SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

OVEX SUSPENSION

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml of suspension contains 100mg mebendazole.
Excipient(s) with known effect:
Sucrose 500mg/5ml
Methylparahydroxybenzoate (E218) 9mg/5ml
Propylparahydroxybenzoate (E216) 1mg/5ml
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral suspension

White homogeneous suspension

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of gastrointestinal infestations of *Enterobius vermicularis* (threadworm).

There is no evidence that Ovex is effective in the treatment of cysticercosis.

4.2 Posology and method of administration

Posology
Adults and children over 2 years: 1 x 5ml (1 dosing cup).
Care should be taken to avoid re-infection and it is strongly recommended that all members of the family are treated at the same time.
It is highly recommended that a second dose is taken after two weeks, if re-infection is suspected.

Method of administration
Oral

4.3 Contraindications

Ovex is contraindicated in pregnancy and in patients who have shown hypersensitivity to the active substance or any of the excipients listed in *section 6.1*.

4.4 Special warnings and precautions for use

Ovex is not recommended in the treatment of children aged under 2 years.

If symptoms do not disappear within a few days, consult your doctor.

A case-control study of a single outbreak of Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) suggested a possible association with the concomitant use of metronidazole with mebendazole. Although there are no additional data on this potential interaction, concomitant use mebendazole and metronidazole should be avoided.

Convulsions in children, including in infants below one year of age, have been reported very rarely during post-marketing experience with Ovex. Ovex Suspension should only be given to very young children if their worm infestation interferes significantly with their nutritional status and physical development.

Glomerulonephritis and agranulocytosis have been very rarely reported with dosages substantially above those recommended and with treatment for prolonged periods of time.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.

Methyl (E218) and propyl (E216) parahydroxybenzoate may cause allergic reactions which could possibly be delayed.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant treatment with cimetidine may inhibit the metabolism of mebendazole in the liver, resulting in increased plasma concentrations of the drug.

Concomitant use of mebendazole and metronidazole should be avoided (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

Since Ovex is contra-indicated in pregnancy patients who think they are or may be pregnant should not take this preparation.

Lactation

Limited data from case reports demonstrate that a small amount of mebendazole is present in human milk following oral administration. Therefore, caution should be exercised when Ovex is administered to breast-feeding women.

Fertility

The effect on human fertility has not been evaluated.

4.7 Effects on ability to drive and use machines

Ovex does not affect mental alertness or driving ability.

4.8 Undesirable effects

Throughout this section adverse reactions are reported. Adverse reactions are adverse events that were considered to be reasonably associated with the use of mebendazole based on the comprehensive assessment of the available adverse event information. A causal relationship with mebendazole cannot be reliably established in individual cases. Further, because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

At the recommended dose, Ovex is generally well tolerated. However, patients with high parasitic burdens when treated with Ovex have manifested diarrhoea and abdominal pain.

The safety of mebendazole was evaluated in 6276 subjects who participated in 39 clinical trials for the treatment of single or mixed parasitic infestations of the gastrointestinal tract. In these 39 clinical trials, no adverse drug reactions (ADRs) occurred in ≥ 1% of mebendazole-treated subjects.

ADRs identified from clinical trials and post-marketing experience with mebendazole are included in Table 1. The displayed frequency categories use the following convention:

Very common (≥ 1/10); Common (≥ 1/100 and < 1/10); Uncommon (≥ 1/1000 and < 1/100); Rare (≥ 1/10,000 and < 1/1000); Very rare (< 1/10,000); Not known (cannot be estimated from the available data).

Table 1: Adverse Drug Reactions Reported in Clinical Trials and Post-Marketing Experience for Mebendazole				
System Organ Class	**Adverse Drug Reactions**			
	Frequency Category			
	Common (≥ 1/100 to < 1/10)	**Uncommon** (≥ 1/1,000 to < 1/100)	**Rare** (≥ 1/10,000 to < 1/1,000)	**Very rare** (< 1/10,000)
Blood and lymphatic system disorders			Neutropenia [b]	Agranulocytosis [a, c]
Immune system disorders			Hypersensitivity including anaphylactic reaction and anaphylactoid reaction [b]	
Nervous system disorders			Convulsions [b] Dizziness [a]	
Gastrointestinal disorders	Abdominal pain [a]	Abdominal discomfort [a]; Diarrhoea [a]; Flatulence [a];		Nausea [b]; Vomiting [b]
Hepatobiliary disorders			Hepatitis [b]; Abnormal liver function tests [b]	
Skin and subcutaneous tissue disorders			Rash [a], Toxic epidermal necrolysis [b]; Stevens-Johnson syndrome [b]; Exanthema [b]; Angioedema [b]; Urticaria [b]; Alopecia [b]	
Renal and urinary disorders				Glomerulonephritis [a, c]

[a] ADR frequency data derived from Clinical Trials or Epidemiological Studies
[b] Adverse reactions reported during post-marketing surveillance
[c] Observed in higher and prolonged doses

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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

In patients treated at dosages substantially higher than recommended or for prolonged periods of time, the following adverse reactions have been reported rarely: alopecia, reversible liver function disturbances, hepatitis, agranulocytosis, neutropenia and glomerulonephritis. With the exception of agranulocytosis and glomerulonephritis, these also have been reported in patients who were treated with mebendazole at standard dosages (see Section 4.8).

