ΠΑΡΑΡΤΗΜΑ 1: ΠΕΡΙΛΗΨΗ ΤΩΝ ΧΑΡΑΚΤΗΡΙΣΤΙΚΩΝ ΤΟΥ ΠΡΟΪΟΝΤΟΣ

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

COGLAVAX, suspension for injection for sheep

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition of one dose vaccine (2 ml):
Toxoids of Cl perfringens *α, β* and *ε* and *Cl septicum*, *Cl novyi B, Cl tetani* and antigen of *Cl chauvoei* in sufficient quantities to induce the following levels of antitoxin or level of protection in the serum of control animals:

Active substances:

Alpha toxoid of *Clostridium perfringens* Type A	min. 2.0IU/ml
Beta toxoid of *Clostridium pergringens* Type C	min.10.0IU/ml
Epsilon toxoid of *Clostridium pergringens* Type D	min. 5.0IU/ml
Toxoid of *Clostridium septicum*	min.2.5IU/ml
Alpha Toxoid of *Clostridium novyi* Type B	min. 3.5IU/ml
Toxoid of *Clostridium tetani*	min. 2.5IU/ml
Anaculture of *clostridium chauvoei*	min. 90% protection

Non active substances:

Alhydrogel (3%$Al(OH)_3$ in buffer solution) expressed in Al^{3+}	0.6-0.8%
Free Formaldehyde (for inactivating)……	.≤0.05% w/v
Sodium chloride isotonic solution	0.85% q.s. to 2 ml

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Injectable suspension.

4. CLINICAL PARTICULARS

4.1 Target species
Sheep.

4.2 Indications for use, specifying the target species
Active immunisation against enterotoxaemia due to *Cl perfringens A, B, C* and *D* and clostridial infections due to *Cl novyi*, *septicum*, *chauvoei* and *tetani.*
As primary or unique agents, these pathogens or their toxins cause the following diseases:

Active ingredient	**Diseases**
Clostridium perfringens Type A	Enterial diseases caused by *Cl perfringens A*

Clostridium perfringens Type B	Lamb dysentery (taking into account the cross-protectiveness of toxoids of *Cl perfringens C and D*)
Clostridium perfringens Type C	Infectious Enterotoxaemia in sheep (Struck)
Clostridium perfringens Type D	Infectious Enterotoxaemia in sheep (Pulpy kidney disease)
Clostridium septicum	Bradsot or malignant oedema of abomasums
Clostridium novyi Type B	Necrotic hepatitis
Clostridium tetani	Tetanus
Clostridium chauvoei	Blackleg

4.3 Contraindications
None.

4.4 Special warnings for each target species
None.

4.5 Special precautions for use
Special precautions for use in animals
-Shake well before use.
-Respect usual aseptic conditions.
-Administer only to healthy animals.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
In case of accidental self-injection, consult a doctor immediately and show him the referring “Directions for use”.

4.6 Adverse reactions (frequency and seriousness)
A mild local reaction at the injection site is expected. According to the safety studies in target species, the swelling appears around in 3 to 5 days after the injection, reaches a maximum size around by the 7th day (19.2±3.78mm). The change is not accompanied by pain, it is significantly during the 21 days (by the 21st day 9.5±3.14mm).

4.7 Use during pregnancy, lactation or lay
According to the safety studies carried out in pregnant ewes during the second half of pregnancy, the vaccine has no effect on pregnancy and lambing performances.

4.8 Interaction with other medicinal products and other forms of interaction

Due to the lack of information on safety and efficacy as being used with other vaccines, it is not recommended to mix or administer it with other vaccines at the same time.

4.9 Amounts to be administered and administration route

One dose of vaccine: 2ml/animal.
Subcutaneous administration.
The vaccination program is based on the results obtained during laboratory and field trials. The program of vaccination is designed to protect the different ages and categories of sheep:

Pregnant ewes:
Vaccination: twice 2 ml with 4 week interval, the second vaccine dose is to be administered 2 to 5 weeks before expected lambing date.
Re-vaccination: booster vaccination should be programmed 2 to 4 weeks before the risk period or 2 to 5 weeks before the expected date of lambing or yearly.

Lambs from vaccinated ewes:
Vaccination: twice 2 ml at 8 and 12 weeks of age.
Re-vaccination: booster vaccination should be programmed 2 to 4 weeks before the risk period or yearly.

Lambs from non-vaccinated ewes:
Vaccination: twice 2 ml at 2 and 6 weeks of age.
Re-vaccination: booster vaccination should be programmed 2 to 4 weeks before the risk period or yearly.

4.10Overdose (symptoms, emergency procedures, antidotes), if necessary

On the basis of the studies performed in the sensitive categories (pregnant ewes, 2 week old lambs) mild local reaction can appear at the injection site by administering the vaccine in multi doses. The swelling appear in 2-3 days after injection and reaches the peak around by the 8th day (28.9±2.1mm). The change is not accompanied by pain and during 28 days it is significantly decreasing (by the 28th day it decreases by 14±1.3mm).

4.11 Withdrawal period

Nil.

