EAZA RMG
EAZA Reproductive Management Group

Taxon: *Giraffidae*

Fact Sheet Compiled by: Veronica Cowl
Last Updated: October 2019
Fact Sheet Reviewed by: Yedra Feltrer Rambaud DVM, MSc(WAH), DipECZM(ZHM), MRCVS & Tobias Knauf-Witzens
We would recommend assessing any contraceptive bout with behavioural and hormone monitoring. For more information on this, please contact contraception@chesterzoo.org
This work is supported by the European Union LIFE NGO funding programme. The European Union is not responsible for the views displayed in publications and/or in conjunction with the activities for which the grant is used.

Contraceptive methods	GnRH agonist (implant)	GnRH agonist (injection)	GnRH vaccine (injection)	Progestagen (oral)	PZP vaccine	Progestagen (implants)	Progestagen (injection)	Surgical/Permanent
Contraceptive Product:	Deslorelin acetate	Luprolide acetate	GnRH protein conjugate	Altrenogest	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).	Etonogestrel 68 mg	medroxyprogesterone acetate;	-
Commercial Name:	Suprelorin ®	Lupron ®	Improvac®	Regu-mate®	Porcine Zona Pellucida vaccine	Implanon® Nexplanon®	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.	Luprolide acetate licenced for human use	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. PZP is available to ship to Europe. It is advised that you check with the licensing authority that manages the import of veterinary drugs to obtain a permit to import PZP. Once all necessary authorisations and approvals have been completed, you can order PZP from: Kimberly M. Frank The Science and Conservation Center 2100 S. Shiloh Road Billings, MT 59106 phone 406-652-9718 fax 406-652-9733 e-mail sccpzp@hotmail.com	Manufactured by Bayer Schering Pharma AG. Available through human drug distributors	Manufactured by Pfizer. Widely available throughout Europe through human drug distributors.	-
Restrictions and/or permit required by Importing Country:	The EAZA RMG recommends that you always check with your local licencing authority.	**Data deficient**	Current knowledge: widely available throughout European countries. The EAZA RMG recommends that you always check with your local licencing authority.	The EAZA RMG recommends that you always check with your local licencing authority.	License required UK and France; all other Countries unknown. The EAZA RMG recommends that you always check with local licencing authority.	The EAZA RMG recommends that you always check with your local licencing authority.	The EAZA RMG recommends that you always check with your local licencing authority.	-
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 results 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 (similar to Suprelorin)	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.	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	-
Insertion/Placement:	Sub-cutaneous, in a place where it can be easily detected or seen for removal at a later date (I.e.base of the ear/neck); refer Suprelorin fact sheet for effective method of implant placement (tunnelisation).	Injectable	Injectable intramuscular or subcutaneously	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	Intramuscular or subcutaneous. The EAZA RMG recommends sub-cutaneous, at the base of the ear/neck for visibility (aid for later removal).	Injectable intramuscular	Surgical
Females		**Data deficient**						
Dose	2 x 9.7mg implants last for at least 1.5-2 years in giraffes[2]. Our records suggest that higher doses of up to 5 implants may need to be administered, as not all females were suppressed at lower doses.	**Data deficient.** Lupron is available in varying dosages from formulations lasting 1-6 months.	For full suppression, two injections of 600µg are given 35 days apart and boosters are usually administered every 2 months. In some cases, a higher dose (800ug may be necessary). Duration can vary between species therefore we would highly recommend monitoring your females for signs of fertility. If the interval between boosters is extended beyond 2 months, it is encouraged that hormonal monitoring is carried out to ensure efficacy.	The dosage is 0.044 mg/kg administered orally daily.	The first injection would consist of 0.5mL PZP + 0.5mL adjuvant and the second injection should be given no less than 14 days after this. For non-seasonal breeders a booster should be given every 7-9 months.	3 to 5 implants (0.068g) are recommended for successful contraception in this species.	The recommended dose is 0.034mg/kg every 45-90 days . If oestrus occurs, increase by increments of 100 mg.	
Latency to effectiveness:	Deslorelin will have a latency to effect of 3-4 weeks during which a stimulation of the reproductive system will occur. For this reason separation of both sexes is recommended for approximately 3-4 weeks. If you cannot separate the sexes, in order to suppress the initial stimulation phase, the first contraceptive bout must be supplemented with an oral progestagen such as megestrol acetate pills (Ovarid) or altrenogest (Regumate®) daily, 7 days before and 8 days after the implant is inserted.	3 weeks average as GnRH analogues initially stimulate the reproductive system. Separation of the sexes OR additional contraception needed during this stimulatory phase (~2mg/kg Megestrol acetate pills or altrenogest (Regumate®) daily, 7 days before and 8 days after can be used to suppress the stimulation phase).	Latency to effectiveness can be up to 6 weeks so separation of the sexes is recommended if possible.	It has been demonstrated that 95% of mares will be suppressed within 3 days. However, the sexes should be separated for 7 days after the contraception is adminstered.	Latency to effectiveness is approximately 2-3 weeks after the final injection in year 1 therefore separation of the sexes from the initial injection until 2 weeks after the final injection is recommended.	Latency to effectiveness can take up to 1 day when inserted on day 1 to 5 of a cycle when replacing oral progestogen. As the right stage during oestrus cycle is often unknown, it is advised to use other contraceptive methods for at least 7 days after insertion of the implant.	Latency to effectiveness after the initial injection is 1-3 days however, if the exact stage of the giraffes cycle is unknown, extra time (1 week) must be allowed, separation of the sexes Is advised for at least one week.	
Oestrus cycles during contraceptive treatment:	Initial oestrus and ovulation (during the stimulatory phase) followed by a period of anoestrus. To suppress the initial oestrus and ovulation you can follow the megestrol acetate/altrenogest protocol mentioned above.	Initial oestrus and ovulation (during the stimulatory phase) followed by a period of anoestrus. To suppress the initial oestrus and ovulation you can follow the megestrol acetate protocol mentioned above.	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.	Ovulation and cycling can occur in adequately contracepted individuals (but is unlikely and the degree of suppression is dose dependent).	PZP normally does not interfere with follicular devlopment and ovulation which means that females should cycle normally	Unlikely to occur	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).	
Use during pregnancy:	**Not recommended, can cause abortion**	**Not recommended**	The effect of Improvac in pregnant individuals is currently unknown however; in a currently unpublished study, one female treated with Improvac while pregnant did abort at approximately 5 months although there may have been other factors involved. However, evidence from a similar study suggests that there may be no issues when used in females with close to term pregnancies[4].	Progestagens are **not recommended** in pregnant animals because of the possibility of prolonged gestation leading to dystocia, stillbirth and abortion in some species.	No known contraindications	Progestagens are **not recommended** in pregnant animals because of the possibility of prolonged gestation leading to dystocia, stillbirth and abortion in some species.	Progestagens are **not recommended** in pregnant animals due to the possibility of prolonged gestation leading to dystocia, stillbirth and abortion in some species.	
Use during lactation:	No known contraindications once lactation has been established.	No contraindications once lactation established	Research suggests that there is no negative effect when used in females that are lactating[4,5].	Considered safe for nursing infant.	No known contraindications	Considered safe for nursing infant.	Considered safe for nursing infant.	

