

Hippopotamidae



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Contraceptive methods:	GnRH agonist (injection)	GnRH Vaccine	Progestagen (injection)	Progestagen (oral)	PZP vaccine	Surgical/ Permanent
Contraceptive Product:	Leuprolide acetate	GnRH protein conjugate	Depot medroxyprogesterone acetate	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).	N/A
Commercial Name:	Lupron®	Improvac®	Depo-Provera®, Depo-Progevera®	Regu-mate®	Porcine Zona Pellucida	Vasectomy
Product Availability:	Leuprolide acetate licenced for human use	Available through veterinary drug distributors.	Manufactured by Pfizer. Widely available throughout Europe through human 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.	N/A
Restrictions and/or permit required by Importing Country:	Data deficient	Current knowledge: widely available throughout European countries. EGZAC recommends: always check with your local licencing authority	EGZAC recommends: always check with your local licencing authority	EGZAC recommends: always checking with your local licencing authority	License required UK and France; all other countries unknown. EGZAC recommends always checking with local licencing authority	N/A
Mechanism of action:	GnRH agonists suppress the reproductive endocrine system, preventing production of pituitary and gonadal hormones. GnRH initially stimulate the reproductive system, which can result in oestrus and ovulation in females or temporary enhancement of testosterone and spermatogenesis in males. Therefore, supplemental contraception is recommended to prevent the stimulation phase.	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.	Progestagens mimic endogenous progesterone. They effect contraception by blocking ovulation, causing thickening of cervical mucus, slowing ovum transport, and/or interfering with fertilization or implantation. Progestagens may not completely suppress follicular development and estrogen production, so some estrous behaviors may persist.	Progestagens mimic endogenous progesterone. They effect contraception by blocking ovulation, causing thickening of cervical mucus, slowing ovum transport, and/or interfering with fertilization or implantation. Progestagens may not completely suppress follicular development and estrogen production, so some estrous behaviors may persist.	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.	Surgical procedure in which the ductus deferens are cut, tied, cauterized, or otherwise interrupted
Insertion/Placement:	Injectable intramuscular or subcutaneously	Injectable intramuscular or subcutaneously	Injectable intramuscular. Administer the injection behind the ear to combat problems with administering the injection due to fatty layer.	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).	Injectable Intramuscular	Surgical
Females						
Dose	There are various formulations lasting 1-6 months. Dosing information is not available; extrapolation from human literature is likely the best place to start.	Two injections of 400-600µg are given 35 days apart. Boosters are usually administered every 3-6 months and may eventually be spaced out to yearly, although duration can vary by species.	The recommended dosage for this taxon is 800mg every 6 weeks.	The standard dose for mares is 0.044 mg/kg daily once for 15 consecutive days. The recommended dose is 1mL per 50kg body weight.	~ 100 ug of protein. Recommended dose is 2 injections given typically 2+ weeks apart then a booster every 8 months for most species. Booster intervals will be advised by the manufacturer.	N/A

Latency to effectiveness:	3 weeks average as GnRH agonists initially stimulate the reproductive system- please refer to Lupron® datasheet for detailed information - separation of the sexes OR additional contraception needed during this time (see product data sheet. ~2mg/kg Megestrol acetate pills daily 7 days before and 8 days after has been used to suppress initial stimulation phase in domestic dogs, but this dose should be extrapolated for other taxa).	Latency to effectiveness can be up to 6 weeks so separation of the sexes is recommended if possible.	1-3 days post injection. However, if the cycle stage is not known then extra time must be allowed; therefore, sexes should be separated for at least 1 week.	Sexes should be separated for 7-14 days after the contraception is administered.	2-3 weeks after the last vaccination during year 1 (primary course of vaccination 2 injections 2-4 weeks apart, preferable 3 injections).	N/A
Oestrus cycles during contraceptive treatment:	Initial oestrus and ovulation (during the 3 weeks of stimulation) then suppression of the oestrus cycle. To suppress the initial oestrus and ovulation, the megestrol acetate protocol above should be followed.	Unknown but it should be suppressed; studies have shown GnRH to be effective at inducing anoestrus in domestic horses.	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).	Ovulation and cycling can occur in adequately contracepted individuals (but is unlikely and the degree of suppression is dose dependent).	PZP should not suppress estrous cycles and may extend the breeding season beyond what is considered typical, resulting in additional estrous cycles.	N/A
Use during pregnancy:	Not recommended	Unknown	Progestagens are not recommended in pregnant animals because of the possibility of prolonged gestation, stillbirth, abortion, etc. in some species, although the effect may depend on dose.	Progestagens are not recommended in pregnant animals because of the possibility of prolonged gestation, stillbirth, abortion, etc. in some species, although the effect may depend on dose.	Does not interrupt pregnancy or affect fetus	N/A
Use during lactation:	No contraindications once lactation established	Unknown	Considered safe for nursing infant.	Considered safe for nursing infant.	No known contraindications	N/A
Use in prepubertals or juveniles:	Data deficient in this group. Because GnRH agonists suppress gonadal steroids, their 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.	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.	The use of synthetic progestagens in pre-pubertals or juveniles has not been fully assessed. Possible long-term effects on fertility are unknown.	PZP-treated prepubertal white-tailed deer and feral horses were fertile as adults. Not associated with side effects in elephants. But there are no data for other species	N/A
Use in seasonal breeders:	Data deficient. Should start at least 1 month prior the breeding season.	Unknown but 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.	Should be injected at least 1 week before the breeding season 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.	N/A
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	Unknown for most species. Improvac® generates short-lived antibodies in the domestic pig (after 7-8 weeks following second injection antibodies start to decline). A full season in mares after the first booster.	Dose dependent: The recommended injection interval for hippos is every six weeks. However, some individuals may be suppressed longer than six weeks.	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 vary between individuals.	Species -dependant: most species 1 year	N/A
Reversibility	Considered reversible but every species has not been tested. Time to reversal extremely variable. There have been no examples of reversibility in this taxon.	Improvac® is designed to be fully reversible; there are no cases currently on the database however studies have shown reversibility in female equids within a two year period.	Designed to be fully reversible and this has been demonstrated in this species although individual variations exist. Four females conceived within a year of their final injection.	Designed to be fully reversible although variations can occur.	Designed to be fully reversible and it has been demonstrated in this species. However, 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.	N/A

