# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT

Moxidectin Tablets, 2 mg

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 2 mg of

moxidectin. Excipients with

known effect:
Lactose

For the full list of excipients, see Section 6.1.

## 3. PHARMACEUTICAL FORM

White to pale yellow, uncoated oval tablets, debossed on one side with “AKKA". Approximate size: 8.13 mm (length) × 4.55 mm (width).

The tablet should not be divided.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Moxidectin Tablets are indicated for the treatment of onchocerciasis due to *Onchocerca volvulus* in adults and children aged 4 years and older *[see Section 5.1].*

### 4.2 Posology and method of administration

Posology

| | |
|---|---|
| **Adults and Children Aged 8 Years and Older** | 8 mg (four 2 mg tablets) |
| **Children Aged 4 to 7 Years** | 4 mg (two 2 mg tablets) |

Method of administration

To be taken orally as a single dose, with or

without food. Special populations

Paediatric Use

The safety and efficacy of moxidectin for the treatment of onchocerciasis due to *O. volvulus* have been established in children with unknown infection status aged 4 years and older and adolescents aged 12 to 17 years with onchocerciasis. Use of Moxidectin Tablets in this indication is supported by evidence from adequate and well-controlled studies in adults and adolescents with additional pharmacokinetic and safety data in children aged 4 years and older [*see Sections 4.8 and 5.2*].

The safety and efficacy of Moxidectin Tablets have not been established in children younger than 4 years old.

*Use in the Elderly*

No overall differences in safety or efficacy were observed in people aged 65 years and over with onchocerciasis compared with younger people participating in clinical trials with Moxidectin Tablets. [*see Section 5.1*].

*Renal Impairment*

No dose adjustment is necessary in mild (creatinine clearance (CrCL) 60 to 89 mL/min) to moderate (CrCL 30 to 59 mL/min) renal impairment. The safety of Moxidectin Tablets in patients with severe renal impairment (CrCL 15 to 29 mL/min) or end stage renal disease, is unknown [*see Section 5.2*].

## 4.3 Contraindications

Hypersensitivity to moxidectin or to any of the excipients listed in Section 6.1.

## 4.4 Special warnings and precautions for use

Adverse Reactions Associated with Efficacy of Treatment

Treatment with Moxidectin Tablets may cause cutaneous, ophthalmological and/or systemic reactions of varying severity (also known as the “Mazzotti reaction”). These adverse reactions are due to allergic and inflammatory host responses to the death of microfilariae *[see Section 4.8].* There is a trend toward an increased incidence of these adverse reactions in people with high microfilarial burden.

The clinical manifestations of Mazzotti reaction include pruritus, headache, pyrexia, rash, urticaria, hypotension (including symptomatic orthostatic hypotension and dizziness) *[see below]*, tachycardia, oedema, lymphadenopathy, arthralgia, myalgia, chills, paresthaesia and asthenia. Ophthalmological manifestations include conjunctivitis, eye pain, eye pruritus, eyelid swelling, blurred vision, photophobia, changes in visual

acuity, hyperaemia, ocular discomfort and watery eyes. These adverse reactions generally occur and resolve in the first week post-treatment. Laboratory changes include eosinophilia, eosinopenia, lymphocytopenia, neutropenia, and increases in alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamyl transferase (GGT) and lactate dehydrogenase (LDH). Proteinuria has also been reported. Symptomatic treatments such as oral hydration, recumbency, intravenous normal saline, antihistamines, analgesics, and/or parenteral corticosteroids have been used. Severe Mazzotti reactions were not observed in clinical trials with moxidectin.

Symptomatic Orthostatic Hypotension

In two clinical studies of people with onchocerciasis, an increased number of those who received Moxidectin Tablets developed symptomatic orthostatic hypotension with inability to stand without support after lying down for 5 minutes (in an orthostatic hypotension provocation test); 47/978 (5%) compared with 8/494 (2%) who received ivermectin. The decreases in blood pressure were transient, managed by resumption of recumbency and most commonly occurred on Days 1 and 2 post-treatment.

People with orthostatic hypotension should be advised to lie down if they feel dizzy or light-headed after taking Moxidectin Tablets until the symptoms resolve. Symptomatic treatments such as oral hydration and recumbency have been used to effectively treat orthostatic hypotension.

