EAZA RMG

EAZA Reproduction Management Group

Species name: Przewalski's horse *(Equus przewalskii)*

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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.

Contraceptive methods	GnRH vaccine	Progestagen (oral)	PZP vaccine	Progestagen (injection)	GnRH vaccine	GnRH agonist (implant)	GnRH agonist (injection)	Surgical/Permanent
Contraceptive Product:	GnRH protein conjugate	Altrenogest	prolligestrone 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
Commercial Name:	Improvac®	Regu-mate®	Porcine Zona Pellucida	Depo-Provera®, Depo-Progevera®	GonaCon™	Suprelorin ®	Lupron ®	Castration/Vasectomy
Product Availability:	Available through veterinary drug distributors	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. Please contact www.sccpzp.org for licensing information.	Manufactured by Pfizer. Widely available throughout Europe through human drug distributors.	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
Restrictions and/or permit required by Importing Country:	Current knowledge: widely available throughout European countries. The EAZA RMG recommends: always check with your local licencing authority	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
Mechanism of action:	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	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	GnRH agonist suppress the reproductive endocrine system, 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. **Ovariectomy:** surgical removal of the ovaries.
Insertion/Placement:	Intramuscular or subcutaneous.	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
Females						**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**	**Not recommended**
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.	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 female perissodactyla	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.	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.	Dosing information is not available; extrapolation from human literature is likely the best place to start.	
Latency to effectiveness:	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 primary vaccination and 100% after the booster vaccination, the interval from treatment to anoestrus was 2-3 weeks.	Usually 1-3 days of treatment, however separation of the sexes or alternative contraception methods 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 or alternative contraception 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 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).	3 weeks average as GnRH agonists initially stimulate the reproductive system- **please refer to Lupron datasheet for 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 used as an alternative method to suppress the stimulation phase).	
Oestrus cycles during contraceptive treatment:	If contraceptive suppression is successful then oestrus should also be suppressed fully; highly successful at inducing anoestrus in domestic horses	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.	
Use during pregnancy:	**Not recommended**	Progestagens are not recommended in pregnant animals unless indicated otherwise (they mimic the corpus luteum). There is a 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**	
Use during lactation:	**Unknown**	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	
Use in prepubertals or juveniles:	**Unknown**	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 juveniles has not been fully assessed. Possible long-term effects on fertility are not known.	**Unknown**	Because 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 dogs and cats. GnRH agonist use in prepubertal domestic cats was followed by reproductive cycles after treatment ceased. However, species differences may occur.	**Data deficient** in this group, see product information sheet	
Use in seasonal breeders:	If used should be done at least 6 weeks prior to the breeding season. Effective in the horse. Use on the onset of the breeding season before cycling starts.	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.	
Duration	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). Mares are suppressed for a full season after the first booster.	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.	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 12 months	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.**	Ovariectomy should not be carried out in females who should breed in future.
Reversibility	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.	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 Przewalski's horses had led to endometritis as a result of mating without a resulting pregnancy, preventing some females from conceiving.	Designed to be fully reversible although individual variations can occur.	**Data deficient.** Reversibility has been reported in white-tailed deer and feral horses.	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 ovariectomy (duration of antibody effect). No oestrus behaviours in mares.	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.	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.	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	
Effects on sexual physical characteristics	Similar to surgical ovariectomy (duration of antibody effect).	**Data deficient**	**Data deficient**	Because it binds readily to androgen receptors and is antiestrogenic, females may experience male-like qualities	Similar to surgical ovariectomy (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.	

Males	Recommended	Not recommended	Not recommended	Not recommended	**Data deficient** - there is potential of similar effects on fertility in males as in females although research in this area is lacking for most species	**Not recommended** **GnRH agonists may not be very effective in equids; deslorelin does not seem to suppress males**	**Data deficient** **GnRH agonists may not be very effective in equids; Lupron does not seem to suppress males**	
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.	0.044 mg/kg or 0.088 mg/kg daily was used in domestic stallions.			A single vaccination of 1-2 ml per male is advised. If longer effects are desired, a second vaccination can be applied			N/A
Latency to effectiveness:	At least 2 weeks following the booster.				**Data deficient.** Assumed to be similar to that of Improvac (~2 weeks) however species-specific information is not known.		Depending on the species there may be fertile sperm present in vas deferens for 6-8 weeks post treatment. Testosterone decreases after 3-4 weeks but sperm can stay fertile for many weeks after. Additional contraception needed during this time or separation of the sexes.	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.
Use in prepubertals or juveniles:	No data available, therefore its use is **not recommended**				**Unknown**		**Data deficient** in this group. See product information sheet.	
Use in seasonal breeders:	If used should be done at least 6 weeks prior to the breeding season. Effective in horses. Use on the onset of the breeding season before cycling starts.				**Data deficient.** Should be given at least 6 weeks prior to the breeding season.		**Data deficient.** Should start at least 2 months prior the breeding season.	
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). Duration of efficacy is a full season in mares after the first booster.	Oral use of regumate will cause suppression of LH, testosterone and other reproductive hormones. Some testicular functions may not be reversed completely after stopping the administration.			**Data deficient.** 2-3 years in white tailed deer.		**Data deficient** but lupron is considered reversible. See product information sheet.	Castration should not be carried out in males who should breed in future.
Effects on Behaviour	Similar to surgical castration (duration of antibody effect). Decrease male aggression due to downregulation of testosterone synthesis.						Testosterone related aggression is likely to decrease. Data deficient in this group, see product information sheet.	
Effects on sexual physical characteristics	Similar to surgical castration (duration of antibody effect).				**Data deficient**		Some dichromatic species may change colour if testosterone related. Decrease in body size, feminisation of males.	
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.	Progestagens likely cause weight gain in all species. Possible deleterious effects on uterine and mammary tissues vary greatly by species. Can cause endometritis in domestic horses and cystic follicles in suids at low doses. The EAZA RMG recommends always reading the manufacturers' 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 Przewalski'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.	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 species that are induced ovulators, may ovulate and become pseudo-pregnant when first treated.	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. Females of a species that are induced ovulators, may ovulate and become pseudo-pregnant when first treated. The EAZA RMG recommends always reading the manufacturer's data sheet.	**N/A**
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 contraindicated for use in females with a previous or current history of uterine inflammation. The EAZA RMG recommends always reading the manufacturer'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.	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 sheet.	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 conjunction with Depo-Provera.	Causes initial gonadal stimulation	The procedure should always be carried out under sterile conditions, potential for infection of the surgical wound.

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

References:

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6) Baker, DL, Powers, JG, Oehler, MO, Ransom, JI, Gionfriddo, J, Nett, TM (2013) Field evaluation of the Immunocontraceptive GonaCon-B in Free-ranging Horses (Equus caballus) at Theodore Roosevelt National Park. *J. Zoo Wildl. Med.* , 44 : S141–S153

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