

**Animal name: Proboscidea**



Fact Sheet Compiled by: Veronica Cowl

Last Updated: May 2016

Fact Sheet Reviewed by: Henk Bertschinger and Yedra Feltrer

We would recommend assessing any contraceptive bout with behavioural and hormone monitoring. For more information, please contact [contraception@chesterzoo.org](mailto:contraception@chesterzoo.org)

Contraceptive methods	GnRH agonist (implant)	GnRH agonist (injection)	Progestagen (implants)	GnRH Vaccine	Progestagen (injection)	Progestagen (injection)	PZP vaccine	Surgical
<b>Contraceptive Product:</b>	Deslorelin acetate	Luprolide acetate	Etonogestrel 68 mg	GnRH protein conjugate	medroxyprogesterone acetate;	proligestrone 100mg/ml	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).	
<b>Commercial Name:</b>	Suprelorin® (0 records)	Lupron®	Implanon® Nexplanon®	Improvac®	Depo-Provera®, Depo-Progevera®	Delvosteron®	Porcine Zona Pellucida	
<b>Product Availability:</b>	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	Manufactured by Bayer Schering Pharma AG. Available through human drug distributors	Available through veterinary drug distributors.	Manufactured by Pfizer. Widely available throughout Europe through human drug distributors.	Manufactured by MSD animal Health UK, Intervet Europe. Licenced for use in female dogs, cats, and ferrets; available through veterinary distributors.	Not commercially available in Europe. Can be imported from the USA. <a href="http://www.sccp.org">www.sccp.org</a>	N/A
<b>Restrictions and/or permit required by Importing Country:</b>	EGZAC recommends: always check with your local licencing authority	Data deficient	EGZAC recommends: always check with your local licencing authority	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 check with your local licencing authority	License for importation is required. licence unavailable in the UK; all other Countries unknown. EGZAC recommends always checking with local licencing authority	N/A
<b>Mechanism of action:</b>	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	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.	Anti-estrogenic activity. 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	The anti-PZP antibodies interfere with fertilisation by binding to the ZP glycoprotein sperm receptors of the zona capsule. This prevents sperm binding, the acrosome reaction and subsequent penetration of the capsule to fertilise the oocyte.	Surgical procedure in which the ductus deferens are cut, tied, cauterized, or otherwise interrupted
<b>Insertion/Placement:</b>	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	Intramuscular or subcutaneous. EGZAC recommends sub-cutaneous, upper inner arm for visibility (aid for later removal)	Deep intramuscular injection only. Avoid intermuscular and fascial tissue	Injectable intramuscular	Injectable subcutaneously - do not inject intradermally or into subcutaneous fat or scar tissue	Injectable: deep intramuscular	Surgical
<b>Females</b>	<b>Not recommended</b>	<b>Not recommended</b>	<b>Not recommended</b>	<b>Data deficient</b>	<b>Data deficient</b>	<b>Not recommended</b>	<b>Recommended</b>	<b>Data deficient</b>
<b>Dose</b>				Two injections of 1000 µg are given 35 days apart and boosters are usually administered every 5 months/yearly, although duration can vary between species. Dose will vary according to animal status and age and formulation used, as they may have different concentrations per ml in different products. <b>Please contact EGZAC for the treatment protocol and specific dosage instructions before treating your animal with Improvac.</b>			Year 1: 400 µg (0.5 ml) with 0.5 ml Freund's modified complete adjuvant (FMA). The two should be emulsified by using a connector between two luer-lock syringes and pushing the mixture forwards and backwards using 60 strokes. This will result in a stable emulsion for injection by hand or by means of a drop-out dart. The booster is given 5 weeks later using 200 µg PZP (0.5 ml) emulsified with 0.5 ml Freund's Incomplete Adjuvant (FIA). Annual boosters using 200µg PZP and FIA at 12-month intervals.	
<b>Latency to effectiveness:</b>				Latency to effectiveness can be up to 6 weeks so separation of the sexes is recommended if possible.			Latency to effect should be 4 week following the second booster.	
<b>Oestrous cycles during contraceptive treatment:</b>				Animals will exhibit anoestrus.			Oestrous cycles continue despite treatment	
<b>Use during pregnancy:</b>				<b>Data deficient</b>			No effects on pregnancy have been seen in ±700 elephant cows.	

