

## **LUPROSTIOL AND LUTALYSE<sup>R</sup> COMPARED FOR HEAT SYNCHRONIZATION**

**BY**

D.G. Landblom, J. L. Nelson and T. J. Newby

Scientists at Norden Laboratories are researching a new, and highly effective luteolytic analog of the prostaglandin F2 alpha, called Luprostiol, which has been marketed to European veterinarians for several years. To apply for marketing clearance for the new compound under the FDA's new drug clearance guidelines, Norden must conduct experiments with the product under field conditions. Dr. T. J. Newby, clinical scientist and research monitor for Norden Laboratories requested participation of the Dickinson Branch Experiment Station in a grant study comparing heat synchronization and artificial breeding with Luprostiol.

Luprostiol, a synthetic analog of the prostaglandin F2 alpha, has been formulated as an injectable solution. Information from pharmacokinetic studies with radiolabelled Luprostiol have shown that the experimental compound is rapidly eliminated from the animal in a manner similar to other prostaglandin analogs.

Dosage and safety studies have shown Luprostiol to be highly effective for estrous cycle control and abortion. Doses above the recommended level have been tolerated with only transient side effects.

The objective of this comparative study is to confirm the luteolytic, or estrus synchronization, effect of Luprostiol with a commonly used compound such as Lutalyse<sup>R</sup> when administered at recommended dosages to normal cycling females.

To complete the outlined objective, 131 cows and heifers were observed for standing heat and inseminated 12 – 14 hours after detection during a five day pre-synchronization period to insure that an adequate number of females would be in the correct stage of their estrous cycle to respond to each of the synchronization compounds.

On the sixth day all cows and heifers that had not been previously inseminated were randomly allotted to either Luprostiol or Lutalyse<sup>R</sup> treatments according to age, breed and calving interval of cows. Then, beginning at 1 pm on the sixth day the remaining cows were injected with either 2 ml of Luprostiol or 5 ml of Lutalyse. As each cow or heifer was being injected, which was considered to be time zero, a 10 ml blood sample was taken, clotted, and a serum sample extracted. Serum samples were collected at 0, 48, and 96 hours after each drug was administered and analyzed for circulating progesterone levels by NDSU reproductive physiologist, Dr. Dale Redmer.

Following the injections, the females were inseminated according to estrus 12 – 14 hours after being detected in standing heat. Heat detection was done visually with the assistance of epididectomized sterile bulls equipped with chin ball marking harnesses.

Pregnancy was determined using a sophisticated ultra sound device and by conventional rectal palpation. Twenty-six days following the average date of insemination, Dr. Pat Hemming, DVM, representing the Bion Corporation, conducted pregnancy determinations using an ultra sound device developed and marketed by Bion. To check for potential early embryonic death that could occur after the ultra sound test, the females were rectally palpated by a local veterinarian fifty-six days after the average date of insemination.

Data accumulated in this investigation have been summarized in Tables 1, 2 and 3.

Mean values for circulating progesterone were determined by radioimmunoassay and are expressed in picograms per milliliter in Table 1. Conception rate as determined by ultra sound and by rectal palpation is summarized in Table 2. Means for body condition score and the hours to standing heat following synchronization with each compound are shown in Table 3.

**Summary:**

The new drug Lutprostirol manufactured by Norden Laboratories and Lutalyse<sup>R</sup> were evaluated in a comparative investigation and were found to be potent and equally efficient luteolytic agents.

The effect of these compounds on the anestrus female was not one of the prescribed objectives. However, anestrus females existed in each treatment, but were not affected by either synchronization substance.

Circulating progesterone was measured at 0, 48 and 96 hours after the administration of each substance. Progesterone levels in females that possessed functional corpus luteums were reduced rapidly by 48 hours and were reduced to stable low levels by 96 hours. Females that demonstrated normal standing heat but did not conceive to artificial breeding are considered in some instances to have been anovulatory. Those females that never cycled during the synchronized breeding period possessed very low circulation progesterone levels throughout the 96 hour sampling period.

First service conception rates as measured by ultra sound (26 days) or rectal palpation (56 days) were similar for both compounds. The percentage of animals pregnant as determined first by ultra sound and subsequently by palpation was 66.7% for Luprostiol and 68.4% and 65.8%, respectively, for Lutalyse<sup>R</sup>.

**Table 1. Mean Values for Circulating Progesterone Measured in Picograms/ml of Serum Among Pregnant, Non-pregnant and Females that Never Cycled Following Synchronization with Either Lutalyse or Luprostiol**

	(No.)	0 Hours	48 Hours	96 Hours
<b>LUPROSTIOL:</b>				
Total animals	36			
Pregnant 1/	24	3352.3	810.9	173.4
Cycled, but open	8	1576.6	1387.5	269.8
Never cycled	4	134.4	646.9	149.9
<b>LUTALYSE:</b>				
Total animals	38			
Pregnant 1/	26	3676	387	165.1
Cycled, but open	3	2810	364.6	149.9
Never cycled	9	803.5	304.8	256.5

1/ Determined by ultra sound.

**Table 2. Estimated Conception Rate as Determined by Ultra Sound and Conventional Pregnancy Testing Procedures**

	26 Day Ultra Sound			56 Day Conventional Pregnancy Test	
	Luprostiol	Lutalyse		Luprostiol	Lutalyse
No. Head	36	38		36	38
No. Pregnant 1/	24	26		24	25
No. cycled, but open	8	3		8	4
No. that never cycled, and open	4	9		4	9
Conception rate	66.7%	68.4%		66.7%	65.7%

1/ Determined by ultra sound.

**Table 3. Body Condition Score and Time Lapse between Injections at Zero Hours and the Onset of Standing Heat**

	Luprostiol	Lutalyse
<b>Pregnant: 1/</b>		
Total hours	1666.0	1857.5
Mean hours	64.0	71.4
Mean range, hours	19 – 139	31 – 129
Body Condition Score	6.5	7.4
<b>Not pregnant, but cycled:</b>		
Total hours	556.0	165.0
Mean hours	69.5	55.0
Mean range, hours	19 – 129	44 – 57
Body Condition Score	7.4	7.6

1/ Determined by ultra sound.