Use in prepubertals or juveniles:	**Data deficient.**	**Data deficient** in this group but likely to have a similar effect to deslorelin	**Data deficient** in giraffes, so caution is advised. Based on the experience of EAZA RMG working group members with Improvac use in elephants, prolonged use of Improvac may bear risk to permanent infertility when administered in prepubertal animals.	The use of synthetic progestagens in pre-pubertals or juveniles has not been fully assessed. Possible long-term effects	PZP-treated prepubertal white-tailed deer and feral horses were fertile as adults. Not associated with side effects in elephants. But there is no data for other species	The use of synthetic progestagens in pre-pubertals or juveniles has not been fully assessed. Possible long-term effects on fertility are not known.	The use of synthetic progestagens in pre-pubertals or juveniles has not been fully assessed. Possible long-term effects on fertility are not known.	
Use in seasonal breeders:	**N/A**	**N/A**	**N/A**	**N/A**	**N/A**	**N/A**	**N/A**	**N/A**
Duration	As a guide, the **minimum** effective period for 4.7mg implants is 6 months, and a **minimum** of 12 months for 9.4mg implants. There is evidence to suggest that 2x9.4mg implants have a duration of efficacy of between 1.5-2 years[2].	**Data deficient**	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). In mares it lasts one to two seasons after the first booster. Long-term use and duration is **data deficient**. Antibodies may not last longer than 2-3 months as boosters are recommended every 2 months.	Duration of effect is 1-3 days and must be administered daily as long as contraception is required. However latency to cycling and conception can vary between individuals.	Duration is related to the antibody titre the persistence of which varies according to species. Boosters are recommended at 6-month intervals to maintain contraception.	The duration of this product can last 2.5 to 3 years.	Dose dependant: 45-90 days in general. However, effects could last 1-2 years in some individuals.	
Reversibility	Deslorelin is designed to be fully reversible and there are 4 records of reversals in giraffes with time to conception varying between 2 months to 2 years after the expected implant expiry date. It is unknown whether implants were removed in these individuals. We would recommend that implants are removed to facilitate reversibility but the risk to the individual of anaesthesia to do so must be carefully considered. As such, implants should be placed in locations with thinner skin e.g. inner thigh, umbilical region, base of the ear.	**Data deficient**	There are two records of reversal in the database for giraffes in which individuals gave birth between 1.5-3 years following their last vaccination. The individuals were treated for 3 and 6 months, respectively. Moreover, studies have shown reversibility in equids within a two year period. It must be taken in to consideration that younger individuals will take longer to reverse in comparison to older individuals and that the longer an individual is treated, the longer it will take them to reverse. We encourage that institutions monitor the reproductive hormones of the animals in which a retun to fertility is desired.	Designed to be fully reversible although this can depend on the individual. There is one record of reversal in the database in which a female giraffe conceived almost immediately after cessation of treatment with regumate for two years; there was immediate male interest one day after treatment end and the female resumed cycling two weeks after treatment end.	Reversibility differs between species; however the longer PZP is given the longer it takes for a female to come back to being fertile. There is potential that individuals are redered infertile following long-term use (>3-4 years). It is therefore suggested that an individual is on PZP for no longer than 3 years if you want the female to breed. (Please visit www.sccpzp.org for more information).	Implanon is designed to be fully reversible however there are no cases of its use or reversibility in the giraffidae family. There are three recorded cases of its use in artiodactyla, but there is no data available on reversal.	Depo-Provera is designed to be fully reversible and reversibility using this product has been demonstrated numerous times. Individuals have been reported as successfully conceiving from 3 months to over 5 years after their final injection.	
Effects on Behaviour	Oestrus behaviour should be suppressed.	**Data deficient**	**Data deficient**	Effects on behaviour have not been studied and individuals may react differently. Further research is necessary.	Since usually the vaccine doesn't suppress oestrus cycles it has almost no effects on social behaviour.	Effects on behaviour have not been studied, every individual may react differently. Further research is necessary.	As Depo-Provera binds readily to androgen receptors and is anti-estrogenic, females may experience male-like qualities such as increased aggression or the development of secondary sex characteristics.	
Effects on sexual physical characteristics	Not reported.	Not reported.		Not reported.	Not reported. No social/behavioural side effects noted in African elephants studied for 12 years	Not reported		
Males	**Not recommended. GnRh agonists have not been proven to be effective in male ungulates.**	**Not recommended. GnRh agonists have not been proven to be effective in male ungulates.**	**Recommended**	**Not recommended**	**Not recommended**	**Not recommended**	**Not recommended**	**Vasectomy/Castration**
Dose	-	**Data deficient.** Lupron is available in varying dosages from formulations lasting 1-6 months.	Two injections of 600ug are given 35 days apart and boosters are usually administered every 2 months, although duration can vary between species. In some cases, a higher dose (800ug may be necessary). From anecdotal experience, we would advise beginning treatment with shorter 2 month intervals, before prolonging the interval period to 5-6 months. We would highly encourage monitoring the animals for any signs of a return to fertility, particularly when extending the booster interval.					-
Latency to effectiveness:	-	**Data deficient**	Latency to effectiveness can be up to 3-4 months for the down regulation of spermatogenesis, so separation of the sexes is recommended if possible. Fertility in males may remain for prolonged periods.					Sperm may survive in the vas deferens for 6-9 weeks
Use in prepubertals or juveniles:	-	**Data deficient**						Vasectomy: Possible with no interuption of puberty; castration: **data deficient**.
Use in seasonal breeders:	**N/A**	**N/A**	**N/A**	**N/A**	**N/A**	**N/A**	**N/A**	**N/A**
Duration and Reversibility	-	**Data deficient**	There are currently no reversals recorded on the database for giraffes however studies have shown reversibility in equids within a two year period. There are a few cases of this being used in male giraffes for controlling aggression which worked well with no side effects however, effects on fertility were not investigated. If future breeding is desired, it must be taken in to consideration that younger individuals will take longer to reverse in comparison to older individuals, and that the longer an individual is treated, the longer it will take them to reverse. There is evidence from the use of Improvac in stallions and African elephants in which Improvac was reversible following short-term (2-3 years) treatment. We have one record of an individual hormonally reversing 3,5 years after 8x 300ug injections.					Vasectomy: Permanent for practical puposes; castration: permanent.
Effects on Behaviour	-	**Data deficient**	Similar to surgical castration but short-acting (duration of antibody effect). Decrease of androgen-related aggressive behaviour due to down-regulation of testosterone synthesis.					Vasectomy: none - androgens maintained; castration: testosterone mediated behaviours e.g. sexual aggression or libido may decrease.

