please contact the National Management Wildlife Centre NWMC@apha.gsi.gov.uk for more information.	4.7mg ('Suprelorin 6') and 9.4 mg ('Suprelorin 12') widely available through veterinary drug distributors in the EU.	Luprolide acetate licenced for human use	N/A
:	The EAZA RMG recommends: always checking with your local licencing authority	License for importation is required. Licence unavailable in the UK; licences have been obtained for France, Austria, and the Netherlands; all other Countries unknown. The EAZA RMG recommends always checking with local licencing authority	The EAZA RMG recommends: always check with your local licencing authority	Not commercially available in Europe. Can be imported from the USA. Please contact the National Management Wildlife Centre NWMC@apha.gsi.gov.uk for more information.	The EAZA RMG recommends: always check with your local licencing authority	Data deficient	N/A
e is ne f	Interference with fertilization by thickening cervical mucus, interrupting gamete transport, disruption of implantation, inhibition of LH surge necessary for ovulation	The PZP antibodies interfere with fertilisation by binding to the ZP glycoprotein receptors that surround the egg of the vaccinated female, blocking the binding and subsequent penetration of sperm.	Anti-estrogenic activity. Interference with fertilization by thickening cervical mucus, interrupting gamete transport, disruption of implantation, inhibition of LH surge necessary for ovulation	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.	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	preventing production of pituitary and gonadal hormones	Castration: Surgical removal of the testes. Vasectomy: Surgical procedure in which the ductus deferens are cut, tied, cauterized, or otherwise interrupted.
	Administered orally in feed or by syringe. Gloves must be worn when administering Regu-mate [®] (absorption through the skin can cause disruption to the menstrual cycle and prolongation of pregnancies in humans).	Injectable intramuscular	Injectable intramuscular	Injectable intramuscular (pregnant women should not be involved in handling or injecting GonaCon and all women should be aware that accidental self-injection may cause infertility)	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	Surgical
					GnRH agonists may not be very effective in equids; deslorelin seems to have a very short duration in mares	GnRH agonists may not be very effective in equids; Lupron seems to have a very short duration in mares	N/A
d s,	0.044 mg/kg daily.	~ 100 ug of protein. Recommended dose is 2 injections given typically 2+ weeks apart then a booster. Booster interval is species dependent and advice will be given by the suppliers. For species with well defined and short (2-3 months) breeding season, give first dose 1-2 months prior to the breeding season and the second inoculation no later than 1 month prior to breeding activity. Year-round breeders booster inoculations should be given every 7 to 8 months.	2-5 mg/kg body weight every 2-3 months. Lack of efficacy in the domestic mare, but proven to be effective in other	A single vaccination of 1-2ml per female is advised. 61%- 93% efficacy has been achieved with a single vaccination; however, if necessary, a 1 ml booster dose can be administered up to three years after the initial vaccination to ensure 100% efficacy.	Data deficient. Dosage depends on the body weight of the individual. 4.7mg is recommended for a minimum duration of 6 months and 9.4mg is recommended for a minimum duration of 12 months. There is recorded use of wild ass treated with 3x9.4mg implants. Please contact The EAZA RMG for species specific dosage recommendations.		