Effects on Behaviour	Data deficient	Similar to surgical castration but short-acting (duration of antibody effect).	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 (increased aggression, development of male secondary sex characteristics, etc.) Further research in the subject is necessary.	Effects on behaviour have not been studied, every individual 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 result in longer than usual breeding season and in some cases this can result in aggression and social disruption.	N/A
Effects on sexual physical characteristics	GnRH agonists may cause the suppression of physical secondary sexual characteristics.	Similar to surgical castration but short-acting (duration of antibody effect).	Because it binds readily to androgen receptors and is antiestrogenic, females may experience male-like qualities (increased aggression, development of male secondary sex characteristics, etc.)	None reported	None reported	N/A
Males			Not Recommended	Not Recommended	Not Recommended	
Dose	Males usually require a higher dose than females. There are various formulations lasting from 1-6 months. Data Deficient	Two injections of 400µg are given 35 days apart and boosters are usually administered every 6 months/yearly, although duration can vary between species.	N/A	N/A	N/A	N/A
Latency to effectiveness:	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 live sperm may remain for many weeks after. Additional contraception needed during this time or separation of the sexes.	Unknown for most species, minimum of 6 weeks.	N/A	N/A	N/A	N/A
Use in prepubertals or juveniles:	Data deficient in this group, see product information sheet	Data deficient	N/A	N/A	N/A	N/A
Use in seasonal breeders:	Data deficient. Should start at least 2 months prior the breeding season.	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.	N/A	N/A	N/A	N/A
Duration and Reversibility	Data deficient, but Lupron is considered reversible. See product information sheet.	Unknown for most species. Improvac® generates short lived antibodies in the domestic pig (after 7-8 weeks following second injection antibodies start to decline). Lasts about 5 to 9 months in bull elephants when used for the control of musth. It must be taken into consideration that younger males will take longer to reverse in comparison to older males.	N/A	N/A	N/A	N/A
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. Can prevent, terminate or reduce aggression/musth behaviour in bull elephants.	N/A	N/A	N/A	N/A
Effects on sexual physical characteristics	Some dichromatic species may change colour if testosterone dependent. Decrease in body size, feminisation of males.	Similar to surgical castration but short-acting (duration of antibody effect).	N/A	N/A	N/A	N/A
General:						
Side effects	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. Males may become the size (weight) of a female.	Occasional swelling at the vaccination site - need to inject deep intramuscular in elephants and horses. EGZAC recommends always reading the manufacturer's data sheet	Possible weight gain. EGZAC recommends always reading the manufacturer's data sheet.	Possible weight gain. EGZAC recommends always reading the manufacturer's 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 result in longer than usual breeding season (aggression and social disruption)	N/A

<p>Warnings</p>	<p>Causes initial gonadal stimulation. Should not be used in conjunction with Depo-Provera.</p>	<p>It should be handled with extreme care to avoid handler accidents. EGZAC recommends always reading the manufacturer's data sheet</p>	<p>Do not administer to any pregnant female because of the possible duration of efficacy extending beyond the expected time of parturition which has the potential for deadly effects. There are possible deleterious effects on the uterine and mammary tissues. Caution must be taken when using this product as very high doses can cause serious side effects, and may affect immune response. EGZAC recommends always reading the manufacturer's data sheet</p>	<p>Progestagens are not recommended in pregnant animals because of the possibility of prolonged gestation, stillbirth, abortion, etc. in some species, although the effect may depend on dose. There are contra indications for use in mares with a history of uterine infection. Data is deficient for other species.</p>	<p>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. In rabbits and possibly canids PZP vaccine can cause depletion of oocytes, and in some primates it can cause temporary cessation of oestrous cycles. There are few data for its use in carnivores, aside from pinnipeds and bears, and recent research with felids indicates that the antibodies will not cross-react with the sperm receptors.</p>	<p>Infection of the surgical wound might occur. Intradermal closure of the skin is advised together with prophylactic antibiotic treatment and NSAID</p>
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Reporting Requirements: In order to increase our knowledge of the efficacy of contraception methods in the Hippopotamidae family it is recommended that all individuals on contraception be reported to EGZAC

References:

- 1)
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Disclaimer: EGZAC 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