GENTAMOX®

Clinical trials

Vocation of leadership.

That is what has always marked the activity of Hipra: a **veterinary pharmaceutical** company dedicated to the research, production and marketing of products for Animal Health.

Our history spans more than half a century and do currently occupy one of the top positions amongst pharmaceutical companies manufacturing **Phamacologicals & Biologicals** for the veterinary industry worldwide. It is the combination of our experience, advanced technology and fully dedicated team to developing innovative products that provides differential advantages to our customers.

This is the reason why we develop products with the most advanced components that give solutions and benefits that, up to now, have not been covered by the other products available in the industry and which take care of unmet needs in today's animal production.

This booklet contains GENTAMOX® clinical trials which confirms that GENTAMOX® is a valuable synergistic antibiotic association to treat various species on different pathologies.

GENTAMOX®

CATTLE

CATTLE

CLINICAL TRIAL 1

Objective of the test. To check for the therapeutic efficacy of GENTAMOX® in the treatment of calves affected by a diarrhoea process produced by *E. coli.*

Characteristics of the animals used in the trial

Species	Cattle
Animals	30
Breed	Asturian
Age	10-15 days
Approximate weight	40-45 kg.
Sex	Male
Production stage	Suckling
System of breeding and/or housing	Groups of 10 calves on a straw bed

Current state of the animals used in the trial. The process begins with the appearance of a yellow coloured diarrhoea, more or less fluid in 8 animals. Within 24 hrs one calf dies and 7 more have diarrhoea, the group in general is apathetic and take milk badly, 2 calves show symptoms of dehydration and all in general, have rough skin and look bad.

Diagnosis of the process and the technique used to carry it out (analysis data, antibiograms, etc...). Because of the clinical symptoms and the age of those calves a colibacillary process was suspected, which was confirmed by the cultures done from the calf which died and *E. coli* is isolated from the liver and small intestine, the antibiogram gives Strep + Neom + Gent +++ Amox. ++ Cmp. -Poly - Ty. + coli +++.

Trial data

Animals treated	20	5 ml GENTAMOX® IM, 3 consecutive days
Control animals	10	150-200 mg colymycin, 5 consecutive days

Results of the trial. 24 hrs. after starting the treatment the faeces of the treated animals begin to acquire normal consistency. After 48 hours the calves begin to take milk with interest and out of the 20 treated only 3 continue to have some diarrhoea, which disappears progressively and on the 4th day the faeces can be considered normal. 3 to 4 days after the start of the treatment the group is almost totally recovered. The positive controls progress well and with 5 days treatment the 10 calves are perfect.

Conclusions. GENTAMOX® is active against enteric processes produced by *E. coli*. The application of this product to young cattle at the recommended dosage and guidelines, totally lacks of local and/or general side effects.

CATTLE

CLINICAL TRIAL 2

Objective of the test. To see the therapeutic efficacy of GENTAMOX® compared with a similar treatment based on tylosin, trimethoprim and sulphamides in calves with a pneumonic process.

Characteristics of the animals used in the trial

Species	Cattle
Animals	110
Breed	Asturian
Age	20-30 days
Approximate weight	50-60 kg.
Sex	Male
Production stage	Suckling
System of breeding and/or housing	In groups on a straw bed

Current state of the animals used in the trial (in the case of sick animals, description of the clinical symptomatology). In general the group shows cough, slight lacrimation and various calves present abdominal respiration the majority take milk with difficulty and the general aspect is affected, the skin is rough and there is generalised apathy. 10 of most affected animals had their rectal temperature taken and in all cases it was greater than 40ºC which makes us suspect a generalised viral process(PI-3).

Diagnosis of the process and the technique used to carry it out (analysis data, antibiograms, etc...). After 24 hrs one calf dies and in the necropsy petequias in the pericardium, hepatic cardiac lobe and congested lung are observed: cultures are carried out from the lung and the PI-3 virus and *Mannheimia haemolytica* whose antibiogram is as follows, are isolated: Ty +++ Ts ++ Neo - Gen +++ Amox +++ Strep + Ery ++ Spi ++, in general very sensitive.

