

# ausrichter equine newsletter

Number 46

## 'Tying Up' – Enerseen™ Injection

### Horses & 'Tying Up'

Transient exertional rhabdomyolysis<sup>1</sup>, is described as a disease in which horses become stiff in their limbs while performing exercise, or soon afterwards. The stiffness and soreness may be so severe that the horse cannot move.

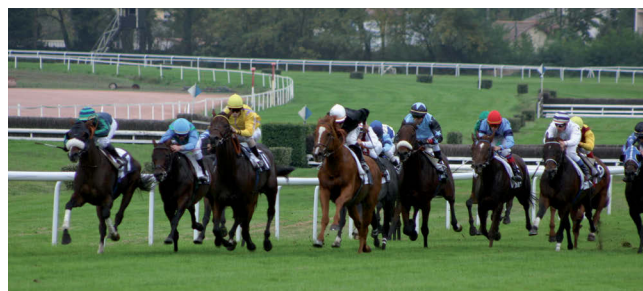
'Tying up' is generally less severe and is described as damage or injury to or of the skeletal muscles (generally back and rump required for movement). It is an insidious muscle disease of horses and racing dogs.

'Tying up' has been known in horses for many years. It is an important on-going disease of muscles. A challenge for both veterinarians and trainers of horses. It seems to occur in high performing and race winning horses with the ability to perform at a high level.

Fillies and mares seem prone to 'tying up' with a number of reports and studies indicating a higher incidence. It negatively impacts training and racing and restricts training and racing schedules.

Surveys of thoroughbreds and standardbreds report 'tying up' in horses resulted in increased days lost to training. Studies have quantified numbers of missed races and events. This results in loss of prize money when horses cannot participate in planned events.

1. Saunders comprehensive dictionary 3 ed, 2007.



### Tying Up (External Rhabdomyolysis [ER])

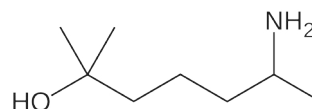
'Tying up' (exertional rhabdomyolysis [ER]) occurs in horses of any age, breed, and both sexes. Veterinarians typically see horses with adequate performance histories with issues of sporadic ER including:

- ▶ **Muscle trauma** – Horses with muscle injuries (commonly back and rump) from struggling when cast often experience 'tying up'.
- ▶ **Overexertion** – Increased exercise without adequate conditioning. Overexertion has been blamed for the high level of ER in polo ponies in the United States.
- ▶ **Exhaustion** – ER commonly occurs in endurance and race horses. Signs, include weakness, ataxia (in coordination) rapid breathing, muscle twitches, sweating and collapse. Horses often have elevated temperature and CK levels.
- ▶ **Dietary and electrolyte imbalances** – ER episodes may be related to diet. Vitamins and minerals should be appropriate for the horse. Vitamin E and Selenium can help prevent ER.

AAEP Convention 12th February 2013.

### Heptaminol – essential for the management of 'Tying up' in horses

#### Heptaminol



Heptaminol hydrochloride has a number of pharmacological effects that benefit 'Tying Up' in horses. It is very important that it is included in the treatment.

#### Heptaminol HCl

- ▶ Directs support for muscle contraction
- ▶ Increases blood circulation, for oxygenation of muscles
- ▶ Promotes blood flow to increase circulation of muscle protecting actives
- ▶ Improves blood circulation to muscles; improves healing time of injuries.



Heptaminol is a prohibited substance under the rules of racing for horses and dogs and for horses participating in events. Currently there are many essential therapeutics that have withholding times after treatment and before racing or an event including Penicillin, Dexamethasone, Clenbuterol, Phenylbutazone and Flunixin, to name a few.

Treatment of horses or dogs within 24 hours of racing is illegal; generally therapeutics administered within 24 hours are easily detected.

The administration of Enerselen Injection close to or within 72 hours of racing is of no practical therapeutic benefit. The important actives in Enerselen Injection need some time to be converted to the enzymes important for protecting the muscles from 'tying up'. This is particularly the case for Selenium (Sodium selenite) which needs to be converted to the muscle protecting Glutathione peroxidase.

## Excretion of Heptaminol HCl in animals:

The European Agency for the Evaluation of Medical Products [EMA /MRL/043/95-FINAL] reported the pharmacokinetics and excretion of Heptaminol HCl.

The various studies indicate Heptaminol HCl is quickly excreted, even at higher doses within 24 hours. There are no reports of accumulation in man or animals.

A withholding time after the last treatment and 72 hours would seem conservative.

Dogs were administered 300 mg of Heptaminol orally. 82 to 87% of the administered dose was recovered in urine within 10 hours, and elimination was total within 24 hours.

In a laboratory animal study (rats) intravenous administration of <sup>14</sup>C – Heptaminol (radio labelled) at 8 mg/kg bodyweight or oral administration at 12 mg/kg bodyweight, no evidence of accumulation of Heptaminol in tissue was seen. (Chanoine F *et al.* *Arzn. – Forchung*; 1981, 31 (9) 1430-1435).