Encephalopathy in *Loa loa* Co-infected Patients

People with onchocerciasis who are also infected with *Loa loa* have developed serious or even fatal encephalopathy following treatment with other macrocyclic lactone medicines. This may also occur following treatment with moxidectin.

Moxidectin Tablets have not been studied in patients co-infected with *Loa loa*. Therefore, it is recommended that individuals who warrant treatment with Moxidectin Tablets and have had exposure to *Loa loa*-endemic areas undergo diagnostic screening for loiasis prior to treatment.

Oedema and Worsening of Onchodermatitis

Patients with hyper-reactive onchodermatitis (sowda) may be more likely than others to experience severe oedema and worsening of onchodermatitis following the use of Moxidectin Tablets.
Symptomatic treatment has been used to manage oedema and

worsening of onchodermatitis. Excipients

Lactose
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

## 4.5 Interaction with other medicinal products and other forms of interaction

Midazolam (CYP3A4 substrate)

In healthy adult subjects, concomitant administration of a single 8 mg oral dose of Moxidectin Tablets did not affect the pharmacokinetics of midazolam [*see Section 5.1*]. Moxidectin can be co-administered with CYP3A4

substrates. In Vitro Studies

CYP Enzymes: Moxidectin is not a substrate or inhibitor of CYP enzymes.

Uridine 5'-diphospho-glucuronosyltransferases (UGTs): Moxidectin is not a UGT substrate.

Transporter Systems: Moxidectin is not a substrate of P-glycoprotein (P-gp) nor breast cancer resistance protein 1 (BCRP1).

Paediatric population

Interaction studies have only been performed in adults.

## 4.6 Fertility, pregnancy and lactation

Pregnancy and Fertility

There are limited data from the use of moxidectin in pregnant women. It is recommended to avoid the use of moxidectin during pregnancy.

See section 5.3 for information on animal reproductive studies.

Breastfeeding

Moxidectin passes into human milk. Treatment of mothers who intend to breast-feed should only be undertaken when the risk of delayed treatment to the mother outweighs possible risk to the newborn. Women who are breast-feeding should not be given moxidectin during the first week after giving birth (see 5.2).

## 4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. Some people may experience side effects such as dizziness [*see Section 4.8*], which could affect the ability to drive or use machines. Patients should be advised not to drive or operate machines until any such effects have resolved.

## 4.8 Undesirable effects

Summary of safety profile

The following clinically significant adverse reactions have been reported with the use of Moxidectin Tablets:

- Adverse Reactions Associated with Efficacy of Treatment *[see Section 4.4]*
- Symptomatic Orthostatic Hypotension *[see Section 4.4]*

Tabulated list of adverse reactions

The most frequently (≥1/10) reported adverse reactions are listed in Table 1 below.

There were no withdrawals from either trial due to adverse reactions. Adverse reactions reported in more than 10% of subjects with onchocerciasis treated with Moxidectin Tablets in the Phase 3 trial are summarised in Table 1. Most were related to physical, vital signs and laboratory changes associated with the Mazzotti reaction *[see Section 4.4]*.

**Table 1: Adverse Reactions Occurring in > 10% of Moxidectin-treated Subjects with Onchocerciasis in the Phase 3 trial**

| MEDRA System Organ Class | Adverse Reaction | Moxidectin N = 978 n (%) | Ivermectin N = 494 n (%) |
|---|---|---|---|
| **Blood and lymphatic system disorders** | Eosinophilia | 721 (74) | 390 (79) |
| | Lymphocytopenia* | 470 (48) | 215 (44) |
| | Leukocytosis | 240 (25) | 125 (25) |
| | Neutropenia** | 197 (20) | 112 (23) |
| | Lymph node pain | 129 (13) | 28 (6) |
| **Skin and subcutaneous tissue disorders** | Pruritus | 640 (65) | 268 (54) |
| | Rash [e] | 358 (37) | 103 (21) |
| **Musculoskeletal and connective tissue** | Musculoskeletal pain [a] | 623 (64) | 257 (52) |

| | | | |
|---|---|---|---|
| **disorders** | | | |
| **Nervous system disorders** | Headache | 566 (58) | 267 (54) |
| | Dizziness | 121 (12) | 44 (9) |
| **Cardiac Disorders** | Tachycardia [b] | 382 (39) | 148(30) |
| | Orthostatic tachycardia [c] | 333 (34) | 130 (26) |
| | Non-orthostatic tachycardia [d] | 179 (18) | 57 (12) |