Trial data

Animals treated	32	5 ml GENTAMOX® IM, 3 days 400 mg of erythromycin in the milk daily for 5 days
Control animals	10	6 ml (100 mg of tylosin, 125 mg of sulphametoxazol and 25 g of trimethoprim per ml) per day for 3 consecutive days 400 mg of erythromycin in their milk for 5 days

Results of the trial. Of the 32 calves treated, 2 died 24 hours after the start of treatment, the necropsy report is similar to the first calf which died, the 30 remaining began to recuperate. After the 2nd day of treatment the cough clears up, the rectal temperature goes down and the appetite reappears. After 5 days all the calves are fine. The 10 control calves also recuperate well and in only 1 of them is it necessary to inject for 2 more days. In general the group when observed after 10 days is totally recuperated.

Laboratory tests used for observation of the results (Description of techniques and methods): The results are obtained after the clinical observation of the symptoms and the favourable evolution of the process, some of the symptoms taken as favourable evolution is the descent of rectal temperature and the disappearance of anorexia.

Conclusions. GENTAMOX® is effective for the treatment of lactating calves affected by pneumonic processes. Its application lacks local or general side effects.

CATTLE

CLINICAL TRIAL

4

Objective of the test. To test the efficacy of GENTAMOX® in a group of calves affected by a bronchopneumonic process.

Characteristics of the animals used in the trial

Species	Cattle
Animals	12
Breed	Virados (country)
Age	8-9 months
Approximate weight	150-170 kg.
Sex	Male and female
Production stage	Fattening
System of breeding and/or housing	Intensive diet, closed unit, animals tied in a collective box

Current state of the animals used in the trial (in the case of sick animals, description of the clinical symptomatology). After treatment the animals recovered perfectly and at this time none of them presented any clinical symptoms, perhaps in one calf there was a certain delay in growth but this was because the animal suffered more seriously from the process.

Trial data

Animals treated	12	15 ml GENTAMOX® IM per animal 3-4 consecutive days
Control animals	-	-

No control animals were left in the test, as all the animals were in the throws of the process.

Results of the trial. The control of the state of the animals was carried out by following the rectal temperature of the animals.

The animals had recovered their normal state after 4 days of treatment.
The cough and nasal mucus observed in the animals subsided in all of them.

Conclusions. The clinical test with GENTAMOX® was positive and no side effect whatsoever has been shown.

GENTAMOX®

SWINE

SWINE

CLINICAL TRIAL

Objective of the test. To test the efficacy of GENTAMOX® against processes of Colibacillosis after weaning in swine.

Characteristics of the animals used in the trial

Species	Swine
Animals	60
Breed	Landrace x B. Belgian
Age	21 days
Approximate weight	5-6 kg live weight

Current state of the animals used in the trial (in the case of sick animals, description of the clinical symptomatology). Three to four days after weaning in a group of 6 weaned swine a gastroenteric process appeared (yellowish green diarrhoea) which affected almost all the animals, and treatment was carried out as is specified further on.

Diagnosis of the process and the technique used to carry it out (analysis data, antibiograms, etc...). Given that the problem requires rapid treatment, laboratory confirmation of the colibacillary process was not waited for and the affected animals were treated. The isolated germ was a strain of haemolytic *E. coli*, sensitive above all to the gentamicin and trimethoprim sulphamides and in a lesser degree to amoxicillin and chloramphenicol.

Trial data

Animals treated	30	2 ml of GENTAMOX® IM, 3-5 consecutive days
Control animals	29	sulphametazine, trimethoprim and arsanilic (90 mg, 15 mg and 50 mg respectively per g. of product) at a dosage of 2 g/l of water for 7 consecutive days

Results of the trial. In the 30 animals injected with GENTAMOX® the gastroenteric process disappeared completely except in 2 of them, which had to be injected for a further 2 days, 1 of which died with strong symptoms of cachexia through intense dehydration and serious alterations of the intestinal mucous membrane. Of the 29 animals treated through drinking water, 25 of them recovered after 8 days, another 2 died on the 3rd and 4th days post-treatment and 8 days after treatment another 2 showed clear signs of cachexia, with progressive weight loss.

Conclusions. GENTAMOX® eliminates the gastroenteric colibacillary process in recently weaned swine, between the 2nd and 3rd day of treatment in the majority of them, without affecting normal development.