In humans, oral administration of 2 x 150 mg tablets were rapidly and entirely absorbed. All the given dose was recovered unchanged in urine within 24 hours.

The dose of Heptaminol HCl horses and dogs receive at the label dose of Enerselen Injection is 2 mg/kg bodyweight.

The dose of Heptaminol HCl in the studies reported were:

1. Dogs received 300 mg = 20 mg/kg bodyweight
2. Laboratory animals (rats) = 8 mg/kg bodyweight
3. Laboratory animals (rats) = 12 mg/kg bodyweight
4. Human study dose received = 4 mg/kg bodyweight (assumed weight of 75 kg bodyweight of the recipients).



## Summary:

From the independent information from the laboratory studies available it can be seen even at higher doses of Heptaminol HCl orally or by injection it is excreted quickly (within 24 hours), and is reported not to accumulate in man or animal.

From this information it can be assumed that 'positive swabs' to Heptaminol HCl occurs because of its administration within 24-48 hours of racing or an event.

## Reports of the incidence of 'Tying up' in racing horses

### STANDARDBREDS

A study of Standardbreds in Sweden indicated 6.4% of horses had a history of 'tying up'. The incidence was higher in mares with a nervous temperament. The standard breeds that 'tyed up' in this study generally had faster lap times and a higher winning percentage than horses not affected by 'tying up'.

This study indicates:

- ▶ Nervous mares had a higher level of 'tying up'
- ▶ Higher incidence of 'tying up' in horses with faster lap times
- ▶ Horses with higher race winnings had a higher frequency of 'tying up'
- ▶ Trainers that routinely measured CK and AST better identified low grade 'tying up' incidence.

Pone.0011594/ Published: July 14, 2010

### THOROUGHBREDS

A survey in UK of 34 yards with 1,276 thoroughbreds in race training reported an incidence of 'tying up' of 6.7%. About half the horses were blood tested and increases in Creatine Kinase (CK) and Aspartate aminotransferase (AST) were noted. Most trainers had at least one horse 'tying up'. In the 6.7% with 'tying up' 74% of those horses were 'tying up' with an average loss of 6 days of training. Horses 'tying up' were identified as female, having a nervous, excitable temperament, or were two year olds.

This study in thoroughbred racing horses identifies:

- ▶ The incidence of 'tying up' was 6.7%. In 74% of those horses 'tying up' reoccurred
- ▶ That most stables had at least one horse 'Tying Up'
- ▶ The loss of six training days because of an episode of 'Tying Up'
- ▶ 'Tying up' occurred more frequently in nervous females and two year olds.

McGowan CM<sup>1</sup>, Fordham T, Christley RM. *Vet Rec.* 2002 Nov 23;151(21):623-6.

## How to use Enerselen™ Injection in the management and treatment during training and exercise – 'Tying up'?

Reports and surveys indicate that 'tying up' occurs in up to 10% of thoroughbred horses being prepared for racing or are racing. The levels of 'tying up' in standardbreds is slightly lower. The level in polo ponies was reported as 10%. Fillies and mares and nervous males had a higher incidence of 'tying up' and are easily identified by trainers. Comments by trainers indicate that horses with proven racing ability, or potential winners are the horses that frequently 'ty up'. The incidence of 'tying up' interrupts training and racing programs and add cost to the preparation and training of horses.

## A guide to treatment of horses with injection:

**2 Year Olds:** As horses begin exercise and training, administer Enerselen Injection @ 4 mL/100 kg bodyweight twice weekly for two weeks, then once a week or once every two weeks, depending on response. Allow 72 hours (3 days) waiting period after treatment and before racing or trialing. Administer a dose following racing/trialing to replace the active used up by strenuous exercise.

**Fillies/Mares:** Have a higher incidence of 'tying up'. Begin administering Enerselen Injection to fillies and mares when they enter the stables and begin exercise and training – twice a week for two weeks, then once a week @ 4 mL/kg bodyweight up until racing; allow 72 (3 days) waiting period after the last dose and before racing or trialing. Administer Enerselen Injection following racing or trialing.

**Nervous Horses:** Follow the same treatment schedule as for Fillies/Mares.

**Standardbreds:** Have more intense training for longer periods. A Swedish study indicated a higher level of 'tying up' in standardbreds than thoroughbreds. Faster horses and race winners had a higher incidence of 'tying up'. Enerselen Injection treatment (see table) is administered to build levels of the actives. Continue Enerselen Injection once or twice per week depending on response. Allow 72 hours waiting time after treatment and before racing.

**Jumpers, Eventers, Polo Ponies, Endurance Horses:** Enerselen Injection treatment is both for 'tying up' and minor muscle injuries. It should be the same treatment and administration schedule as for racing horses. A withholding period of 72 hours after the last treatment and before an event should be allowed.