| MEDRA System Organ Class | Adverse Reaction | Moxidectin N = 978 n (%) | Ivermectin N = 494 n (%) |
|---|---|---|---|
| **Gastrointestinal disorders** | Abdominal pain [f] | 305 (31) | 173 (35) |
| | Diarrhea/Gastroenteritis/Enteritis | 144 (15) | 84 (17) |
| **Vascular disorders** | Hypotension [g] | 289 (30) | 125 (25) |
| | Orthostatic hypotension [h] | 212 (22) | 81 (16) |
| | Peripheral swelling | 107 (11) | 30 (6) |
| **General disorders and administration site conditions** | Pyrexia/Chills | 268 (27) | 88 (18) |
| **Infections and infestations** | Influenza like illness | 226 (23) | 102 (21) |
| **Respiratory, thoracic and mediastinal disorders** | Cough | 168 (17) | 88 (18) |
| **Renal and urinary disorders** | Hyponatremia | 112 (12) | 65 (13) |

[a] Includes "myalgia", "arthralgia", "musculoskeletal pain", "pain" and "back pain"
[b] Includes "orthostatic heart rate increased", "postural orthostatic tachycardia syndrome", "heart rate increased" and "sinus tachycardia"
[c] Includes "orthostatic heart rate increased" and "postural orthostatic tachycardia syndrome"
[d] Includes "heart rate increased", "tachycardia", and "sinus tachycardia"
[e] Includes "rash," "papular rash" and "urticaria"
[f] Includes "abdominal pain", "abdominal pain upper" and "abdominal pain lower"
[g] Includes "orthostatic hypotension", "blood pressure orthostatic decreased", "blood pressure decreased", "mean arterial pressure decreased", "hypotension"
[h] Includes "orthostatic hypotension", and "blood pressure orthostatic decreased"
*Lymphocytopenia is defined as absolute lymphocyte count less than 1 x $10^9$/L
**Neutropenia is defined as absolute neutrophil count less than 1 x $10^9$/L

The most common adverse reactions in subjects with onchocerciasis (n = 38) treated with an 8 mg dose (4 x 2 mg) of Moxidectin Tablets were similar to the adverse reactions described in Table 1 above.

Description of Selected Adverse Reactions

The following adverse reactions occurred in less than 10% of subjects with onchocerciasis receiving Moxidectin Tablets in the Phase 3 trial:

Ocular Adverse Reactions: In the Phase 3 trial, the most common ocular adverse reactions occurring in moxidectin-treated patients were eye pain (78%) and conjunctivitis (64%).

Hepatobiliary Adverse Reactions

More subjects with onchocerciasis in the moxidectin arm experienced elevation in bilirubin above the upper limit of normal and elevation in transaminases > 5x upper limit of normal. Twenty-seven (2.8%) subjects in the moxidectin arm and 3 (0.6%) subjects in the ivermectin arm had hyperbilirubinemia. Most had single measurements of hyperbilirubinemia without concurrent elevation in transaminases.

Nine (1%) subjects in the moxidectin arm and 2 (0.4%) subjects in the ivermectin arm had elevation in ALT of more than 5x upper limit of normal; ten (1%) subjects in the moxidectin arm and 3 (0.6%) subjects in the ivermectin arm had elevation in AST to more than 5x upper limit of normal.

Paediatric Population

In the Phase 3 trial, adolescents aged 12 to 17 years with known onchocerciasis infection experienced efficacy related adverse events (Mazzotti reactions) such as abdominal pain, tachycardia, pyrexia, rash, peripheral swelling, and lymph node pain at a prevalence and severity similar to infected adults. Overall, the safety profile relative to age was similar across all age groups studied.

In the paediatric pharmacokinetic study in 36 children aged 4 to 17 years with unknown infection status from a known onchocerciasis endemic area, the adverse event profile was no different to that observed in adults. Safety endpoints in the study included the incidence and severity of adverse events, physical examination findings, changes in vital signs, and laboratory safety parameters at all time points to Week 24 after treatment. Moxidectin was well tolerated in all age cohorts, with no treatment-limiting adverse events identified during 24 weeks of follow-up and no adverse events leading to early study withdrawal. All adverse events were mild or moderate and none were considered related to moxidectin.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