SWINE

CLINICAL TRIAL

Objective of the test. To test the efficacy of GENTAMOX® against a generalised process of M.M.A (Mastitis, Metritis and Agalaxia), in breeding sows.

Characteristics of the animals used in the trial

Species	Swine
Animals	25 sows
Breed	White Belgian
Age	2 - 5 years
Approximate weight	130-160 kg body weight
Sex	Female
Production stage	Lactation

Current state of the animals used in the trial (in the case of sick animals, description of the clinical symptomatology). During gestation and lactation of almost all the swine on the farm, an intermittent vaginal flow with a neonatal mortality in piglets of between 20-30% was observed. Mastitis was also detected in the first days after birth, with varying levels of intensity and approximately 40 % of recurrences.

25 sows treated with GENTAMOX®

- 2 with mastitis: 8%
- 1 with vaginal flow: 4%
- 4 recurrences: 16%

Sows not treated with GENTAMOX®

- 70% with post-partum mastitis
- 80% with vaginal flow
- 40% recurrences

Diagnosis of the process and the technique used to carry it out (analysis data, antibiograms, etc...). The vaginal flow was collected from some swine through swabs, which were sown in specific culture media, isolating most frequently, bacterial strains of *E. coli*, *Streptococcus, Staphylococcus* and sensitive *Corynebacterium* sensitive according to the antibiograms carried out, to amoxicillin and ampicillin and in a greater degree to gentamicin, trimethoprim - sulphamides and penicillin.

Trial data

Animals treated	25 sows	10 ml of GENTAMOX® IM in one application

We consider control animals those sows which had previously presented the M.M.A syndrome and had not been preventively treated.

Results of the trial. Of the 25 sows treated preventively or curatively with GENTAMOX®, two of them produced Mastitis. There were four more sows which between 18 and 22 days after the mating period came into rut and in only one of them was vaginal flow observed during lactation.

Laboratory tests used for observation of the results (Description of techniques and methods): Laboratory analyses were carried out with 7 vaginal swabs from 7 of the 25 sows treated. These were sown in specific cultures to detect possible bacterial strains.

Results of the laboratory tests. Of the 7 samples in only one of them was there intense contamination with colonies of *E. coli*, *Staphylococcus* and *Streptococcus* which coincided with one of the sows which produced mastitis, in spite of being injected preventively with GENTAMOX®. In the rest of the swabs only normal saprophyte germs of the swine' vaginal flora were observed.

Conclusions. GENTAMOX® injected preventively immediately after the birth, to sows coming from farms prone to the M.M.A syndrome produces a noticeable lessening of genital flows (metritis), post-partum mastitis and diminishes the % of recurrences.

SWINE

CLINICAL TRIAL

Objective of the test. To test the efficacy of GENTAMOX® against a pathological respiratory process in swine.

Characteristics of the animals used in the trial

Species	Swine
Animals	120
Breed	Landrace x B. Belgian
Age	4-5 months
Approximate weight	50-60 kg body weight
Sex	Male and Female
Production stage	Fattening

These swine were 2 months old and weighed approximately 18 kg when they entered the fattening unit. 4-5 days later they suffered a colibacillary diarrhoea process in more than 40% of the animals, also being observed oedemas in some swine. There was a total of 10 losses but the 120 remaining recovered perfectly.

Current state of the animals used in the trial (in the case of sick animals, description of the clinical symptomatology). When the trial began almost all the animals presented the following symptoms: temperature higher than 40.5ºC, almost generalised anorexia, deep, dry cough and dyspnea in 10% of the animals. There were, moreover, 4 animals housed in different compartments which began to show cyanosis in the ears due to the advanced state of septicaemia.

Diagnosis of the process and the technique used to carry it out (analysis data, antibiograms, etc...). Given that the pathological process required rapid treatment and no animals had yet died no necropsy was carried out before treating them. Then, 2 days after treatment when one of them died, a strain of *Actinobacillus pleuropneumoniae* was isolated from the bronchial tubes and lungs.