5. IMMUNOLOGICAL PROPERTIES

ATCvet code: QI04AB01
Pharmacotherapeutic group: inactivated clostridial vaccine for sheep

Main immunological properties demonstrated during the efficacy trials
Ewes
Protection of the ewes.

Primo-vaccination: tests have shown that after two administrations of the vaccine at 4 weeks interval when the second one is administered 2 to 5 weeks before expected lambing date, toxin specific neutralising antibodies reach a peak above protective levels 2 weeks after the last injection.
These antibodies are against:
Toxoids produced from *Alpha, Beta, Epsilon toxins* induced by *Clostridium perfringens* A, C and D.
Toxoids of *Clostridium septicum*, *novyi* and *tetani*.
(In therapeutic term the Alpha, Beta, Epsilon toxins expressed by *Clostridium perfringens* A, B, C and D, furthermore the toxins of *Clostridium septicum*, *novyi* and *tetani*).
Protection of their lambs (passive immunisation): antibodies against Beta and Epsilon toxins expressed by *Clostridium perfringens* C and D (In therapeutic term the Beta and Epsilon toxins expressed by *Clostridium perfringens* B, C and D) are detected in the colostrums of the vaccinated ewes.
Lambs receiving colostrums within 12 hours after birth will have detectable antibodies against the same toxins.
Booster vaccination: is recommended before lambing or the risk period but latest in 1 year after primo-vaccination.

Lambs born from vaccinated ewes
Primo-vaccination: tests have shown that after two administrations of the vaccine at 8 and 12 weeks of age, toxin specific neutralising antibodies reach at peak 2 weeks after the last injection.
These antibodies are against:
Toxoids produced from Alpha, Beta, Epsilon toxins induced by *Clostridium perfringens* A, C and D.
Toxoids of *Clostridium septicum, novyi* and *tetani.*
(In therapeutic term the Alpha, Beta and Epsilon toxins expressed by the Clostridium perfringens A, B, C and D and the toxoids of Clostridium septicum, novyi and tetani)
Booster vaccination: should be programmed depending on the risk period. Re-vaccination should be carried out not later than 1 year after primo-vaccination.

Lambs from non-vaccinated ewes
Primo-vaccination: tests have shown that two administrations of the vaccine at 2 and 6 weeks of age, specific neutralising antibodies reach at peak 2 weeks after the last injection.
These antibodies are against:
Toxoids produced from Alpha, Beta, Epsilon toxins induced by *Clostridium perfringens* A, C and D.
Toxoids of *Clostridium septicum*, *novyi* and *tetani.*
(In therapeutic term the Alpha, Beta and Epsilon toxins expressed by the Clostridium perfringens A, B, C and D and the toxoids of *Clostridium septicum*, *novyi* and *tetani)*

Re-vaccination: tests have shown that 2 weeks after booster vaccination the maximum level of antibodies against the above components were reached.
Booster vaccination: should be programmed depending on the risk period. Re-vaccination should be carried out not later than 1 year after primo-vaccination.

In laboratory species
Guinea pigs vaccinated twice at 4 week interval with 1 dose are protected at the level of 90% against a Clostridium chauvoei challenge carried out 2 weeks after the last injection of vaccine.

Consequences
Diseases caused by *C. perfringens* A, B, C and D, *C novyi, septicum* and *tetani.*
The action of neutralising antibodies is known to be determinant in the protection of sheep against enterotoxaemia due to C. perfringens A, B, C and D and clostridial infections due to *C. novyi*, *septicum* and *tetani.*

Challenge tests were not carried out, either because there are no standardised models (enterotoxaemia are multi-factorial disease) or because this is too cruel (Clostridium tetani component – animal welfare reasons). But, this is not detrimental to the demonstration of efficacy as the protective levels of antibodies in sheep are known for all these components.

Clostridium chauvoei component: challenge tests were not carried out, either on the target species, for the same reasons: *Clostridium chauvoei* – animal welfare. Furthermore, there is no technique allowing to measure the specific immune response in the target species.
However, this is not detrimental to the demonstration of efficacy for the following reasons:
-The challenge results on laboratory animals is the best reliable practice to ensure adequate level of potency for the vaccine.
-Published studies have shown that vaccines passing the requirements on laboratory animals are efficient against Blackleg disease in the target species.

Vaccination should also be carried out taking into account with great care the risk period or lambing date. If appropriate vaccination programme is applied, the high level of antibodies can be present in the animals during the risk period or at time of lambing.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Alhydrogel
Formaldehyde
Sodium chloride

6.2 Incompatibilities
Unknown.

6.3 Shelf life
18 months for the commercial packed veterinary medicinal product.
After opening the vial, use it up immediately.

6.4. Special precautions for storage
The product must be stored between 2º C and 8º C, protected from light.
Keep it away from children.

6.5 Nature and composition of immediate packaging
100 ml (50 doses) in low density polyethylene lense-type container closed with bromobutyl stopper and aluminium cap, in carton.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products
Any unused product or waste materials have to be handled according to the national rules concerning medicinal waste products.

7. MARKETING AUTHORISATION HOLDER
CEVA SANTE ANIMALE
10, avenue de la Ballastiere
33500 Libourne
France

8. MARKETING AUTHORISATION NUMBER(S)
19045

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Renewal: 19/4/2013

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