## 4.9 Overdose

In the event of overdose, general supportive measures including monitoring of vital signs as well as observation of the clinical status of the patient may be adequate. Supportive therapy, if indicated, should include parenteral fluids and electrolytes, respiratory support (oxygen and mechanical ventilation if necessary) and pressor agents if clinically significant hypotension is present.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihelmintics, Antinematodal Agents, ATC code: P02CX03. Pharmacodynamics

*Mechanism of action*

Moxidectin is a macrocyclic lactone, anthelmintic drug. The mechanism by which moxidectin exhibits its effect against *O. volvulus* is not known. Studies with other nematodes suggest that moxidectin binds to glutamate-gated chloride channels (GluCl), gamma-aminobutyric acid (GABA) receptors and/or ATP-binding cassette (ABC) transporters. This leads to increased permeability, influx of chloride ions, hyperpolarization and muscle paralysis. Additionally, there is a reduction in motility of all stages of the parasite, excretion of immunomodulatory proteins, and the fertility of both male and female adult worms.

Moxidectin is active against the microfilariae of *O. volvulus [see Clinical Studies]*. Studies suggest that moxidectin is not effective in killing the adult worms, however, it inhibits intra-uterine embryogenesis and release of microfilariae from the adult worms.

*Mechanisms of resistance*

Studies *in vitro* and in infected animals suggest a potential for development of resistance to moxidectin and cross-resistance with other macrocyclic lactones, such as ivermectin. However, the clinical relevance of these findings is not known.

The mechanism of resistance may be multifactorial that include alteration in the target GluCl, GABA receptors and/or ABC transporters.

Clinical efficacy and safety

*Clinical Studies*

The assessment of the safety and efficacy of Moxidectin Tablets 8 mg in the treatment of onchocerciasis is based on data from two randomized, double-blind, active-controlled trials in patients with *O. volvulus* infection, the Phase 3 trial in 1472 patients, and the Phase 2 trial, a dose-ranging trial. Patients in the trials received a single oral dose of moxidectin or ivermectin, the active control medication.

Efficacy was assessed by skin microfilarial density (microfilariae/mg skin) from the mean of 4 skin snips per person per time point up to 18 months post-treatment.

The Phase 3 trial recruited adults and adolescents with onchocerciasis ≥ 12 years with a body weight
≥ 30 kg and ≥ 10 microfilariae/mg skin. Mean (± SD) age was 25 (± 16.3) years,
height 1.59 (± 0.09) meters, weight 51.6 (± 8.2) kg; 36.1% were female and 100% were black. Mean (± SD) pretreatment skin microfilarial density was 39.5 (± 30.7) microfilariae/mg skin, 69.6% had
≥ 20 microfilariae/mg skin and 39.7% had at least one ocular microfilaria.

Individuals who were not previously exposed to ivermectin treatment programmes were recruited from the sub-Saharan African region (Democratic Republic of Congo, Liberia, and Ghana). Table 5 reports mean skin microfilarial density and the proportion of study subjects with undetectable skin microfilariae at Months 1, 6, and 12.

**Table 2: Mean Microfilarial Density and Percentage of Undetectable Microfilariae in Skin of Study Subjects with *O. volvulus* (12 Years of Age and Older) at Months 1, 6, and 12 in the Phase 3 trial**

| **Endpoint** | **Moxidectin** N = 977 | **Ivermectin** N = 495 | **Difference (95% Confidence Interval)** |
|---|---|---|---|
| **1 month** | | | |
| Mean Microfilarial Density [a] | 0.10 | 2.30 | -2.20 (-2.83, -1.58) p < 0.0001 |
| % Undetectable Microfilariae [b] | 83.4% | 42.9% | 40.5% (35.7, 45.3) p < 0.0001 |
| **6 months** | | | |
| Mean Microfilarial Density [a] | 0.14 | 3.71 | -3.57(-4.11, -3.03) p < 0.0001 |
| % Undetectable Microfilariae [b] | 91.0% | 11.5% | 79.6% (76.3, 82.9) p < 0.0001 |
| **12 months** | | | |

| | | | |
|---|---|---|---|
| Mean Microfilarial Density [a] | 1.79 | 9.83 | -8.04 (-9.11, -6.98)<br>p < 0.0001 |
| % Undetectable Microfilariae [b] | 45.9% | 5.4% | 40.4% (36.7, 44.1)<br>p < 0.0001 |

[a] Mean microfilarial density in skin is the average microfilarial density (microfilariae count/mg skin) over skin snips from four sites.
[b] Proportion of subjects undetectable (defined as a mean skin microfilariae density of zero across all 4 skin snips).