Trial data

Animals treated	60	6 ml of GENTAMOX® IM in the neck muscles for 3-5 consecutive days
Control animals	60	200 mg/litre spiramycin for 7 consecutive days

A product based in spiramycin is administered to these control animals at a ratio of 2 g/litre for 7 consecutive days. Each g of the said product contains 100 mg of spiramycin base.

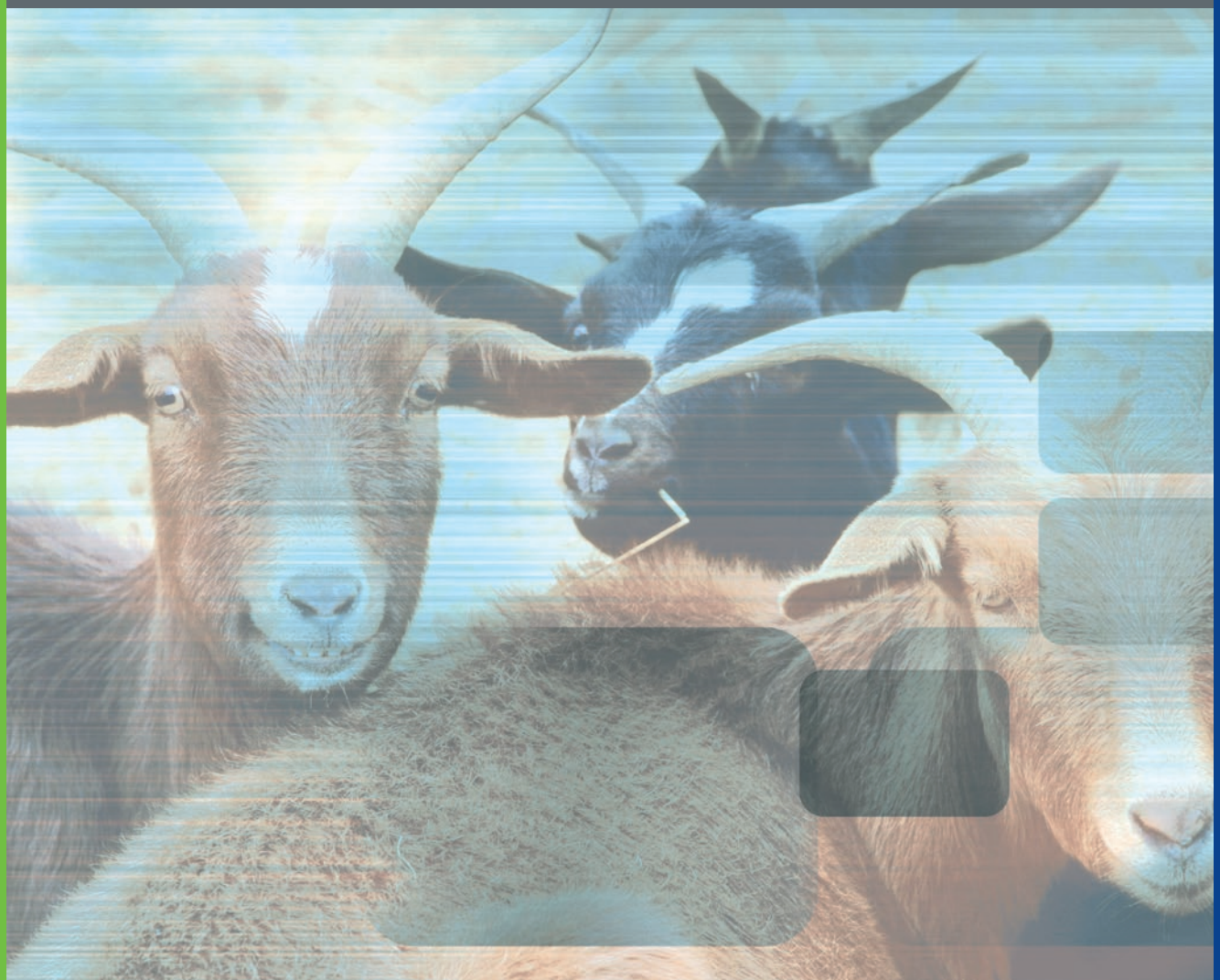
Description of the clinical observations in treated and control animals. Of the sixty animals treated with GENTAMOX® there was only one loss on the 2nd day of treatment. This was a pig which in the first inoculation showed cyanosis in the ears. One of the five swine treated for a further five days, was extremely emaciated on the 15th day after treatment due to the chronic nature of the respiratory process it was undergoing. In the animals treated through the drinking water there were 4 losses and two animals which, 15 days after treatment, showed clear signs of cachexia which as in the previous case was due to the chronic nature of the process.

