Attachment D3 Proposed Package Insert

1.Product name

Mopsion Spot-on Solutions 0.4 mL/tube (for Dogs)

Mopsion Spot-on Solutions 1.0 mL/tube (for Dogs)

Mopsion Spot-on Solutions 2.5 mL/tube (for Dogs)

Mopsion Spot-on Solutions 4.0 mL/tube (for Dogs)

2. Name and Strength of Active Substance(s)

0.4 mL/tube: Imidacloprid 40 mg+ Moxidectin 10 mg

1.0 mL/tube: Imidacloprid 100 mg+ Moxidectin 25 mg

2.5 mL/tube: Imidacloprid 250 mg+ Moxidectin 62.5 mg

4.0 mL/tube: Imidacloprid 400 mg+ Moxidectin 100 mg

3. Product Description

Mopsion Spot-on Solutions 0.4 mL/tube (for Dogs) is a yellow to brownish yellow solution. Each 0.4 ml tube contains 40 mg imidacloprid and 10 mg moxidectin.

Mopsion Spot-on Solutions 1.0 mL/tube (for Dogs) is a yellow to brownish yellow solution. Each 1.0 ml tube contains 100 mg imidacloprid and 25 mg moxidectin.

Mopsion Spot-on Solutions 2.5 mL/tube (for Dogs) is a yellow to brownish yellow solution. Each 1.0 ml tube contains 250 mg imidacloprid and 62.5 mg moxidectin.

Mopsion Spot-on Solutions 4.0 mL/tube (for Dogs) is a yellow to brownish yellow solution. Each 1.0 ml tube contains 400 mg imidacloprid and 100 mg moxidectin.

4. (1) Pharmacodynamics

Imidacloprid, 1-(6-Chloro-3-pyridylmethyl)-N-nitro-imidazolidin-2-ylideneamine is an ectoparasiticide belonging to the chloronicotinyl group of compounds. Chemically, it is more accurately described as a chloronicotinyl nitroguanidine. Imidacloprid is effective against larval flea stages and adult fleas. Flea larvae in the pet's surroundings are killed after contact with a pet treated with the veterinary medicinal product.

Imidacloprid has a high affinity for the nicotinergic acetylcholine receptors in the post-synaptic region of the central nervous system (CNS) of the flea. The ensuing inhibition of cholinergic transmission in insects results in paralysis and death. Due to the weak nature of the interaction with mammalian nicotinergic receptors and the postulated poor penetration through the blood-brain barrier in mammals, it has virtually no effect on the mammalian CNS. Imidacloprid has minimal pharmacological activity in mammals.

Moxidectin, 23-(O-methyloxime)-F28249 alpha is a second-generation macrocyclic lactone of the milbemycin family. It is a parasiticide which is active against many internal and external parasites. Moxidectin is active against larval stages of *Dirofilaria immitis* (L1, L3, L4) and *Dirofilaria repens* (L1, L3). It is also active against gastrointestinal nematodes. Moxidectin interacts with GABA and glutamate-gated chloride channels. This leads to opening of the chloride channels on the postsynaptic junction, the inflow of chloride ions and induction of an irreversible resting state. The result is flaccid paralysis of affected parasites, followed by their death and/or expulsion. The drug has a persistent action and protects dogs for 4 weeks after a single application against re-infection with the following parasites: *Dirofilaria immitis*, *Dirofilaria repens*, *Angiostrongylus vasorum*.

(2) Pharmacokinetics

After topical administration of the veterinary medicinal product, imidacloprid is rapidly distributed over the animal's skin within one day of application. It can be found on the body surface throughout the treatment interval. Moxidectin is absorbed through the skin, reaching maximum plasma concentrations approximately 4 to 9 days after treatment in dogs.

Following absorption from the skin, moxidectin is distributed systemically throughout the body tissues but due to its lipophilicity it is concentrated mainly in the fat. It is slowly eliminated from the plasma as manifested by detectable moxidectin concentrations in plasma throughout the treatment interval of one month.

The $t_{1/2}$ in dogs is about 28.4 days.

Studies evaluating the pharmacokinetic behaviour of moxidectin after multiple applications have indicated that steady state serum levels are achieved following approximately 4 consecutive monthly treatments in dogs.