Additionally, safety and efficacy were assessed in a smaller single ascending dose trial (the Phase 2 trial) comparing 2 mg (n = 44), 4 mg (n = 45) (2 mg and 4 mg are not approved doses) and 8 mg
(n = 38) single doses of moxidectin to ivermectin. The Phase 2 trial was conducted in Ghana in adults aged ≥ 18 to ≤ 60 years with *O. volvulus* infection. Analysis of the baseline-to-12-month change in skin microfilarial density for the moxidectin 8 mg dose showed statistically significant superiority to ivermectin, $p < 0.001$.

## 5.2 Pharmacokinetic properties

### Pharmacokinetics

The pharmacokinetic parameters of moxidectin following a single 8 mg oral dose of Moxidectin Tablets to healthy subjects and subjects with onchocerciasis under fasted conditions are shown in Table 4. Mean moxidectin $C_{max}$ and AUC increased approximately proportionally to dose over a dose range of 2 to 36 mg (0.25 to 4.5 times the approved recommended dose) assessed in healthy subjects under fasted conditions.

**Table 3: Mean (± SD) Pharmacokinetic Parameters of Moxidectin Following a Single 8 mg Oral Dose of Moxidectin Tablets to Healthy Subjects and Patients with Onchocerciasis Under Fasted Conditions**

| **PK Parameter** | **Healthy Subjects (N = 27)** | **Patients with Onchocerciasis (N = 31)** |
|---|---|---|
| **Cmax (ng/mL)** | 58.9 ± 12.5 | 63.1 ± 20.0 |
| **Tmax* (hours)** | 4 (2, 8) | 4 (1, 4) |
| **AUCinf (ng•h/mL)** | 3387 ± 1328 | 2738 ± 1606 |
| **Half-life (hours)** | 784 ± 347 | 559 ± 525 |

Cmax = maximum plasma concentration; Tmax = time to reach Cmax; AUCinf = area under the plasma concentration-time curve from time 0 to infinity; * Median (range)

Absorption

*Effect of Food*

Moxidectin mean $C_{max}$ and AUC increased on average by 34% and 39%, respectively, when administered with a standard high fat meal (900 calories, with a nutritional distribution of approximately 55% fat, 31% carbohydrates and 14% protein), compared to fasted conditions *[see Dosage and Administration]*.

Distribution

The apparent mean ± SD volume of distribution of moxidectin is 2421 ± 1658 L in adults with onchocerciasis. The plasma protein binding in humans is 99.92%.

Elimination

The mean terminal half-life of moxidectin in adults with onchocerciasis is 23.3 days (559 hours) following a single 8 mg dose of Moxidectin Tablets. The apparent mean ± SD total clearance of moxidectin is approximately 3.50 ± 1.23 L/hour in adults with onchocerciasis.

*Metabolism*

The hepatic metabolism of moxidectin is minimal.

*Excretion*

Following administration of a single 8 mg oral dose of Moxidectin Tablets to healthy subjects, 2% of the dose is eliminated unchanged in the feces within the first 72 hours. Renal elimination of intact drug is negligible.

Specific Populations

In clinical studies, no clinically significant differences in the pharmacokinetics of moxidectin were observed based on age (18 to 60 years), sex, weight (42.7 to 107.2 kg), or renal impairment (creatinine clearance (CrCL) 47 to 89 mL/min, estimated by Cockcroft-Gault). The pharmacokinetics of

moxidectin in patients with CrCL less than 47 mL/min is unknown. The pharmacokinetics of moxidectin in patients with hepatic impairment is unknown.

*Patients with Renal Impairment*

Based on a population pharmacokinetic analysis and the fact that renal elimination of intact drug is negligible, mild (creatinine clearance (CrCL), estimated by Cockcroft-Gault of 60 to 89 mL/min) and moderate (CrCL 30 to 59 mL/min) renal impairment is not likely to have an impact on moxidectin exposure. The effect of severe renal impairment (CrCL 15 to 29 mL/min) or of end-stage renal disease on the pharmacokinetics of moxidectin is unknown.