Results of the laboratory tests. 15 days after the treatment of the sixty animals treated with GENTAMOX® the cough had disappeared in the 59 survivors and the 10 chosen at random had a body temperature less than 39.5ºC. They all had a normal appetite, a fine and silky coat and had a good weight, with the exception of one. Of the group of 60 swine treated through the drinking water, 56 survivors presented the same general state as the previous ones, with the exception of two, which showed signs of cachexia with progressive weight loss.

Conclusions. GENTAMOX® injected into swine which showed an acute pneumonic process due to bacterial infection (in this case, *Actinobacillus pleuropneumoniae*) produces the recovery of the majority of the swine affected during the second and fourth day of treatment.

GENTAMOX®

GOATS



GOATS

CLINICAL TRIAL

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Objective of the test. To test the therapeutic effectivity of GENTAMOX® in an enteric process in goats.

Characteristics of the animals used in the trial

Species	Goats
Animals	15
Breed	Granadina
Age	15 - 20 days
Approximate weight	5 - 8 kg.
Sex	Male and females
Production stage	Lactation
System of rearing and/or housing	Semiextensive grazing

Clinical record of the animals used in the trial. 15 young goats (between 15 - 20 days) started to show a liquid diarrhoea with milk clots, they refused taking mother's milk and their attitude was too quite, sad and apathetic. All of them had fever (between 39 and 41 ºC) and the second-third day the diarrhoea started to have blood in some cases. One of the animals suddenly died.

Protocol of the trial

Animals treated	10	1 ml of GENTAMOX® per animal and day by IM route during 3 days
Control animals	15	Gentamicin-Trimethoprim Sulfamide (COLIPRA-JET) 2.4 ml/day/animal during 5 days

Results of the trial. The treated group started to improve from the 3rd day of treatment, but one of them needed to be injected one more day. The control group started to improve from the 5th day. After one weeks the whole group can be considered recovered.

Conclusions. Bearing in mind the results, we can conclude that GENTAMOX® is effective in enteric processes caused by *E. coli*.

GOATS

CLINICAL TRIAL

11

Objective of the test. To test the therapeutic effective of GENTAMOX® in a generalised case of Salmonellosis in goats.

Characteristics of the animals used in the trial

Species	Goats
Animals	75
Breed	Nubia, Granadina, and NxG
Age	Between 10 weeks and 4 years
Approximate weight	30 - 50 kg.
Sex	Males and females
Production stage	From lactation to reproduction
System of rearing and/or housing	Semiextensive grazing

Clinical record of the animals used in the trial. The first affected were the younger animals which showed a several mucous, thin, malodorous; admixture of blood, grey to dark grey and in some cases off-white mucous flakes (Fibrin) diarrhoea. 3 days later some of the animals showed also this kind of diarrhoea. In one week, the diarrhoea affects 60 % of the animals (45). Three young affected animals died in two days. They had high temperature (40.5 ºC) and severe dehydration. In general, all the animals had high fever and were anorectic, apathetic and some of them were very dehydrated.

Protocol of the trial

Animals treated	62	2 to 10 ml/day/ animal GENTAMOX® by IM route 3-5 days Sulphonamide by oral route during 5 to 6 days
Control animals	10	Sulphonamide by oral route during 5 to 6 days

Results of the trial. In the treated group, about 80 % (50) of the animals started to improve from the third day. 15 of them were treated for 2 more days and in 10 days the whole group were really recovered. Only 3 of them (the youngest) were still anorectic and apathetic and they still had diarrhoea. They were slaughtered.
The 10 control animals started to improve from the 7th day and in 12 days, 8 of them were nearly recovered and two of them needed to be treated for 2 more days but no results were obtained and they were slaughtered.

