1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Avishield IBD Plus, lyophilisate for use in drinking water, for chickens

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose contains
Active substance:
Attenuated live Infectious Bursal Disease virus,
Intermediate plus strain G6 $10^{1.9}$ - $10^{3.2}$ EID_{50}*

*EID_{50} = 50% embryo infective dose

Excipients:

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Lyophilisate for use in drinking water.
Cream to red-brown coloured lyophilisate.

4. CLINICAL PARTICULARS

4.1 Target species

Chickens (broilers, future layers and breeders).

4.2 Indications for use, specifying the target species

For active immunisation of chickens (broilers, future layers and breeders) with maternally derived antibodies (break-through titre: ≤500 IDEXX ELISA units) to reduce clinical disease and bursal lesions due to infection caused by Avian Infectious Bursal Disease (IBD) viruses.
Chickens can be vaccinated from 10 days of age.

Onset of immunity: 2 weeks after vaccination
Duration of immunity: 5 weeks after vaccination

4.3 Contraindications

None.

4.4 Special warnings for each target species

See section 4.9.
Vaccinate healthy animals only.

4.5 Special precautions for use

Special precautions for use in animals

The vaccine strain can spread to susceptible, unvaccinated chickens following vaccination for at least 5 days. The spread does not induce clinical signs.

It is possible that the vaccine virus spreads to non-target susceptible species.
Care should be taken to ensure that the vaccine virus does not spread to unvaccinated birds. Therefore, all birds in a flock should be vaccinated at the same time to reduce the risk of bird to bird transmission. Vaccinated birds should not be mixed with unvaccinated birds. Hygiene measures should be taken to prevent spread to other flocks. Vaccination of all chickens on the premises is recommended. Housing needs to be disinfected prior to restocking.

Given that this vaccine is an intermediate plus strain of IBDV, this vaccine should only be used after it has been determined that there is an epidemiological need.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

Wash and disinfect hands and equipment after vaccination.

4.6 Adverse reactions (frequency and seriousness)

In laboratory studies after administration of a 10-fold overdose significant lymphocyte depletion in the bursa of Fabricius (in 26-50% of the follicles) was observed very commonly 7 days after vaccine take. Lymphocyte repopulation is observed from 21 days post vaccination onwards. At 28 days post vaccination there is still some depletion remaining (1-25 % of follicles). Complete repopulation of the bursae by lymphocytes has taken place by 35 days after vaccination.
The vaccine-related lymphocyte depletion was not associated with immunosuppression.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Do not use in birds in lay and within 4 weeks before the onset of the laying period.

4.8 Interaction with other medicinal products and other forms of interaction

No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product. A decision to use this vaccine before or after any other veterinary medicinal product therefore needs to be made on a case by case basis.

4.9 Amounts to be administered and administration route

One dose of vaccine should be administered to each chicken by drinking water route from 10 days of age depending on MDA level.

The optimal vaccination date is influenced by a number of factors, such as status of maternally derived antibodies, type of bird, infection pressure, housing and management conditions.
Maternally derived antibodies (MDA) can interfere with the immunity induced by live IBD vaccines, so the optimum age for vaccination depends on both the level of residual MDA against IBD in the

flock and ability of the vaccine strain of avian IBD virus to induce the required level of immunity in the presence of MDA. To predict the age when the MDA titre has sufficiently decreased to allow effective vaccination (break-through titre), testing of serum samples of at least 18 chicks by serology and use of the Deventer Formula is advised. When high titres are expected, later sampling (i.e. on day 7) will give a more reliable estimation of time of vaccination than sampling on day 0. A break-through titre of 500 (IDEXX standard ELISA) should be used. If other ELISA kits are used, obtained titre values need to be corrected to correspond to IDEXX standard ELISA kit.

The Deventer formula is as follows:
Vaccination age = { (log2 titre bird% - log2 breakthrough) x t _ } + age at sampling + correction 0-4

In which
Bird% = percentage of the flock that can be efficaciously vaccinated (having MDA titres below break-through titre)
Log2 titre bird % = ELISA titre to be used is the highest ELISA titre in certain percentage of all serums taken on sampling day, after their antibody titres are ranked from the lowest to the highest. This percentage of samples corresponds to the percentage of flock that can be efficaciously vaccinated (having MDA titres below break-through titre)
breakthrough = breakthrough (ELISA) titre of the vaccine to be used
t _ = half-life time (ELISA) of the antibodies in the type of chickens being sampled Age sampling = age of the birds at sampling
Correction 0-4 = extra days when the sampling was done at 0 to 4 days of age.