5.Target Species: Dogs (Canine)

6. Indication

For dogs suffering from, or at risk from, mixed parasitic infections. The veterinary medicinal product is only indicated when use against fleas and one or more of the other target parasites is indicated at the same time:

- the treatment and prevention of flea infestation (*Ctenocephalides felis*),
- the treatment of biting lice (*Trichodectes canis*),
- the treatment of ear mite infestation (*Otodectes cynotis*), sarcoptic mange (caused by S*arcoptes scabiei* var. *canis*), demodicosis (caused by *Demodex canis*),

- the prevention of heartworm disease (L3 and L4 larvae of *Dirofilaria immitis*),
- the treatment of circulating microfilariae (*Dirofilaria immitis*),
- the treatment of cutaneous dirofilariosis (adult stages of *Dirofilaria repens*),
- the prevention of cutaneous dirofilariosis (L3 larvae of *Dirofilaria repens*),
- the reduction of circulating microfilariae (*Dirofilaria repens),*
- the prevention of angiostrongylosis (L4 larvae and immature adults of *Angiostrongylus vasorum*),
- the treatment of *Angiostrongylus vasorum* and *Crenosoma vulpis*,
- the prevention of spirocercosis (*Spirocerca lupi*),
- the treatment of *Eucoleus* (syn. *Capillaria*) *boehmi* (adults),
- the treatment of the eye worm *Thelazia callipaeda* (adults),
- the treatment of infections with gastrointestinal nematodes (L4 larvae, immature adults and adults of *Toxocara canis*, *Ancylostoma caninum* and *Uncinaria stenocephala*, adults of *Toxascaris leonina* and *Trichuris vulpis*).

The veterinary medicinal product can be used as part of a treatment strategy for flea allergy dermatitis (FAD).

7. Recommended dose

To ensure a correct dosage, body weight should be determined as accurately as possible. The recommended minimum doses are 10 mg/kg bodyweight imidacloprid and 2.5 mg/kg bodyweight moxidectin, equivalent to 0.1 ml/kg bodyweight of the veterinary medicinal product.

For treatment or prevention of infestations with the parasites indicated for use of this veterinary medicinal product, the need for and frequency of re-treatment(s) should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle.

Weight of canine（kg）	Applicable type	Volume（mL）	Imidacloprid（mg/kg body weight）	Moxidectin（mg/kg body weight）
≤4 kg	Small canine	0.4	Not less than 10	Not less than 2.5
＞4～10 kg	Medium canine	1.0	10～25	2.5～6.25
＞10～25 kg	Large canine	2.5	10～25	2.5～6.25
＞25～40 kg	Extra-large canine	4.0	10～16	2.5～4
＞40 kg	Use a combination of products of appropriate volumes.			

Flea treatment and prevention (Ctenocephalides felis)

One treatment prevents future flea infestation for 4 weeks. Existing pupae in the environment may emerge for 6 weeks or longer after treatment is initiated, depending upon climatic conditions. Therefore, it may be necessary to combine the veterinary medicinal product treatment with environmental treatments aimed at breaking the flea life cycle in the surroundings. This can result in a more rapid reduction in the household flea population. The veterinary medicinal product should be administered at monthly intervals when used as part of a treatment strategy for flea allergy dermatitis.

Treatment of biting lice (Trichodectes canis)

A single dose should be administered. A further veterinary examination 30 days after treatment is recommended as some animals may require a second treatment.

Treatment of ear mite infestation (Otodectes cynotis)

A single dose of the veterinary medicinal product should be administered. Loose debris should be gently removed from the external ear canal at each treatment. A further veterinary examination 30 days after treatment is recommended as some animals may require a second treatment. Do not apply directly to the ear canal.

Treatment of sarcoptic mange (caused by Sarcoptes scabiei var. canis)

A single dose should be administered twice 4 weeks apart.

Treatment of demodicosis (caused by Demodex canis)

The administration of a single dose every 4 weeks for 2 to 4 months is efficacious against *Demodex canis* and leads to a marked improvement of clinical signs particularly in mild to moderate cases.

Especially severe cases may require more prolonged and more frequent treatment. To achieve the best possible response in these severe cases, at the discretion of the veterinarian, the veterinary medicinal product can be applied once a week and for a prolonged time. In all cases it is essential that the treatment should be continued until skin scrapings are negative on at least 2 consecutive monthly occasions. Treatment should be stopped in dogs that show no improvement or do not respond in mite count after 2 months treatment. Alternative treatment should be administered. Seek the advice of your veterinarian.