Conclusions. Having in account the results, we conclude that GENTAMOX® is effective in the treatment of Salmonellosis in goats.

GENTAMOX®

SHEEP

GENTAMOX®

12

SHEEP

CLINICAL TRIAL

Objective of the test. To test the therapeutical effectivity of GENTAMOX® in a generalised process of Colibacillosis in lambs.

Characteristics of the animals used in the trial

Species	Sheep
Animals	50
Breed	Aragonesa
Age	1 -3 weeks
Approximate weight	5 - 10 kg.
Sex	Males and females
Production stage	Lactation

Clinical record of the animals used in the trial. In a farm with 250 sheep, 50 lambs were born. From the 5th day, about 25 started to be apathetic. Temperature was taken to 15 animals at random and the values oscillated between 40 - 41 ºC. The affected animals were depressed and prostrated and 1 day after, a painful diarrhoea appeared which became more and more fluid and white to greasy colour. One animal died in the first 24 hours after the beginning of the process.

Protocol of the trial

Animals treated	50	1 ml of GENTAMOX® /animal/day IM route during 3 days
Control animals	4	Gentamicin-Sulphamides-Trimethoprim association by oral route, during 4 days

Bacteriological sows were carried out and *E. coli* was isolated which in the antibiograms showed sensibility to: Gentamicin, Amoxicillin, Colistin and Enrofloxacin.

Results of the trial. The 20 affected animals treated with GENTAMOX® started to improve from the 3rd day. The temperature decreased from the 3rd day and was normal up to the 5th day. They started to show appetite and the diarrhoea decreased from the 4th day and disappeared up to 5th day.
The 4 control animals followed a similar processes, being recovered up to the 6th day.

Conclusions. Bearing in mind the results, we can conclude that GENTAMOX® is effective in enteric processes caused by E. coli.

GENTAMOX®

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SHEEP

CLINICAL TRIAL

Objective of the test. To test the therapeutical effectivity of GENTAMOX® in a generalised case of dysentery in lambs.

Characteristics of the animals used in the trial:

Species	Sheep
Animals	20
Breed	Ripollesa
Age	2 - 3 weeks
Approximate weight	10 - 15 kg.
Sex	Males and females
Production stage	Lactation

Clinical record of the animals used in the trial. This is a farm where 30 lambs had born and 15 to 20 days later some animals started to show clear digestive symptoms with swollen and painful abdomen (gas formation) and a severe, liquid, painful, dark malodorous and with blood diarrhoea. They are quite depressed and apathetic.

Protocol of the trial

Animals treated	30	1.5 ml of GENTAMOX®/day/ animal IM route during 3 days
Control animals	-	-

By intramuscular route 1.5 ml of GENTAMOX®/ day/animal during 3 days were administered.

Results of the trial. After 3 days only 10 of the 30 affected lambs seemed to be better, so we decided to go on with the treatment for 2 more days. After this period of time only 5 animals needed to be injected once more. The rest of the group stopped suffering from diarrhoea and started looking better. After 10 days the whole group was recovered except 2 lambs which were slaughtered due to the persistent diarrhoea.

Conclusions. Bearing in mind the results, we can conclude that GENTAMOX® is effective in dysentery processes.

GENTAMOX®

EQUINE

EQUINE

CLINICAL TRIAL

15

Objective of the test. To test the therapeutic effectivity of GENTAMOX® in one case of Foal pneumonia.

Characteristics of the animals used in the trial:

Species	Equine
Animals	1
Breed	Arabian
Age	4 months
Approximate weight	120 kg
Sex	Female
Production stage	Growing
System of rearing and/or housing	With the mother

Clinical record of the animals used in the trial. One month after birth the foal started to be depressed and one week later showed the following symptoms: increase of respiratory rate, depressed attitude, anorexia, nasal discharge and cough, arthritis and fever.