For examples and more information about the use of the Deventer Formula please refer to *de Wit 2001: Gumboro disease: Estimation of optional time of vaccination by the Deventer formula, or contact the marketing authorisation holder*.

In drinking water use

- Suspend the vaccine in a small amount of cool and clean water without traces of chlorine, other disinfectants or impurities, in a number of doses corresponding to the number of birds to be vaccinated. Where the number of birds is between the standard dosages, the next higher dosage should be used.
- Vaccine should be suspended immediately before use.
- Measure the correct volume of water for the number of birds to be vaccinated. The volume of water for dilution depends on the age of the birds, breed, housing conditions and weather conditions.
- The resuspended vaccine should be diluted in the amount of water which will be consumed within 1.5 to 2.0 hours (taking into account the different types of drinking systems for poultry).
- In order to determine the quantity of water in which the vaccine will be diluted, measure the volume of water consumed within a two hours period one day before vaccination.
- As an orientation guide for younger chickens (until 3rd week of life), apply the reconstituted vaccine to cold and fresh water at the rate of 1000 doses of vaccine to 1 litre of water per day of age for 1000 chickens, e.g. 10 litres would be needed for 1000, 10 days old chickens.
- In order to make the birds thirsty, withdraw the supply of drinking water up to 2 hours prior to immunisation (birds' drinking behaviour varies, depending on the air temperature, type of birds, breed, management, weather conditions).
- The drinking system should be clean, without traces of chlorine, other disinfectants or impurities.
- If needed, turn the lights down low when the water is turned off. After the vaccine is in the drinking system, increase light intensity again. Increased light intensity will stimulate the birds to look for food and water.
- Always make sure that there is food available when vaccinating. Birds will not drink if they have no food to eat.

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

After the administration of a 10-fold overdose, no adverse reactions other than those described in section 4.6 were observed.

4.11 Withdrawal period(s)

Zero days.

5. IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: avian infectious bursal disease virus (gumboro disease).
ATCvet code: QI01AD09.

To stimulate active immunity against Infectious Bursal Disease virus in chickens.

The vaccine strain is an intermediate plus strain with an average bursal lesion score of 0.4 at 28 days after administration of 10-times the maximum dose.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Povidone K-25
Monosodium glutamate
Bacto peptone
Potassium dihydrogen phosphate
Potassium hydroxide

6.2 Major incompatibilities

Do not mix with any other veterinary medicinal product.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after reconstitution according to directions: 3 hours.

6.4. Special precautions for storage

Store in a refrigerator (2°C–8°C).
Protect from light.
Do not freeze.

6.5 Nature and composition of immediate packaging

The vaccine is filled into 4 ml (1000 doses) or 10 ml (2500 or 5000 doses) colourless glass vials (type I), which are closed with bromobutyl rubber stoppers and sealed with aluminium caps.
Cardboard box with 10 vials of 1,000 doses of vaccine.
Cardboard box with 10 vials of 2,500 doses of vaccine.

Cardboard box with 10 vials of 5,000 doses of vaccine.
Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Genera Inc.
Svetonedeljska cesta 2, Kalinovica
10436 Rakov Potok
Croatia
Tel: +385 1 33 88 888
Fax: +385 1 33 88 650
E-mail: info.hr@dechra.com

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

{carton box with 10 glass vials}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Avishield IBD Plus, lyophilisate for use in drinking water, for chickens

2. STATEMENT OF ACTIVE SUBSTANCES

Each dose contains:
Attenuated live Infectious Bursal Disease virus, intermediate plus strain G6 $10^{1.9}$ - $10^{3.2}$ EID_{50}

3. PHARMACEUTICAL FORM

Lyophilisate for use in drinking water

4. PACKAGE SIZE

10 x 1000 doses
10 x 2500 doses
10 x 5000 doses

5. TARGET SPECIES

Chickens (broilers, future layers and breeders).

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

In drinking water use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Withdrawal period: zero days

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Once reconstituted use within 3 hours.

11. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Protect from light.
Do not freeze.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Dispose of waste material in accordance with local requirements.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

GENERA Inc.
Svetonedeljska cesta 2, Kalinovica,
10436 Rakov Potok
Croatia

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

{Glass vials with 1000, 2500 or 5000 doses}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Avishield IBD Plus, lyophilisate for use in drinking water, for chickens

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Each dose contains:
Attenuated live Infectious Bursal Disease virus, intermediate plus strain G6 $10^{1.9}$ - $10^{3.2}$ EID_{50}

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

1000 doses
2500 doses
5000 doses

4. ROUTE(S) OF ADMINISTRATION

In drinking water use.

5. WITHDRAWAL PERIOD(S)

Withdrawal period: zero days

6. BATCH NUMBER

Lot {number}

7. EXPIRY DATE

EXP {month/year}
Once reconstituted use within 3 hours.

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Avishield IBD Plus, lyophilisate for use in drinking water, for chickens

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder and manufacturer responsible for batch release:
GENERA Inc.
Svetonedeljska cesta 2, Kalinovica,
10436 Rakov Potok
Croatia

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Avishield IBD Plus, lyophilisate for use in drinking water, for chickens

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Each dose contains:

Active substance:
Attenuated live Infectious Bursal Disease virus,
Intermediate plus strain G6 $10^{1.9}$ - $10^{3.2}$ EID_{50}*

*EID_{50} = 50% embryo infective dose

Cream to red-brown coloured lyophilisate.

4. INDICATION(S)

For active immunisation of chickens (broilers, future layers and breeders) with maternally derived antibodies (break-through titre: ≤500 IDEXX ELISA units) to reduce clinical disease and bursal lesions due to infection caused by Avian Infectious Bursal Disease (IBD) viruses.
Chickens can be vaccinated from 10 days of age.

Onset of immunity: 2 weeks after vaccination
Duration of immunity: 5 weeks after vaccination

5. CONTRAINDICATIONS

None.

6. ADVERSE REACTIONS

In laboratory studies after administration of a 10-fold overdose significant lymphocyte depletion in the bursa of Fabricius (in 26-50% of the follicles) was observed very commonly 7 days after vaccine take. Lymphocyte repopulation is observed from 21 days post vaccination onwards. At 28 days post vaccination there is still some depletion remaining (1-25 % of follicles). Complete repopulation of the bursae by lymphocytes has taken place by 35 days after vaccination.

The vaccine-related lymphocyte depletion was not associated with immunosuppression.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon. Alternatively you can report via your national reporting system {national system details}.

7. TARGET SPECIES

Chickens (broilers, future layers and breeders).

8. DOSAGE FOR EACH SPECIES, ROUTE AND METHOD OF ADMINISTRATION

One dose of vaccine should be administered to each chicken by drinking water route from 10 days of age depending on MDA level.

The optimal vaccination date is influenced by a number of factors, such as status of maternally derived antibodies, type of bird, infection pressure, housing and management conditions.
Maternally derived antibodies (MDA) can interfere with the immunity induced by live IBD vaccines, so the optimum age for vaccination depends on both the level of residual MDA against IBD in the flock and ability of the vaccine strain of avian IBD virus to induce the required level of immunity in the presence of MDA. To predict the age when the MDA titre has sufficiently decreased to allow effective vaccination (break-through titre), testing of serum samples of at least 18 chicks by serology and use of the Deventer Formula is advised. When high titres are expected, later sampling (i.e. on day 7) will give a more reliable estimation of time of vaccination than sampling on day 0. A break-through titre of 500 (IDEXX standard ELISA) should be used. If other ELISA kits are used, obtained titre values need to be corrected to correspond to IDEXX standard ELISA kit.
The Deventer formula is as follows:
Vaccination age = { (log2 titre bird% - log2 breakthrough) x t _ } + age at sampling + correction 0-4

In which
Bird% = percentage of the flock that can be efficaciously vaccinated (having MDA titres below break-through titre)
Log2 titre bird % = ELISA titre to be used is the highest ELISA titre in certain percentage of all serums taken on sampling day, after their antibody titres are ranked from the lowest to the highest. This percentage of samples corresponds to the percentage of flock that can be efficaciously vaccinated (having MDA titres below break-through titre)Break-through = break-through (ELISA) titre of the vaccine to be used
t _ = half-life time (ELISA) of the antibodies in the type of chickens being sampled
Age sampling = age of the birds at sampling
Correction 0-4 = extra days when the sampling was done at 0 to 4 days of age.

