Animal name: Mishmi takin (*Budorcas taxicolor taxicolor*)

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We would recommend assessing any contraceptive bout with behavioural and hormone monitoring. For more information on this, please contact contraception@chesterzoo.org

Contraceptive methods	GnRH agonist (implant)	GnRH agonist (injection)	GnRH vaccine (injection)	Progestagen (implants)	Progestagen (injection)	Progestagen (oral)	Progestagen (oral)	PZP vaccine	Surgical/Permanent
Contraceptive Product:	Deslorelin acetate	Luprolide acetate	GnRH protein conjugate	Etonogestrel 68 mg	medroxyprogesterone acetate;	Altrenogest	Chlormadinone	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).	-
Commercial Name:	Suprelorin ®	Lupron ®	Improvac®	Implanon® Nexplanon®	Depo-Provera®, Depo-Progevera®	Regu-mate®	ertil®, Belara®, Prostan®, Lutei	Porcine Zona Pellucida	Castration; Vasectomy
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.	Manufactured by Bayer Schering Pharma AG. Available through human 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.	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	-
Restrictions and/or permit required by Importing Country:	The EAZA RMG recommends: always check with your local licencing authority	Data deficient	Current knowledge: widely available throughout European countries. The EAZA RMG recommends: always check with your local licencing authority	The EAZA RMG recommends: always check with your local licencing authority	The EAZA RMG recommends: always check with your local licencing authority	EGZA recommends: always checking with your local licencing authority	The EAZA RMG recommends: always checking with your local licencing authority	License required UK and France; all other Countries unknown. The EAZA RMG recommends always checking with 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 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	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	Anti-estrogenic activity. Interference with fertilization by thickening cervical mucus, interrupting gamete transport, disruption of implantation, inhibition of LH surge necessary for ovulation	Interference with fertilization by thickening cervical mucus, interrupting gamete transport, disruption of implantation, inhibition of LH surge necessary for ovulation	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.	**Castration:** Surgical procedure in which the testes are removed; **Vasectomy:** Surgical procedure in which the ductus deferens are cut, tied, cauterized, or otherwise interrupted
Insertion/Placement:	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	Injectable intramuscular or subcutaneously	Intramuscular or subcutaneous. The EAZA RMG recommends sub-cutaneous, upper inner arm for visibility (aid for later removal)	Injectable intramuscular	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).	Administered orally	Injectable Intramuscular	Surgical
Females									