Protocol of the trial

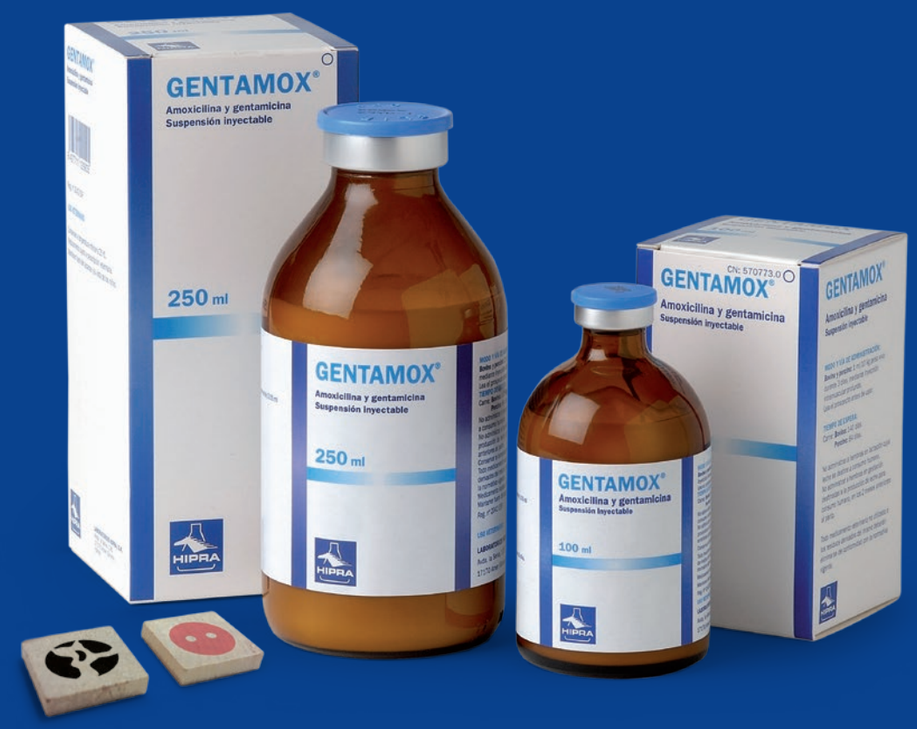
Animals treated	1	15 ml/day GENTAMOX® were administered during 4 days
Control animals	-	-

Techniques and methods used for diagnosis:

- Radiography: accumulation of exudate in the lungs was observed.
- Transtracheal aspiration: *Actinobacillus equili* were isolated.
- Blood sample: mild lymphopenia, moderate neutrophilic leukocytosis (15.000 W.B.C.).

Results of the trial. The animal started to improve from the 3rd day and it was clearly better after the 5th day. After one week we could consider that it was completely recovered.

Conclusions. Bearing in mind the results, we can consider that GENTAMOX® is effective in the treatment of Foal pneumonia.



GENTAMOX® Amoxicillin and gentamicin, in injectable suspension. **Composition per ml:** Amoxicillin trihydrate 150 mg; Gentamicin (as sulphate) 40 mg; Oil excipient q.s. **Indications:** Swine: Pneumonia, Colibacillosis, Metritis, Diarrhoea and Mastitis. Sheep: Pneumonia, Diarrhoea, Pasteurellosis and Colibacillosis. Cattle: Pneumonia, Diarrhoea, Mastitis, Metritis and Cutaneous abscesses. Horse: Pneumonia, Diarrhoea, Genito-urinary infections, Strangles, abscesses and Foot infections. **Administration route:** Deep intramuscular. When large volumes are administered (e.g. cattle and horses) it is advisable to divide the product between two inoculation points, to favour absorption. **Dosage:** Generally: 1 ml/ 10 kg b.w./ day, for 3 days. Swine and Sheep: 5 to 10 ml/adult animal/day; and 1 to 5 ml/young animal/day. Cattle: 30 to 40 ml/cow/day and 10 to 15 ml/calf/day. Horses: 30 to 50 ml/adult horse/day and 5 to 15 ml/foal/day. **Overdose:** In the case of an intoxication due to an overdose, discontinue treatment and administer a symptomatic therapy. To avoid this type of problem, do not administer more than 3 ml/10 kg b.w. **Withdrawal period**: Meat: 30 days. Milk: 2 days (4 milkings). **Packaging:** 100 ml bottle, pack with 12 bottles of 100 ml. **Reg nº:** 2.042 ESP. Under veterinary prescription. FOR VETERINARY USE ONLY.

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