Effects on sexual physical characteristics	-	**Data deficient**	Similar to surgical castration but short-acting (duration of antibody effect).					Vasectomy: none - androgens maintained; castration: males may experience a loss of secondary sexual characteristics.
General:								
Side effects	In general weight gain as would be seen with ovariectomy or castration.	Effects on weight should be similar to those from 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.	Occasional swelling at the vaccination site - need to inject deep intramuscular in elephants, horses and giraffes.	Possible weight gain. **The EAZA RMG recommends that you always read the manufacturer's data sheet.**	Treatment for over 5 years has been associated with ovarian failure in some species (species differences). In some species the failure to conceive can result in longer than usual breeding season (aggression and social disruption)		Possible weight gain. The EAZA RMG recommends that you read the manufacturer's data sheet.One report of uterine pathology on post mortem in a giraffe treated for more than two years with Depo-Provera	Possible surgical complications. Epididymal spermatic granulomas seen in sheep and goats.
Warnings	Duration may be reduced if implant is broken. Do not cut the implant. Should not be used in conjunction with Depo-provera or any other long-acting injectable progestagen.	Should not be used in conjuction with Depo-Provera or any other long-acting injectable progestagen.	It should be handled with extreme care to avoid handler accidents. The EAZA RMG recommends that you read the manufacturer's data sheet. Do not treat females with previous or current history of endometritis/metritis. The use of progestins can exacerbate existing uterine inflammation/infection. sheet	Do not treat females with previous or current history of endometritis/metritis. The use of progestins can exacerbate existing uterine inflammation/infection.	The only adjuvants used with PZP are Freund's modified complete and incomplete adjuvants. **The complete adjuvant does not cause false positive TB results.** Injection site reactions are less than 0.05%. Following the initial treatments, boosters are required, using only Freund's Incomplete adjuvant.		Please be aware that there is one report of a post-mortem on a giraffe where they found uterine pathologies following >2 years of treatment with Depo-Provera.	Make sure that the vas deferens was in fact located. Confirm the presence of sperm in the excised portion.