Dose	Dosage depends on the body weight of the individual. 3-4 x 4.7 mg implants are recommended for a **minimum** duration of 6 months and 3-4 x 9.4 mg implants are recommended for a **minimum** duration of 12 months.	There are various formulations available lasting from 1-6 months. Dosing information is not available; extrapolation from human literature is likely the best place to start. **Please contact the EAZA RMG with specific dosage advice.** 1 mg (formulation unknown) has been successfully used in Sichuan takin.	Two injections of 400ug are given 4 weeks apart and boosters are usually administered every 6 months. Please note that the duration can vary between species and booster intervals have not been well established for this species.	1-2 implants (0.068g) are recommended for successful contraception in this species. As a guideline 1 implant/100kg.	As a guide 2.5-5mg/kg BW every 45-90 days. Doses in our database range between 2.7-5.7 mg/kg BW and were most frequently readministered every 3 months.	For contraception, 0.044mg/kg daily Regu-mate® Equine or Porcine daily: for oestrus synchronisation Regu-mate® Porcine: 5ml daily. Product should be administered orally through feed or syringe.	½ a tablet should be administered daily (~10-12 mg, although this varies depending on the product).	100 µg protein is recommended. 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. In species with longer breeding season, if the vaccine is given at a time other than prior to the breeding season the primary vaccination course should be given at day 0, day 21 and day 45; booster should be administered every 7-8 months. If a seasonal breeder with a well defined and short breeding season (2-3 months) then it is 1-2 months before the breeding season.	-
Latency to effectiveness:	3 weeks average as GnRH agonists initially stimulates the reproductive system- **please refer to the 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 stimulates the reproductive system- **please refer to Deslorelin datasheet for detailed information** - separation of the sexes OR supplemental 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).	Latency to effectiveness can be up to 6 weeks so separation of the sexes is recommended if possible.	In general inhibition of ovulation after 1 day when inserted on day 1-5 of cycle or 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 7-14 days after insertion of the implant depending on administration route (IM or SC).	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.	In mares, 95% treated with Regu-mate will be suppressed within 3 days[7] however separation of the sexes should be used for 7-14 days after contraceptive methods, if this not possible then other contraception methods should be used for this time.	Latency to effectiveness should be approximately 3 days; however it is recommended that the sexes are either separated for one week, or alternate contraception is used at this time.	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 (primary course of vaccination 2 injections 2-4 weeks apart, preferable 3 injections).	-
Oestrus cycles during contraceptive treatment:	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.	In a group of 57 mares, 80% were anoestrus after the primary vaccination and 100% after the booster vaccination, the interval from treatment to anoestrus was 2-3 weeks.[2]	Oestrus behaviour may be observed. Cycling and even ovulation can occur in adequately contracepted individuals (but is unlikely and the degree of suppression is dose dependent).	Oestrus behaviour may be observed. Cycling and even ovulation can occur in adequately contracepted individuals (but is unlikely and the degree of suppression is dose dependent).	Oestrus in Inhibited	**Data deficient.**	PZP should not suppress oestrous cycles and may extend the breeding season beyond what is considered typical, resulting in additional oestrous cycles.	-
Use during pregnancy:	**Not recommended**	**Not recommended** as may cause abortion.	**Data deficient.** Studies in elk[3] and bison[4] have demonstrated that females who were vaccinated with the GnRH vaccine GonaCon while pregnant, delivered healthy calves.	Progestagens are not recommended in pregnant animals because of the possibility of prolonged gestation leading to dystocia, stillbirth and abortion in some species, although the effect may depend on dose.	Not recommended for use in pregnant animals because of the risk of prolonged gestation, stillbirth or abortion, etc. in some species, although the effect may depend on dose.	Not recommended for use in pregnant animals because of the risk of prolonged gestation, stillbirth or abortion.	Not recommended for use in pregnant animals because of the risk of prolonged gestation, stillbirth or abortion.	Does not interrupt pregnancy or affect foetus.	-
Use during lactation:	No known contraindications once lactation has been established; however, treatment during pregnancy may impede proper mammary development.	No contraindications once lactation established; however, treatment during pregnancy may impede proper mammary development.	**Data deficient.** In dairy cattle, lactation and milk production were unaffected by vaccination with Improvac.[5]	Considered safe for nursing; Does not affect lactation, but etonogestrel is excreted in milk.	Considered safe for nursing infant.	Considered safe for nursing infant.	**Data deficient.** Considered safe for nursing infant.	No known contraindications.	-
Use in prepubertals or juveniles:	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.	Lupron® may prevent epiphyseal closure of the long bones, resulting in taller individuals.	**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 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.	**Data deficient.** The use of synthetic progestogens in pre-pubertals or juveniles has not been fully assessed. Possible long-term effects on fertility are not known.	PZP-treated prepubertal white-tailed deer and feral horses were fertile as adults, but there is little data for other species.	-
Use in seasonal breeders:	Treatment should be given more than 2 months prior to expected breeding season.	**Data deficient**. Should start at least 2 months before start of breeding season.	Unknown but if used should be done at least 6 weeks prior to the breeding season. Effective in the horse. Use before cycling starts at the onset of the breeding season.		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.	**Data deficient.** 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.	-