Use during lactation:				Data deficient			No negative effects on lactation. Cows will stop lactating if treatment is continued longer than 5 years after birth of the last calf.	
Use in prepubertal or juveniles:				May cause permanent ovarian shut-down especially after repeated use			No negative effects have been observed in pubertal cows. However, the lack of a calf may affect social behaviour.	
Use in seasonal breeders:							Can be used at any time of the year	
Duration				Approximately 6 months after each booster			This depends on how many treatments have been carried out. The longer treatment has been continued the longer the duration. It is dependent on the waning of antibody titres.	
Reversibility				Improvac is not designed to be reversible however reversibility has been demonstrated in free ranging African elephants following 2 years of Improvac use. Please be advised that younger elephants will take longer to reverse than older individuals.			Reversal has been demonstrated after 5 years of yearly treatments. Long-term treatment may result in follicular depletion.	
Effects on Behaviour				Will suppress oestrus associated behaviours			Cows continue to cycle and thus an increased incidence of oestrus is noted in individuals or a group. Behavioural studies in free-ranging elephants where a population had been treated for 10 years showed no effects on behaviour. It is recommended to allow young cows to have their first calf prior to treatment and, in a group, to allow individuals to reverse from time to time. This important for the social behaviour of the family group.	
Effects on sexual physical characteristics				Data deficient			None have been noted	
Males	Not recommended	Not recommended	Not recommended	Recommended	Not recommended	Not recommended	Not recommended - Does not work in males	Vasectomy
Dose				Two injections of 1000 µg are given 35 days apart and boosters are usually administered every 5 months/yearly to maintain downregulation of testicular function, although duration can vary between species. Dose will vary according to animal status and age and formulation used, as they may have different concentrations per ml in different products. Please contact EGZAC for the treatment protocol and specific dosage instructions before treating your animal with Improvac.				A laparoscopic technique is detailed in reference 2.
Latency to effectiveness:				Serum testosterone concentrations decline rapidly after the primary vaccination course and are undetectable 3-5 months after the first booster vaccination. They continue to remain baseline if boosters are continued. Androgen-dependent behaviour improves steadily after the first booster. In African elephant bulls all sperm were found to be dead 5 months after the first booster. No sperm were present in 11 of 12 bulls 12 months after the first booster where treatment was continued. Treatment of an Asian bull treated with 600 µg GnRH protein conjugate successfully arrested sperm production in an Asian elephant bull. N.B. this male had previously also been treated with 2.0ml Equity® which ensured the same delivery of GnRH protein conjugate. This bull received booster injections every 3-4 weeks for 6 months. 1.5 years following the first GnRH vaccination, injection intervals were increased to 2 years apart, with a sustained suppression of serum testosterone.				
Use in prepubertal or juveniles:				Administration during the onset of puberty may result in decreased testes and penis size compared to untreated bulls. It may also cause irreversible infertility.				
Use in seasonal breeders:				NA				

Duration and Reversibility				After the primary and 1st booster in African bulls reversal as seen by an increase in aggressive behaviour starts 5-6 months after the booster. No data is available for reversal after prolonged treatment. Adult bulls that were treated for three years have failed to either show a rise in serum testosterone (2 captive bulls) or a musth cycle (2 free-ranging bulls) two years after the last treatment.				
Effects on Behaviour				In southern Africa Improvac is primarily used to control androgen-related aggression and musth in captive and free-ranging bulls. Some 50 bulls have been treated successfully to date. The first bull to be treated is now 32 years old and after 13 years of treatment in captivity has shown normal body and tusk growth and remains tractable.				
Effects on sexual physical characteristics				Persistent treatment in prepuberal bulls may lead feminine appearance of the bull.				
General:								
Side effects				Inject site reactions occur in about 10% of treatments and consist of a painful swelling which may be associated with temporary lameness or stiffness.			Post treatment swellings have been noted in about 10% of cases. These are possibly granulomas resulting from the adjuvant but may also be small abscesses especially where drop-out darts have been used. Lameness or other complications have not been observed.	
Warnings				Prolonged treatment for more than 2-3 years may lead to permanent infertility.			To avoid contamination of skin and especially mucous membranes, protective clothing (especially gloves) and goggles should be worn while preparing the vaccine. Women should be made aware that absorption of the vaccine could cause infertility/sterility.	