	Usually 1-3 days of treatment, however separation of the sexes should be used for 7- 14 days after first treatment.	2-3 weeks after the last vaccination during year 1 (primary course of vaccination 2 injections 2-4 weeks apart, preferable 3 injections).	1-3 days post injection. However, if the cycle stage is not known then extra time must be allowed; therefore, separation of the sexes should be used for at least 1 week.	Data deficient. Latency to effect may be similar as with Improvac (~8 weeks) however there is no species-specific data available.	3 weeks average as GnRH agonists initially stimulate the reproductive system- please refer to Deslorelin datasheet for detailed information - separation of the sexes OR supplementary contraception is recommended during this time (see product data sheet. Megestrol acetate pills, or another oral progestin, daily 7 days before and 8 days after implant insertion have been used to suppress stimulation phase. The dose for domestic dogs is 2mg/kg, but must be extrapolated for other taxa). (See Product data sheet. Regumate, 0.02 - 0.4 mg/kg daily 7 days before and 8 days after implant placement can also be used as an alternative method to suppress the stimulation phase).	detailed information - separation of the sexes OR supplementary contraception is recommended during this time (see product data sheet. Megestrol acetate pills daily 7 days before and 8 days after implant insertion have been used to suppress stimulation phase. The dose for domestic dogs is 2mg/kg, but must be extrapolated for other taxa). (See Product data sheet. Regumate, 0.02 - 0.4 mg/kg daily 7 days before and 8 days after implant placement can also be	
us t	Ovulation and cycling can occur in adequately contracepted individuals (but is unlikely and the degree of suppression is dose dependent).	PZP should not suppress oestrous cycles (but will render individuals infertile) and may extend the breeding season beyond what is considered typical, resulting in additional oestrous cycles.	Oestrus behaviour may be observed. Ovulation and cycling can occur in adequately contracepted individuals (but is unlikely and the degree of suppression is dose dependent).	If contraceptive suppression is successful then oestrus should also be suppressed fully	Initial oestrus and ovulation (during the 3 weeks of stimulation) then down-regulation. To prevent the stimulation phase, the megestrol acetate protocol described above is recommended.	Initial oestrus and ovulation (during the 3 weeks of stimulation) then down-regulation. To prevent the stimulation phase, the megestrol acetate protocol described above is recommended.	
	Progestagens are not recommended in pregnant animals because of the possibility of prolonged gestation, still birth, abortion, etc.	Is compatible with pregnant animals and should not interfere with the development of the foetus.	Progestagens are not recommended in pregnant animals because of the possibility of prolonged gestation, still birth, abortion, etc.	Does not interrupt pregnancy or affect foetus	Not recommended	Not recommended	
	Considered safe for nursing infant.	Does not interrupt pregnancy or affect foetus	Considered safe for nursing infant.	Unknown	No known contraindications once lactation has been established; however, treatment during pregnancy may impede proper mammary development.	No contraindications once lactation established	
	The use of synthetic progestagens in pre-pubertals or juveniles has not been fully assessed. Possible long-term effects on fertility are not known.	PZP-treated prepubertal feral horses were fertile as adults. But there is no data for other species. Dependent on length of treatment, if used long term (approx. 4 years) then infertility may occur.	The use of synthetic progestagens in pre-pubertals or inveniles has not been fully assessed. Possible long-term	Unknown	Because deslorelin suppresses gonadal steroids, its use may delay epiphyseal closure of the long bones, resulting in taller	Data deficient in this group, see product information sheet	
5	Treatment should begin at least one month before the anticipated onset of the breeding season.	Can be used in seasonal breeders but initial treatment and annual boosters should be carried out 2 and 1 months before the start of the breeding season respectively.	Should be injected at least 1 month before the breeding season starts.	If injected during gestation, pregnancy will go to term and most females will become infertile after giving birth	Treatment should be given more than 2 months prior to expected breeding season	Data deficient. Should start at least 1 month prior the breeding season.	
s 3 D er	Duration may not be more than one day, so has to be administered daily. Clearance of regumate from the system can occur in a few days, however latency to conception can very between individuals.	Boosters vaccination required at regular intervals. Is used for short term use for no more than 3-4 years.	Dose dependant: 45-90 days in general. However, effects could last 1-2 years in some individuals.	Minimum 1 year following a single vaccination that will make 61-93% of the mares infertile, although suppression can last up to 5 years. In white-tailed deer, if a longer effect is desired, a second vaccination can be given during the course of the first year to boost the contraceptive effect.	4 Y /Img will be attactive for a minimum of 17 months. Duration	Not well established, duration of effect being likely related to the dose. Higher doses result in longer duration of effect. This is extremely data deficient.	
g or	Generally short-acting. Designed to be fully reversible although variations can occur.	Species differences on reversibility. Treatment for over 5 years has been associated with ovarian failure in some cases. The possibility of ovarian damage makes this method unsuitable for animals highly valuable to captive breeding programmes or where reversibility is important. We have three records of reversal in equid species, with time to conception ranging between 5-6 months after the estimated expiry of the contraceptive. Consecutive use for over 3-4 years can lead to possible reversal failure. There is concern that use in Przewalksi's horses had led to endometritis as a result of mating without a resulting pregnancy, preventing some females from conceiving.		Data deficient. Reversibility has been reported in white- tailed deer and feral horses. Rates of foaling among treated mares was similar to control mares treated with saline, 4 years after one GonaCon treatment.	Deslorelin is designed to be fully reversible, however there are currently no cases of this within this taxon on the database. Cases of reversibility have been demonstrated, but this is individual and taxon dependent.	Considered reversible but every species has not been tested. Duration to reversibility extremely variable.	