Symptoms
In the event of accidental overdosage, abdominal cramps, nausea, vomiting and diarrhoea may occur.

Management
There is no specific antidote. Activated charcoal may be given if considered appropriate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic classification: Anthelmintic for oral administration, benzimidazole derivatives

ATC code: P02CA01

In vitro and *in vivo* work suggests that mebendazole blocks the uptake of glucose by adult and larval forms of helminths, in a selective and irreversible manner. Inhibition of glucose uptake appears to lead to endogenous depletion of glycogen stores within the helminth. Lack of glycogen leads to decreased formation of ATP and ultrastructural changes in the cells.

There is no evidence that Ovex is effective in the treatment of cysticercosis.

5.2 Pharmacokinetics properties

Absorption
Following oral administration, approximately 20% of the dose reaches the systemic circulation, due to incomplete absorption and to extensive pre-systemic metabolism (first-pass effect). Maximum plasma concentrations are generally seen 2 to 4 hours after administration. Dosing with a high fat meal leads to a modest increase in the bioavailability of mebendazole.

Distribution
The plasma protein binding of mebendazole is 90 to 95%. The volume of distribution is 1 to 2 L/kg, indicating that mebendazole penetrates areas outside the vascular space. This is supported by data in patients on chronic mebendazole therapy (e.g., 40 mg/kg/day for 3-21 months) that show drug levels in tissue.

Biotransformation
Orally administered mebendazole is extensively metabolized primarily by the liver. Plasma concentrations of its major metabolites (amino and hydroxylated amino forms of mebendazole) are substantially higher than those of mebendazole. Impaired hepatic function, impaired metabolism, or impaired biliary elimination may lead to higher plasma levels of mebendazole.

Elimination
Mebendazole, the conjugated forms of mebendazole, and its metabolites likely undergo some degree of enterohepatic recirculation and are excreted in the urine and bile. The apparent elimination half-life after an oral dose ranges from 3 to 6 hours in most patients.

Steady-state Pharmacokinetics
During chronic dosing (e.g., 40 mg/kg/day for 3-21 months), plasma concentrations of mebendazole and its major metabolites increase, resulting in approximately 3-fold higher exposure at steady-state compared to single dosing.

5.3 Preclinical safety data

Acute oral toxicity of mebendazole in a number of species is low with a large margin of safety. Chronic oral toxicity studies in rats at 40 mg/kg/day and above, showed altered liver weights with some slight centrilobular swelling and hepatocellular vacuolation, and altered testicular weights with some tubular degeneration, desquamation and marked inhibition of spermatogenic activity.

In genotoxicity studies mebendazole was aneugenic in mammalian somatic cells above a threshold plasma concentration of 115 ng/mL, but had no mutagenic or clastogenic activity. In limited long term studies in mice and rats no carcinogenic effects were seen.

Mebendazole has shown embryotoxic and teratogenic activity in pregnant rats and mice at oral doses of 10 mg/kg/day and above and in rats at a single dose of 10 mg/kg, approximately equivalent to the human dose of 100mg on a body surface area (mg/m^2) basis.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose

Microcrystalline cellulose and carmellose sodium

Methylcellulose 15 mPa.s

Methylparahydroxybenzoate (E218)

Propylparahydroxybenzoate (E216)

Sodium laurilsulfate

Banana flavour

Citric acid, monohydrate

Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Amber glass flask containing 30 ml suspension, with either:

- Pilfer-proof screw cap. Cork insert in cap is coated on both sides with polyvinylchloride

or

- Child-resistant polypropylene screw cap, lined inside with a LDPE insert.

A 5ml natural polypropylene (food-grade) dosing cup is also provided, graduated for 2.5 ml and 5 ml.

6.6 Special precautions for disposal and other handling

Shake well before use.
No special requirements for disposal.
Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

MCNEIL PRODUCTS LIMITED

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SL6 3UG
UNITED KINGDOM

8 MARKETING AUTHORISATION NUMBER(S)

PL 15513/0313

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

24/11/2004

10 DATE OF REVISION OF THE TEXT

27/03/2018