As demodicosis is a multi-factorial disease, where possible, it is advisable to also treat any underlying disease appropriately.

Prevention of heartworm disease (D. immitis)

Dogs in areas endemic for heartworm, or those which have travelled to endemic areas,

may be infected with adult heartworms. Therefore prior to treatment with the veterinary medicinal product, the advice provided in section Warnings and Precautions should be considered.

For prevention of heartworm disease, the veterinary medicinal product must be applied at regular monthly intervals during the time of the year when mosquitoes (the intermediate hosts which carry and transmit *D. immitis* larvae) are present. The veterinary medicinal product may be administered throughout the year. The first dose may be given after first possible exposure to mosquitoes, but not more than one month after this exposure. Treatment should continue at regular monthly intervals until 1 month after the last exposure to mosquitoes. To establish a treatment routine, it is recommended that the same day or date be used each month. When replacing another heartworm preventative product in a heartworm prevention programme, the first treatment with the veterinary medicinal product must be given within 1 month of the last dose of the former medication.

In non-endemic areas there should be no risk of dogs having heartworm. Therefore, they can be treated without special precautions.

Prevention of cutaneous dirofilariosis (skinworm) (D. repens)

For prevention of cutaneous dirofilariosis, the veterinary medicinal product must be applied at regular monthly intervals during the time of the year when mosquitoes (the intermediate hosts which carry and transmit *D. repens* larvae) are present. The veterinary medicinal product may be administered throughout the year or at least 1 month before the first expected exposure to mosquitoes. Treatment should continue at regular monthly intervals until 1 month after the last exposure to mosquitoes. To establish a treatment routine, it is recommended that the same day or date be used each month.

Treatment of microfilariae (D. immitis)

The veterinary medicinal product should be administered monthly for two consecutive months

Treatment of cutaneous dirofilariosis (skinworm) (adult stages of Dirofilaria repens)

The veterinary medicinal product should be administered monthly for six consecutive months.

Reduction of microfilariae (skin worm) (D. repens)

The veterinary medicinal product should be administered monthly for four consecutive months.

Treatment and prevention of Angiostrongylus vasorum

A single dose should be administered. A further veterinary examination 30 days after treatment is recommended as some animals may require a second treatment.

In endemic areas regular monthly applications will prevent angiostrongylosis and patent infection with *Angiostrongylus vasorum*.

Treatment of Crenosoma vulpis

A single dose should be administered.

Prevention of spirocercosis (Spirocerca lupi)

The veterinary medicinal product should be administered monthly.

Treatment of Eucoleus (syn. Capillaria) boehmi (adults)

The veterinary medicinal product should be administered monthly for two consecutive months. It is advisable to prevent auto-coprophagia between the two treatments in order to prevent possible reinfection.

Treatment of the eye worm Thelazia callipaeda (adults)

A single dose of the veterinary medicinal product should be administered.

Roundworm, hookworm and whipworm treatment (Toxocara canis, Ancylostoma caninum, Uncinaria stenocephala, Toxascaris leonina and Trichuris vulpis)

In areas endemic for heartworm, monthly treatment may significantly reduce the risk of re-infection caused by the respective round-, hook- and whipworms. In areas non-endemic for heartworm, the veterinary medicinal product can be used as part of a seasonal prevention programme against fleas and gastrointestinal nematodes.

Studies have shown that monthly treatment of dogs will prevent infections caused by *Uncinaria stenocephala*.

8. Mode of administration

External use. In order to prevent canines from licking, this product can be dropped on the skin between the two shoulder blades of the canine's back to the buttocks, and it can be dropped in 3 to 4 places.

Remove one tube from the package. Then hold the tube in an upright position, and twist and pull off the cap. Reverse the cap and use it to twist and remove the seal from the tube.

For dogs up to 25 kg:

With the dog in a standing position, part the coat between the shoulder blades until the skin is visible. Wherever possible apply to undamaged skin. Place the tip of the tube on the skin and squeeze the tube firmly several times to empty its contents directly onto

the skin.

For dogs of more than 25 kg:

For easy application the dog should be standing. The entire contents of the tube should be applied evenly as 3 or 4 spots along the top of the back, from between the shoulders to the base of the tail. At each spot, part the coat until the skin is visible. Wherever possible apply to undamaged skin. Place the tip of the tube on the skin and gently squeeze the tube to expel a portion of its contents directly onto the skin. Do not apply an excessive amount of solution at any one spot, as that could cause some of the veterinary medicinal product to run down the animal's side.