Effects on Behaviour	Similar to surgical castration (duration of antibody effect). No oestrus behaviours in mares.	Effects on behaviour individual m
Effects on sexual physical characteristics	Similar to surgical castration (duration of antibody effect).	Dat
Males	Recommended	Not re
Dose	Two injections of 400µg are given 35 days apart and boosters are usually administered every 6-7 months, although duration can vary between species and individuals.	
Latency to effectiveness:	At least 2 weeks following the booster.	
Use in prepubertals or juveniles:	No data available, therefore its use is not recommended	
Use in seasonal breeders:	If used should be done at least 6 weeks prior to the breeding season. Effective in horses.	
Duration and Reversibility	Reversibility is unknown for most of species. Improvac [®] generates short lived antibodies in the domestic pig (after 7-8 weeks following second injection antibodies start to decline). Plasma testosterone remains low for at least 6 months after initial treatment in domestic stallions. In a study of 5 stallions, only 70% had pre-treatment concentrations of testosterone after 1 year, whereas 15% did not reverse even after two years. Reversibility occurs on an individual basis.	
Effects on Behaviour	Similar to surgical castration (duration of antibody effect). Decrease male aggression due to downregulation of testosterone synthesis. The social position of treated males may decrease.	
Effects on sexual physical characteristics	Similar to surgical castration (duration of antibody effect).	
General:		
Side effects	Painful swelling at the vaccination site may occur - need to inject deep intramuscular in equids. The EAZA RMG recommends always reading the manufacturer's data sheet.	
Warnings	It should be handled with extreme care to avoid handler accidents. The EAZA RMG recommends always reading the manufacturer's data sheet.	This product is contraine previous or current histo EAZA RMG recom manufact
Reporting Requirements: In orde	r to increase our knowledge of the efficacy of contrace	eption methods in <i>equida</i>
References:		
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•	scher, SB, Annandale, CH, Guthrie, AJ & Bertschinger, HJ	(2013) Reversibility of the
3) Gray, ME, Thain, DS, Cameron, E		(2013) Reversibility of the e-roaming feral horses wit
3) Gray, ME, Thain, DS, Cameron, E 4) Killian, G, Wagner, D & Miller, L	scher, SB, Annandale, CH, Guthrie, AJ & Bertschinger, HJ Z & Miller, LA (2010) Multi-year fertility reduction in fre	(2013) Reversibility of the e-roaming feral horses wit e GonaconTM in Male Whi
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Disclaimer: The EAZA RMG endeavours to provide correct and current information on contraception from various sources. As these are prescription only medicines it is the responsibility of the veterinarian to determine the dosage and best treatment for an individual

r have not been studied, every may react differently.	Since usually the vaccine doesn't suppress oestrus cycles it has almost no effects on social behaviour, and no undesirable behavioural effects have been registered in free-ranging elephants treated for up to 9 years. In some species the failure to conceive can results in longer than usual breeding season and in some cases this can results in aggression and social disruption.	Effects on behaviour have not been studied, every individual may react differently. Because it binds readily to androgen receptors and is antiestrogenic, females may experience male- like qualities. Further research in the subject is necessary.
ata deficient	Data deficient	Because it binds readily to androgen receptors and is antiestrogenic, females may experience male-like qualities
recommended	Not recommended	Not recommended
cause weight gain in all species. effects on uterine and mammary species. Can cause endometritis in estic follicles in suids at low doses. ommends always reading the cturers' data sheet.	Treatment for over 5 years has been associated with ovarian failure in some species (species differences). Significant ovarian disruption has been noted in dogs, rabbits, mice and domestic sheep. Oophoritis unknown if transient or permanent. In some species the failure to conceive can results in longer than usual breeding season (aggression and social disruption). There is concern that use in Przewalksi's horses had led to endometritis as a result of mating without a resulting pregnancy, preventing some females from conceiving.	Possible deleterious effects on the endometrium following prolonged use. Progestins are likely to cause weight gain in all species. Because it binds readily to androgen receptors and is anti-estrogenic, females may experience masculinisation (increased aggression, development of male secondary sex characteristics). The EAZA RMG recommends always reading the manufacturer's data sheet.