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

References:

1) Asa, C.S. & Porton, I.J. (eds.) (2005) *Wildlife Contraception: Issues, Methods, and Applications* . The Johns Hopkins University press: Baltimore.

2) Patton, M.L., Bashaw, M.J., del Castillo, S.M., Jöchle, W., Lamberski, N., Nieches, R., Bercovitch, F.B. (2005) Long-term suppression of fertility in female giraffe using the GnRH agonist deslorelin as a long-acting implant. *Theriogenology* , 66(2):431-438.

3) Borkowski, R., Citino, S., Bush, M., Wollenman, P., Irvine, B. (2008) Surgical Castration of Subadult Giraffe (Giraffa camelopardalis). *Journal of Zoo and Wildlife Medicine* , 40(4):786-790.

4) Miller, L.A., Rhyan, J.C., Drew, M. (2004) Contraception of bison by gnRH vaccine: a possible means of decreasing transmission ofbrucellosis in bison. *Journal of Wildlife Diseases* , 725-730.

4) Balet, L., Janett, F., Hüsler, J., Piechotta, M., Howard, R., Amatayakul-Chantler, S., Steiner, A., Hirsbrunner, G. (2014) Immunization against gonadotropin-releasing hormone in dairy cattle: Antibody titres, ovarian function, hormonal levels, and reversibility. *Journal of Dairy Science,* 97:2193-2203.