For examples and more information about the use of the Deventer Formula please refer to *de Wit 2001: Gumboro disease: Estimation of optional time of vaccination by the Deventer formula, or contact the marketing authorisation holder*.

9. ADVICE ON CORRECT ADMINISTRATION

In drinking water use

- Suspend the vaccine in a small amount of cool and clean water without traces of chlorine, other disinfectants or impurities, in a number of doses corresponding to the number of birds to be vaccinated. Where the number of birds is between the standard dosages, the next higher dosage should be used.
- Vaccine should be suspended immediately before use.
- Measure the correct volume of water for the number of birds to be vaccinated. The volume of water for dilution depends on the age of the birds, breed, housing conditions and weather conditions.
- The resuspended vaccine should be diluted in the amount of water which will be consumed within 1.5 to 2.0 hours (taking into account the different types of drinking systems for poultry).
- In order to determine the quantity of water in which the vaccine will be diluted, measure the volume of water consumed within a two hours period one day before vaccination.
- As an orientation guide for younger chickens (until 3rd week of life), apply the reconstituted vaccine to cold and fresh water at the rate of 1000 doses of vaccine to 1 litre of water per day of age for 1000 chickens, e.g. 10 litres would be needed for 1000, 10 days old chickens.
- In order to make the birds thirsty, withdraw the supply of drinking water up to 2 hours prior to immunisation (birds' drinking behaviour varies, depending on the air temperature, type of birds, breed, management, weather conditions).
- The drinking system should be clean, without traces of chlorine, other disinfectants or impurities.
- If needed, turn the lights down low when the water is turned off. After the vaccine is in the drinking system, increase light intensity again. Increased light intensity will stimulate the birds to look for food and water.
- Always make sure that there is food available when vaccinating. Birds will not drink if they have no food to eat.

10. WITHDRAWAL PERIOD

Zero days.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Store in a refrigerator (2°C–8°C).
Protect from light.
Do not freeze.

Do not use this veterinary medicinal product after the expiry date which is stated on the label and carton.

Shelf life after reconstitution according to directions: 3 hours.

12. SPECIAL WARNING(S)

Special warnings for each target species:
See section Dosage for each species, route and method of administration.
Vaccinate healthy animals only.

Special precautions for use in animals:

The vaccine strain can spread to susceptible, unvaccinated chickens following vaccination for at least 5 days. The spread does not induce clinical signs.

It is possible that the vaccine virus spreads to non-target susceptible species.
Care should be taken to ensure that the vaccine virus does not spread to unvaccinated birds. Therefore, all birds in a flock should be vaccinated at the same time to reduce the risk of bird to bird transmission. Vaccinated birds should not be mixed with unvaccinated birds. Hygiene measures should be taken to prevent spread to other flocks. Vaccination of all chickens on the premises is recommended. Housing needs to be disinfected prior to restocking.

Given that this vaccine is an intermediate plus strain of IBDV, this vaccine should only be used after it has been determined that there is an epidemiological need.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Wash and disinfect hands and equipment after vaccination.

Lay:
Do not use in birds in lay and within 4 weeks before the onset of the laying period.

Interaction with other medicinal products and other forms of interaction:
No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product. A decision to use this vaccine before or after any other veterinary medicinal product therefore needs to be made on a case by case basis.

Overdose (symptoms, emergency procedures, antidotes):
After the administration of a 10-fold overdose, no adverse reactions other than those described in section *Adverse reactions* were observed.

Incompatibilities:
Do not mix with any other veterinary medicinal product.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

The vaccine stimulates active immunity against Infectious Bursal Disease virus in chickens.
For animal treatment only – to be supplied only on veterinary prescription.

Packaging sizes:
Cardboard box with 10 vials of 1000 doses of vaccine.
Cardboard box with 10 vials of 2500 doses of vaccine.
Cardboard box with 10 vials of 5000 doses of vaccine.
Not all pack sizes may be marketed.

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.