ndicated for use in females with a tory of uterine inflammation. The nmends always reading the cturer's data sheet.	The only adjuvant used with PZP is Freund's Modified adjuvant, which DOES NOT CAUSE TB+ TEST RESULTS, and injection site reactions are less than 0.05%. Following the initial treatments, boosters are required, using only Freund's Incomplete adjuvant.	Interaction with other drugs are known to occur and may influence protection against pregnancy. In some diabetic animals progestagens has led to an increased insulin requirement, as such this product is not recommended in diabetic animals. The EAZA RMG recommends always reading the manufacturer's data sheet.
ae it is recommended that all ind	ividuals on contraception be reported to the EAZA RMG	

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Vhite-Tailed Deer (*Odocoileus virginianus*). *Wildlife Damage Management Conferences - Proceedings* . Paper 133.

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of estrus in cycling mares. *Journal of Equine Veterinary Science*, 29:140-145.

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e Report: Suppression of Harem Stallion Behavior and Fertility Following Anti-Gonadotropin-Releasing Hormone Vaccination of a Captive Wild Przewalski's Horse (Equus ferus przewalskii). Frontiers in Veterinary Science; 7(901). Doi: 10.3389/fvets.2020.569185

No oestrus behaviours in mares. As a 2 ml dose, GonaCon induced swelling at injection site in 80% of the mares.	Deslorelin is likely to supress some hormonal related behaviours and it has been used previously for aggression in the Somali Wild Ass with positive results.	Same as deslorelin	
Similar to surgical castration (duration of antibody effect).	Similar to gonadectomy. GnRH agonists may cause the suppression of physical secondary sexual characteristics.	Similar to gonadectomy. GnRH agonists may cause the suppression of physical secondary sexual characteristics.	
Not recommended	Not recommended GnRH agonists may not be very effective in equids; deslorelin does not seem to suppress males	Not recommended	
			N/A
			There will be a latency period of ~ 6-8 weeks in which there may still be fertile sperm present. Please use additional contraception during this time, or keep the sexes separated.
			Permanent. Castration should not be carried out in males who should breed in future.
Swelling at the vaccination site may occur - need to inject deep intramuscular in equids. The EAZA RMG recommends always reading the manufacturer's data sheet.	Similar to gonadectomy; especially weight gain. Females of a	In general weight gain as would be seen with ovariectomy or castration. Increased appetite will result in weight gain, especially in females. Males may lose muscle and overall weight if not replaced by fat. Males may become the size (weight) of females. The EAZA RMG recommends always reading the manufacturer's data sheet.	N/A
deep intramuscular in equids. The EAZA RMG recommends	Similar to gonadectomy; especially weight gain. Females of a species that are induced ovulators, may ovulate and become pseudo-pregnant when first treated. Causes initial gonadal stimulation. Duration may be reduced if implant is broken. Do not cut the implant. Implants are	castration. Increased appetite will result in weight gain, especially in females. Males may lose muscle and overall weight if not replaced by fat. Males may become the size (weight) of females. The EAZA RMG recommends always	
deep intramuscular in equids. The EAZA RMG recommends always reading the manufacturer's data sheet. Product should be handled with extreme care to avoid handler accidents. There is a possibility that treated individuals will be rendered permanently infertile. The EAZA RMG recommends always reading the manufacturer's data	Similar to gonadectomy; especially weight gain. Females of a species that are induced ovulators, may ovulate and become pseudo-pregnant when first treated. Causes initial gonadal stimulation. Duration may be reduced if implant is broken. Do not cut the implant. Implants are designed to be left in and fully reversible, but removal of the implant may also aid reversibility. Should not be used in	castration. Increased appetite will result in weight gain, especially in females. Males may lose muscle and overall weight if not replaced by fat. Males may become the size (weight) of females. The EAZA RMG recommends always reading the manufacturer's data sheet.	N/A The procedure should always be carried out under sterile conditions, potential
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