Duration	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.	Lupron® is available in various formulations lasting from 1 to 6 months, but because the release of hormone from the depot formulation varies by individual, actual duration of efficacy can vary considerably.	Unknown for most of species. Improvac® induces an immune response that generates short-lived antibodies in the domestic pig (antibody production starts to decline ~7-8 weeks following second injection). Suppresses oestrus for a full season in mares after the first booster.	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.	No more than one dose each day. Regu-mate® must be given daily to maintain suppression of oestrus.	No more than one dose each day. Chlormadinone must be given daily to maintain suppression of oestrus.	Species -dependant: most species 1 year	Permanent
Reversibility	Deslorelin is designed to be fully reversible, however there are currently no cases of reversibility in this species. Cases of reversibility have been demonstrated in other bovid, with time to conception ranging from 1.3 - 8.6 months after implant placement. We would advise that implants are removed to facilitate reversibility and that they should therefore be placed in locations with thinner skin e.g. the inner thigh, umbilicus, or armpit.	Lupron® is designed to be fully reversible however there are no current cases of reversal in bovidae.	It must be taken in to consideration that younger individuals will take longer to reverse in comparison to older individuals. Improvac is not designed to be reversible, but reversibility has been demonstrated in some wild animal species. We do not have any records of reversal in this species.	Implanon is designed to be fully reversible however, we do not have any records of reversal in this species.	Designed to be fully reversible but individual variation can occur. We have two records of reversal in takin, where time to conception ranges between 19 - 24 months after the final vaccination.	It should be reversible after cessation of treatment. Signs of oestrus in equids have been observed 5 days after the end of treatment but will vary depending on the individual. However there are no cases of reversal in bovids.	Chlormadinone should in theory be reversible, however this has not been researched in this species.	Species differences on reversibility. Reversibility differs between species; however the longer PZP is given the longer it takes for a female to become fertile again. 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. It is therefore suggested that an individual is on PZP for no longer than 3 years if you want the female to breed. We have one record of an Eastern bongo giving birth to live young 5 years after she began treatment.	-
Effects on Behaviour	Deslorelin is likely to supress some hormonal related behaviours.	**Data deficient**	Similar to surgical castration but short-acting (duration of antibody effect). No oestrus behaviour in mares.	**Data deficient**	Effects on behaviour have not been studied; there may be individual variation in response. Medroxyprogesterone acetate binds readily to androgen receptors and are antiestrogenic; females may experience male-like qualities (increased aggression , development of male secondary sex characteristics, etc.) Further research in the subject is necessary.	Regu-mate® can be used to alleviate temperament changes and aggression. Synthetic progestins may not suppress follicle growth and some signs of oestrus behaviour may be present.	Effects on behaviour have not been studied; there may be individual variation in response.	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 sexual physical characteristics	Similar to gonadectomy. GnRH agonists may cause the suppression of physical secondary sexual characteristics.	GnRH agonists may cause the suppression of physical secondary sexual characteristics.	Similar to surgical castration but short-acting (duration of antibody effect).		Because medroxyprogesterone acetate binds readily to androgen receptors and is antiestrogenic, females may experience male-like qualities (increased aggression, development of male secondary sex characteristics, etc.)	**Data deficient**	**Data deficient**	**Data deficient**	-
Males	**Not Recommended as GnRH agonists are seemingly not effective in male ungulates**	**Not Recommended as GnRH agonists are seemingly not effective in male ungulates**		**Not recommended**	**Not recommended**	**Not recommended**	**Not recommended**	**Not recommended**	
Dose	-	-	Two injections of 400ug are given 4 weeks apart and boosters are usually administered every 6 months, although duration can vary between species. Please note that the duration can vary between species and booster intervals have not been well established for this species.	-	-	-	-	-	-
Latency to effectiveness:	-	-	Latency to effectiveness can be up to 6 weeks so separation of the sexes is recommended if possible.	-	-	-	-	-	Depending on species and individual, perhaps as long as 2 months or more
Use in prepubertals or juveniles:	-	-	**Data deficient**	-	-	-	-	-	**Data deficient**
Use in seasonal breeders:	-	-	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.	-	-	-	-	-	-

Duration and Reversibility	-	-	Unknown for most species. Improvac® induces an immune response that generates short-lived antibodies in the domestic pig (antibody production starts to decline ~7-8 weeks following second injection). This lasts ~ 5 to 9 months in bull elephants when used for the control of musth. Improvac is designed to be fully reversible; there are currently no reversals on the database however; studies have shown reversibility in equids within a two year period.[6] It must be taken in to consideration that younger individuals will take longer to reverse in comparison to older individuals.	-	-	-	-	-	The procedure should not be used in males likely to be recommended for subsequent breeding as reversal is unlikely
Effects on Behaviour	-	-	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.	-	-	-	-	-	Vasectomy will not affect androgen-dependant behaviours
Effects on sexual physical characteristics	-	-	Similar to surgical castration but short-acting (duration of antibody effect).	-	-	-	-	-	-
General:									
Side effects	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. Some dichromatic species may change colour. The EAZA RMG recommends always reading the manufacturer's data sheet	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. Some dichromatic species may change colour. The EAZA RMG recommends always reading the manufacturer's data sheet	Occasional swelling at the vaccination site - need to inject deep intramuscular in elephants and horses. The EAZA RMG recommends always reading the manufacturer's data sheet		Possible deleterious effects on the endometrium following prolonged use. Progestins are likely to cause weight gain in all species. In the human literature, Depo-Provera® has been linked to mood changes. Because it binds readily to androgen receptors and is anti-estrogenic, females may experience masculinisation (increased aggression, development of male secondary sex characteristics, in dichromatic species, aspects of male colouration, etc.) 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.	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)	-
Warnings	Causes initial gonadal stimulation. Duration may be reduced if implant is broken. Do not cut the implant. If implant is not completely removed at the end of treatment, residual circulating levels of deslorelin may affect time to reversal. **Should not be used in conjunction with Depo-Provera.**	Causes initial gonadal stimulation	It should be handled with extreme care to avoid handler accidents. The EAZA RMG recommends always reading the manufacturer's data sheet		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, it is advised that the product be used with caution in diabetic animals and that urine glucose levels are carefully monitored during the month after dosing. 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	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.	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 takin it is recommended that all individuals on contraception be reported to the EAZA RMG

References:

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4) Miller LA, Rhyan JC, Drew M (2004) Contraception of bison by GnRH vaccine: a possible means of decreasing transmission of brucellosis in bison. J Wildl Dis 40:725–730.

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7) Card, C. (2009) Hormone therapy in the mare IN Equine Breeding Management and Artificial Insemination. Samper, JC. Saunders: St. Louis.