*Paediatric population*

A pharmacokinetic study was conducted in 36 children aged 4 to 17 years with unknown infection status who were administered a single dose of moxidectin (single 4, 6 or 8 mg doses). Population pharmacokinetic modeling and simulations showed that when single doses of moxidectin are administered to a pediatric population (4 mg to children ages 4 to 7 years; 8 mg to children ages 8 to 11 years; and, 8 mg to adolescents ages 12 to 17 years), the predicted exposures are similar to predicted exposures in adults following administration of a single dose of moxidectin 8 mg, shown to be efficacious and well-tolerated in adults and adolescents. Body weight was identified as a key covariate in the population pharmacokinetic model, and allometric scaling of body weight provided the best predictions of exposure across the range of ages. Analyzing pharmacokinetic data in participants with, or at risk of, onchocerciasis (98 adults (33.0% of overall population), 9 adolescents (12 to 17 years; 3.0% of overall population), and 27 children (4 to 11 years; 9.1% of overall population)) together with 162 healthy adult volunteers, the population pharmacokinetic model estimated a mean apparent clearance (CL/F) of 3.86 L/h (inter-individual variability (IIV) of 22.4%) and apparent central volume of distribution (Vc/F) of 120 L (IIV of 42.0%) for an adult with a weight of 70 kg.

*Lactation*

A pharmacokinetic study in twelve healthy adult lactating women who were 21 to 100 weeks post partum evaluated the concentrations of moxidectin in plasma and breast milk collected over a period of 28 days following a single 8 mg dose of Moxidectin Tablets. The mean (± SD) exposure ratio of moxidectin present in human breast milk to that of human plasma was approximately 1.77 (± 0.66) over a collection period of 28 days. The estimated mean (± SD) total infant dose, assuming the infants would consume all the breast milk collected during the study, was 0.056 mg (± 0.024 mg), which would be approximately 0.70% (± 0.30%) of the maternal

dose. Based on a 5 Kg infant, the relative infant dose was estimated to be 8.73% (± 0.024 mg). The effects of moxidectin or its metabolites on the breast-fed child or milk production were not evaluated.

### 5.3 Preclinical safety data

Nonclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, and carcinogenic potential.

Effects in nonclinical studies were observed only at exposures in excess of human exposures with the recommended dose based on frequency of administration and dose administered.

Animal Toxicology and/or Pharmacology

In a pre-postnatal study in rats, maternal daily oral gavage administration of moxidectin at a dose approximately 11 times the recommended human dose based on body weight comparison (resulting in concentrations approximately 5 times the maximum plasma concentration after a clinical dose of 8 mg in breastfeeding women) during the lactation period resulted in adverse clinical signs, weight loss, and

increased mortality in rat pups suggesting moxidectin in the milk was responsible for the adverse effects.

In embryo-fetal development studies in rats and rabbits, moxidectin did not produce foetal malformations in rats or rabbits in the absence of toxicity in the mother. Developmental toxicity was observed at daily doses of 12 mg/kg in rats, consisting of a significantly increased foetal (but not litter) incidence of a malformation, cleft palate, and incidence of a skeletal variation, wavy ribs. These findings were attributed to maternal toxicity. In rabbits, no developmental effects were observed at the highest tested dose of 10 mg/kg/day.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

The Tablets are uncoated, and include the following excipients:

- colloidal silicon dioxide
- croscarmellose sodium
- lactose anhydrous
- magnesium stearate
- microcrystalline cellulose
- sodium lauryl sulfate.

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

Packaged shelf life: 24 months.

In-use shelf life: 14 days from first opening.

### 6.4 Special precautions for storage

Store below 30°C.

Protect from light.

### 6.5 Nature and contents of container

Each high-density polyethylene bottle contains 500 tablets, silica gel desiccant and rayon pharmaceutical coil.

### 6.6 Special precautions for disposal

Moxidectin is potentially harmful to aquatic life. Do not dispose into waterways or public sewer systems. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

## 7. MARKETING AUTHORIZATION HOLDER AND MANUFACTURING SITE ADDRESS

Medicines Development for Global Health
Address: Level 1, 18 Kavanagh Street, Southbank, Victoria, 3006
Country: Australia
Telephone: +61 399122400
Telefax: none
E-Mail: sarah.kilpatrick@medicinesdevelopment.com

## 8. MARKETING AUTHORIZATION NUMBER

FDA/GD.245-110321

## 9. DATE OF FIRST AUTHORIZATION/RENEWAL

**Nov/2024**

## 10. DATE OF REVISION OF TEXT

**June 2025**