9. Contraindication

Do not use in puppies under 7 weeks of age.

Do not use in cases of hypersensitivity to the active substances or to any of the excipients.

Do not use in dogs classified as Class 4 for heartworm disease as the safety of the product has not been evaluated in this animal group.

Do not use in cats. Instead, the corresponding “Mopsion Spot-on Solutions (for Cats)” product (0.4 or 0.8 ml), which contains 100 mg/ml imidacloprid and 10 mg/ml moxidectin, must be used for cats.

Do not use in ferrets.

Do not use on canaries.

10. Warnings and Precautions

During the monthly treatment interval, brief contact with water on one or two occasions is unlikely to significantly reduce the efficacy of the veterinary medicinal product. However, frequent shampooing or prolonged immersion in water following treatment may potentially decrease its efficacy.

Consideration should be given to the possibility that other animals in the same household may act as a source of re-infestation with fleas, mites, gastrointestinal nematodes, heartworm and/or lungworm, and such animals should be treated with an appropriate product as necessary.

Unnecessary use of antiparasitic agents, or use not in accordance with the instructions, may increase antiparasitic resistance selection pressure and result in reduced efficacy. The use of the product should be based on confirmation of the parasitic species and infestation burden, or on the risk of infestation determined by epidemiological characteristics for each individual animal.

Efficacy against adult *Dirofilaria repens* has not been tested under field conditions.

Special precautions for safe use in the target species:

The treatment of animals weighing less than 1 kg should be based on a benefit-risk assessment.

Experience with the use of the veterinary medicinal product in sick or debilitated animals is limited; therefore, the product should only be used in these animals following a benefit-risk assessment.

Do not apply the product into the mouth, eyes or ears of the animal.

Care should be taken to ensure that the veterinary medicinal product is not ingested by animals and does not come into contact with the eyes or mouth of the treated animal and/or other animals.

Careful attention should be paid to the correct application method, the product should be applied to the specified site to minimise the risk of the animal licking the application site.

Do not allow recently treated animals to groom each other. Treated animals should not come into contact with untreated animals until the application site is dry.

When the veterinary medicinal product is applied in 3 to 4 separate spots (see section Method of Administration), specific care should be taken to prevent the animal licking the application sites.

This veterinary medicinal product contains moxidectin (a macrocyclic lactone), therefore special care should be taken with Collie or Old English Sheep dogs and related breeds or crossbreeds, to correctly administer the veterinary medicinal product as described under section Method of Administration; in particular, oral uptake by Collie or Old English Sheep dogs and related breeds or crossbreeds should be prevented.

The safety of the veterinary medicinal product has only been evaluated in dogs classified as either Class 1 or 2 for heartworm disease in laboratory studies and in a few Class 3 dogs in a field study. Therefore, the use in dogs with obvious or severe symptoms of the disease should be based on a careful benefit-risk assessment by the treating veterinarian.

Although experimental overdosage studies have shown that the veterinary medicinal

product may be safely administered to dogs infected with adult heartworms, it has no therapeutic effect against adult *Dirofilaria immitis*. It is therefore recommended that all dogs 6 months of age or more, living in areas endemic for heartworm, should be tested for existing adult heartworm infection before being treated with the veterinary medicinal product. At the discretion of the veterinarian, infected dogs should be treated with an adulticide to remove adult heartworms. The safety of the veterinary medicinal product has not been evaluated when administered on the same day as an adulticide.

Imidacloprid is toxic for birds, especially canaries.

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

This veterinary medicinal product may cause irritation to the skin, eyes or mouth.

In very rare cases, the product may cause skin sensitisation or transient skin reactions such as numbness, irritation, burning or tingling.

In very rare cases, the product may cause respiratory irritation in susceptible individuals.

People with known hypersensitivity to benzyl alcohol, imidacloprid or moxidectin should administer the product with caution.

Avoid contact with skin, eyes or mouth.

Do not eat, drink or smoke during application.

Wash hands thoroughly after use.

Do not stroke or groom animals until the application site is dry.

In case of accidental spillage onto the skin, wash immediately with soap and water.

If the product accidentally gets into the eyes, rinse thoroughly with water.

If skin or eye symptoms persist, or if the product is accidentally ingested, seek medical advice immediately and show the package leaflet or label to the doctor.

