เอกสารกำกับยาสำหรับแพทย์ภาษาอังกฤษ

FUGACAR®

1. Name of the Medicinal Product

FUGACAR® (INN: mebendazole)

2. Qualitative and Quantitative Composition

Each tablet contains 500 mg mebendazole.

For excipients, see *section 6.1 List of Excipients.*

3. Pharmaceutical Form

Tablet

FUGACAR 500 mg tablet: Cream-coloured, circular, flat, bevel-edged tablet with the inscription "JANSSEN" on one side and "Me" on the other side.

500

4. Clinical Particulars

4.1 Therapeutic indication

Anthelmintic against thread worm and round worms.

4.2 Posology and method of administration

Dosage

For thread worm and round worms infection: 1 tablet once only.

Administration

Oral use.

Tablet

Tablets may be chewed or swallowed whole. The tablet must be crushed before it is given to a young child. A child must always be supervised while they are taking FUGACAR.

4.3 Contraindication

FUGACAR is contraindicated in persons with a known hypersensitivity to the drug or its excipients.

4.4 Special warning and precautions

1. Do not use in children under 2 years old

2. Should not be administered in pregnant woman during the first three months of pregnancy and patients suffering from liver disease.

There have been rare reports of reversible liver function disturbances, hepatitis, and neutropenia described in patients who were treated with mebendazole at standard dosages for indicated conditions (see *section 4.8 Undesirable effects*). These events, along with glomerulonephritis and agranulocytosis, have also been reported with dosages substantially above those recommended and with treatment for prolonged periods of time.

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 of mebendazole and metronidazole should be avoided.

Convulsions in children, including in infants below 1 year of age, have been reported very rarely during post-marketing experience (see *section 4.8 Undesirable effects*). Fugacar has not been extensively studied in children below the age of 2 years.

Fugacar should only be given to very young children if their worm infestation interferes significantly with their nutritional status and physical development.

4.5 Interaction with other medicinal products and other forms of interactions

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

Concomitant use of mebendazole and metronidazole should be avoided (see *section 4.4 Special warning and precautions*).

4.6 Fertility, pregnancy and lactation

Mebendazole has shown embryotoxic and teratogenic activity in rats and in mice. No harmful effects on reproduction were noted in other animal species tested (see *section 5.3 Preclinical Safety Data*).

The possible risks associated with prescribing FUGACAR 500 mg during pregnancy, particularly during the first trimester, should be weighed against the expected therapeutic benefits.

Breast-feeding

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 FUGACAR 500 mg is administered to breast-feeding women.

4.7 Effect on ability to drive and use machine

FUGACAR 500 mg does not affect the 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 Fugacar based on the comprehensive assessment of the available adverse event information. A causal relationship with Fugacar 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.

The safety of Fugacar 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 Fugacar-treated subjects.

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

Very common (≥1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1000 to <1/100); Rare (≥1/10,000 to <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 Fugacar

System Organ Class	Adverse Drug Reactions		
	Frequency Category		
	Common (≥ 1/100 to < 1/10)	**Uncommon** (≥ 1/1000 to < 1/100)	**Rare** (≥1/10,000 to <1/1000)
Blood and Lymphatic System Disorders			Neutropenia[b] Agranulocytosis[b] *
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[a], Vomiting[a]	
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[b] *

[a] ADR frequency data derived from Clinical Trials or Epidemiological Studies

[b] ADRs not observed in clinical trials and frequency calculated based on 6276 patients exposed in clinical trials and epidemiological studies, divided by 3 (Frequency = 1/2092).

* Observed in higher and prolonged doses

4.9 Overdose

Agranulocytosis and glomerulonephritis are adverse reactions for Echinococcosis treatment for which the dosage is higher and used for prolonged periods of time compared with other indications; therefore, these are expected symptoms of overdose for non-Echinococcosis indications (see *section 4.8 Undesirable effects*).

Signs and symptoms

In the event of accidental overdose, abdominal cramps, nausea, vomiting and diarrhea may occur.

Treatment

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

5. Pharmacological Properties

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: 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 Fugacar is effective in the treatment of cysticercosis.

5.2 Pharmacokinetic Properties

Absorption

Following oral administration, <10% of the dose reaches the systemic circulation, due to incomplete absorption and to extensive pre-systemic metabolism (first-pass effect). The majority of an orally administered dose remains in the gastrointestinal tract. Maximum plasma concentrations are generally seen 2 to 4 hours after administration.

Dosing with a high fat meal increases the bioavailability of mebendazole, although the overall effect of food on the amount of drug remaining in the gastrointestinal tract is not expected to be substantial.

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.

Metabolism

Orally administered mebendazole is extensively metabolized primarily by the liver. Plasma concentrations of its major metabolites (hydrolyzed and reduced forms of mebendazole)

are 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

In animal reproduction studies, adverse developmental effects (i.e., skeletal malformations, soft tissue malformations, decreased pup weight, embryolethality) were observed when mebendazole was administered to pregnant rats and mice throughout the period of organogenesis or as a single oral dose as low as 10 mg/kg in rats (approximately 0.2-fold the maximum recommended human dose (MRHD)). Maternal toxicity was present at the highest of these doses. Dosing of hamsters and rabbits did not result in embryotoxicity or teratogenicity. Doses up to 40 mg/kg in rats (0.8-fold the MRHD, based on mg/m^2), given to males for 60 days and to females for 14 days prior to gestation, had no effect upon fetuses and offspring.

No mutagenic activity was observed with mebendazole in bacterial reverse mutation tests. Mebendazole was mutagenic when tested in the mouse lymphoma thymidine kinase assay and aneugenic in vitro in mammalian somatic cells. In the in vivo mouse micronucleus assay, orally administered mebendazole induced an increased frequency of micronucleated polychromatic erythrocytes with evidence suggestive of aneugenicity.

Mebendazole had no carcinogenic effects at doses as high as 40 mg/kg/day when administered daily in the diet over 2 years in carcinogenicity tests in mice and rats (0.4 to 0.8-fold the MRHD, based on mg/m^2).

6. Pharmaceutical Particulars

6.1 List of excipients

colloidal anhydrous silica

lactose monohydrate

magnesium stearate

maize starch

methylcellulose

microcrystalline cellulose

sodium starch glycolate

6.2 Incompatibilities

None known.

6.3 Shelf life

See expiry date on the outer pack.

6.4 Special precautions for storage

Store below 30° C.

Keep out of the sight and reach of children.

6.5 Nature and contents of container

500 mg, Pack of 1 tablet.

1 carton contains 1 blister. Each blister contains 1 tablet.

Instructions for Use and Handling

Not applicable.

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Manufactured by

Lusomedicamenta Sociedade Técnica Farmacêutica, S.A., Barcarena, Portugal

Product Name	Marketing Authorization Numbers	Date of Authorization
FUGACAR®	1C 15021/64	19 March 2021

Imported by

Janssen-Cilag Ltd., Bangkok, Thailand

To report Suspected Adverse Reactions, please contact us at aepqcjacth@its.jnj.com

For any product information, please contact us at medinfosea@its.jnj.com