**Travelling Horses:** It is suggested treatment with Enerselen Injection is beneficial to protect muscles during periods of travel. Particularly horses with a history of minor issues of stiffness or cramping after travelling.

**Muscle Injuries:** Muscle injuries have been reported as precursors for 'tying up'. It would be beneficial to include Enerselen Injection in the treatment of horses with diagnosed muscle injuries.

1. [www.thehorse.com/external/rhabdomyolysis-not-just-tying-up/](http://www.thehorse.com/external/rhabdomyolysis-not-just-tying-up/)

## PRODUCT INFORMATION

### Enerselen™ Injection

#### ACTIVE CONSTITUENTS:

2 mg/mL ADENOSINE TRIPHOSPHATE  
1 mg/mL URIDINE TRIPHOSPHATE  
1 mg/mL SODIUM SELENITE  
5 mg/mL HEPTAMINOL HYDROCHLORIDE  
15 mg/mL MAGNESIUM ASPARTATE  
15 mg/mL POTASSIUM ASPARTATE  
0.5 mg/mL CYANOCOBALAMIN

#### THE ACTIVE CONSTITUENTS OF ENERSELEN INJECTION ARE:

**ATP** (adenosine triphosphate), providing an immediate source of muscle energy.

**URDINE TRIPHOSPHATE** is a source of muscle energy, related to ATP.

**SELENIUM** is an essential trace element. For metabolic processes, and energy. Selenium has anti-oxidant properties,



protects muscle from damage. It directly and indirectly prevents 'tying-up' and related muscle problems.

**HEPTAMINOL HCL** increases blood flow for exercise and endurance capacity. It helps build and maintain muscles. A new study indicates HEPTAMINOL delays the onset of muscle fatigue.

**MAGNESIUM ASPARTATE** increases oxygen delivery to muscle tissue. For muscle strength and endurance, and has a role in muscle contraction.

**POTASSIUM ASPARTATE** for glucose/glycogen (i.e., energy) metabolism.

**VITAMIN B<sub>12</sub>** (cyanocobalamin) to stimulate appetite for energy metabolism.

#### INDICATIONS

An aid in the control of muscular dystrophy, and a muscular stimulant, in horses and dogs.

#### DIRECTIONS FOR USE

Inject slowly subcutaneously or intramuscularly.

**Horses:** 4 mL per 100 kg bodyweight.

**Dogs:** 1 mL per 25 kg bodyweight.

**Prevention:** One injection each week for 2-3 weeks.

**Treatment:** One Injection every 3 days for 9-12 days.

#### MEAT WITHHOLDING PERIOD

**DO NOT ADMINISTER less than 28 days before slaughter for human consumption.**

#### RACING/EVENT WITHHOLDING

**Consult racing authorities, stewards, or veterinarians for the withholding time after treatment and before racing or event.**





## FIRST AID

If poisoning occurs, contact a doctor or Poisons Information Centre, phone 131126. If skin contact occurs, remove contaminated clothing and wash skin thoroughly.

DISPOSE of container by wrapping with paper and placing in garbage.

STORE below 30°C (Room Temperature). Protect from light.

Made in Australia

APVM Approval No 41531/1199



## Use and administration of Enerselen™ Injection for 'Tying up' in horses

Horse/activity	Treatment rationale	Dose rate/frequency	Withholding period*
<b>THOROUGHBREDS</b> 2 year olds	Start treatment when horses begin training – to protect muscles. Continue administration during training and racing. Respect rules of racing and WHP.	By injection 4 mL/100 mg B.W. twice weekly for two weeks. Continue weekly administration.	72 hours after last treatment and before racing.
Fillies/mares/nervous horses	Begin administration when horses return to training and racing. Protects and reduces severity of 'tying up'. Respect rules of racing and WHP.	As above.	As above.
<b>STANDARDBREDS</b>	Start treatment when horses return to training. Continue to treat during training and racing to reduce incidence of 'tying up'. Respect rules of racing and WHP.	As above.	As above.
Dressage, Show, Polo, Endurance	Start administration when exercise/training is increased to reduce 'tying up'. Continue administration. Respect WHP after treatment.	As above. Discuss with your veterinarian.	According to the rules of the event.
Travelling horses	Treatment benefits travelling horses. Protects muscles.	By injection 4 mL/100 kg B.W. Frequency as required.	72 hours before racing or according to the rules of the event.
Horses with muscle injuries	Muscle injuries are precursors to 'tying up'. Treatment benefits injured muscles.	By injection 4 mL/100 kg B.W. Frequency as determined by severity of injury.	As above.

\***Racing/Event withholding time:** Consult racing authorities, stewards, veterinarians or event organizers for a withholding time for this product containing Heptaminol Hcl after treatment and before racing or an event.

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