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

References:

- 1) Delsink, A. & Kirkpatrick, J.F. (2012). Free-ranging African Elephant immunocontraception.
- 2) Rubio-Martinez, L. M., Hendrickson, D.A., Stetter, M., Zuba, J.R. & Marais, H.J. (2014). Laparoscopic Vasectomy in African Elephants (*Loxodonta africana*). *Veterinary Surgery* (43), pp 507-514.
- 3) Lueders, I., Hildebrandt, T.B., Gray, C. Botha, S., Rich, S. & Niemuller, C. (2014) Suppression of testicular function in a male Asian elephant (*Elephas maximus*) treated with gonadotropin-releasing hormone vaccines. *Journal of Zoo and Wildlife Medicine* 45(3), pp. 611-619.
- 4) Somgirda, C., Homkong, P., Sripiboon, S., Brown, J.L., Stoute, T.A.E., Colenbrandere, B., Mahasawangkul, S., & Thitaram, C. (2015) Potential of a gonadotropin-releasing hormone vaccine to suppress musth in captive male Asian elephants (*Elephas maximus*). *Animal Reproduction Science* (164), pp. 111-120.
- 5) BERTSCHINGER, H.J., E.S SILLS. (2013) Contraceptive applications of GnRH-analogues and vaccines for wildlife mammals of southern Africa: Current experience and future challenges. In: Gonadotropin-releasing hormone (GnRH). Production, structure and function. ES Sills (ed). Nova Science Publishers Inc., New York, ISBN: 978-1-62808-478-8 (eBook) 278 pp: 85-107
- 6) DELSINK A.K., J. KIRKPATRICK, J.J. VAN ALTENA, M.J. BERTSCHINGER, S.M. FERRERA, R. SLOTOW (2013) Lack of spatial and behavioral responses to immunocontraception application in African elephants (*Loxodonta africana*). *Journal of Zoo and Wildlife Medicine* 44(4): 352-374.
- 7) DELSINK A.K., J. KIRKPATRICK, J.J. VAN ALTENA, M.J. BERTSCHINGER, S.M. FERRERA, R. SLOTOW (2013) Lack of spatial and behavioral responses to immunocontraception application in African elephants (*Loxodonta africana*). *Journal of Zoo and Wildlife Medicine* 44(4): 352-374.
- 8) DELSINK, A.K., VAN ALTENA, J.J., GROBLER, D., BERTSCHINGER, H.J., KIRKPATRICK, J., SLOTOW, R. (2007) Implementing immunocontraception in free-ranging African elephants at Makalali Conservancy. *Journal of the South African Veterinary Association* 78: 25-30
- 9) DE NYS, H.M., H.J. BERTSCHINGER, J.A. TURKSTRA, B. COLENBRANDER, R. PALME, A.M. HUMAN. (2010) Vaccination against GnRH may suppress aggressive behaviour and musth in African elephant (*Loxodonta africana*) bulls – a pilot study. *Journal of the South African Veterinary Association* 81: 8-15.
- 10) Somgird, C., Homkong, P., Sripiboon, S., Brown, J. L., Stout, T. A., Colenbrand, B., ... & Thitaram, C. (2015). Potential of a gonadotropin-releasing hormone vaccine to suppress musth in captive male Asian elephants (*Elephas maximus*). *Animal Reproduction Science*.
- 11) BERTSCHINGER, HENK, AUDREY DELSINK, JJ VAN ALTENA, JAY KIRKPATRICK, HANNO KILLIAN, ANDRE GANSWINDT, ROB SLOTOW, GUY CASTLEY (2008). Chapter 6: Reproductive control of elephants. In: *Elephant Management: A Scientific Assessment for South Africa*. Eds RJ Scholes and KG Mennel: 257-328.

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