Special precautions for the protection of the environment:

The veterinary medicinal product should not be allowed to enter watercourses, as imidacloprid and moxidectin may be dangerous to fish and other aquatic organisms. Dogs should not be allowed to swim in surface waters for 4 days after treatment.

Other precautions:

The solvent contained in the veterinary medicinal product may stain or damage certain materials, including leather, fabrics, plastics and finished surfaces. Contact with such materials should be avoided until the application site is dry.

11. Interactions with other medicaments

During treatment with this veterinary medicinal product, no other antiparasitic macrocyclic lactone products should be administered.

No interactions have been observed between this veterinary medicinal product and routinely used veterinary medicinal products, or during routine medical or surgical procedures.

Safety of the veterinary medicinal product when administered on the same day as an adulticide to remove adult heartworms has not been evaluated.

12. Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation in the target species.

Pregnancy and lactation:

The veterinary medicinal product is not recommended for use during pregnancy and lactation.

Fertility:

The product should not be used in breeding animals.

13. Adverse effects

Dogs:

Common (1 to 10 animals / 100 animals treated):	Diarrhoea[1], Vomiting[1] Cough[1], Dyspnoea[1], Tachypnoea[1] Inappetence[1], Lethargy[1]
Rare (1 to 10 animals / 10,000 animals treated):	Vomiting

Very rare (< 1 animal / 10,000 animals treated, including isolated reports):	Application site greasy fur[2], Application site hair loss[2], Application site itching[2], Application site redness[2] Behavioural disorder (e.g. agitation)[3] Hypersensitivity[4] Neurological signs (e.g. ataxia, muscle tremor)[5] Pruritus Inappetence[3], Lethargy[3]

[1] These signs are common in heartworm positive dogs with microfilariaemia, and there is a risk of gastrointestinal signs and severe respiratory signs that may require prompt veterinary treatment.

[2] These signs disappear without further treatment.

[3] Transiently noted and related to sensation at application site.

[4] This is not a sign of intoxication and disappears within minutes without treatment. Correct application will minimise licking of the application site.

[5] Most neurological signs occur transiently.

14. Overdose and treatment

Up to 10 times the recommended dose was tolerated in adult dogs with no evidence of adverse effects or undesirable clinical signs. Five times the recommended minimum dose applied at weekly intervals for 17 weeks was investigated in dogs aged over 6 months and tolerated with no evidence of adverse effects or undesirable clinical signs.

The veterinary medicinal product was administered to puppies at up to 5 times the recommended dose, every 2 weeks for 6 treatments, and there were no serious safety concerns. Transient mydriasis, salivation, vomiting and transient rapid respiration were observed.

After accidental oral ingestion or overdose, neurological signs (most of which are transient) such as ataxia, generalised tremors, ocular signs (dilated pupils, little pupillary reflex, nystagmus), abnormal respiration, salivation and vomiting may occur in very rare cases.

Ivermectin-sensitive Collie dogs tolerated up to 5 times the recommended dose repeated at monthly intervals without any adverse effects, but the safety of application at weekly intervals has not been investigated in ivermectin-sensitive Collie dogs. When 40% of

the unit dose was given orally, severe neurological signs were observed. Oral administration of 10% of the recommended dose produced no adverse effects.

Dogs infected with adult heartworms tolerated up to 5 times the recommended dose, every 2 weeks for 3 treatments, without any adverse effects.

In case of accidental oral uptake, symptomatic treatment should be administered. There is no known specific antidote. The use of activated charcoal may be beneficial.

15. Withdrawal period(s)

Not applicable.

16. Storage conditions

Seal up, store below 25℃.

17. Shelf life

36 months

18. Dosage form and packaging

Spot-on solution.

Aluminum plastic tube, 0.4 mL/tube OR 1.0 mL/tube OR 2.5 mL/tube, OR 4.0 mL/tube, 3 tubes/box.

19. Name and Address of Manufacturer

Ringpu (Tianjin) Bio-Pharmacy Co., Ltd.

Address: No.6 Liujing Road, Dongli District, Tianjin, China

20. Name and Address of Marketing authorization holder

Medispec (M) Sdn. Bhd.

Address: B-1-07, Jalan SS 25/22, Taman Mayang, 47301 Petaling Jaya, Selangor, Malaysia

21. Date of Revision of Package Insert

May 22, 2026