DATA SHEET

1 PRODUCT NAME

Benztropine Omega 1mg/ml Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL of sterile clear colourless solution contains: 1 mg of Benztropine mesylate and 9 mg of Sodium chloride in Water for injection.
Hydrochloric acid and/or Sodium hydroxide may have been added to adjust the pH.

3 PHARMACEUTICAL FORM

Solution for injection

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Benztropine Omega is recommended for all forms of parkinsonism including arteriosclerotic, postencephalitic, idiopathic, as well as medicine-induced extrapyramidal disorders (except tardive dyskinesia). It can be effective at any stage of the disease, even when a patient has become bedridden.

Benztropine Omega is often helpful in patients who have become unresponsive to other agents. Benztropine Omega is a powerful anticholinergic agent which is mainly effective in relieving tremor and rigidity. Therapy is directed toward control of disturbing symptoms to permit the patient maximum integration of function with minimum discomfort. In non-medicine-induced parkinsonism, partial control of symptoms is usually achieved.

4.2 Dose and method of administration
Benztropine Omega is available as an injection for intravenous and intramuscular use.

Because Benztropine Omega is cumulative in action, therapy should be initiated with a small dose which can then be increased gradually at five- or six-day intervals. Increases in dosage should be made in increments of 0.5 mg to a maximum of 6 mg.

The injection is especially useful for psychotic patients with acute dystonic reactions. There is no significant difference in onset of effect after intravenous and intramuscular injection. Improvement sometimes is noticeable within a few minutes after injection. In emergency situations, when the patient’s condition is alarming, administration of 1 to 2 mL of Benztropine Omega injection usually will provide quick relief. If the signs of parkinsonism begin to return, the dose can be repeated.

Some patients experience greatest relief when taking the entire dose at bedtime; others react more favourably to divided doses, two to four times a day.

Benztropine Omega data sheet dated 22 June 2017
The long duration of action of Benztropine Omega makes it particularly suitable for administration at bedtime when the effects may persist throughout the night. Consequently, Benztropine Omega enables the patient to turn in bed more easily and to rise in the morning.

Therapy with other agents for parkinsonism should not be terminated abruptly when Benztropine Omega is started, but reduced or discontinued gradually. Many patients obtain the greatest relief with a combination of Benztropine Omega and other medicines.

Benztropine Omega may be administered concomitantly with levodopa/carbidopa (in combination), or with levodopa, in which case periodic dosage adjustment may be required in order to maintain optimum response.

**Arteriosclerotic, Idiopathic and Postencephalitic Parkinsonism**

The usual daily dosage of Benztropine Omega is 1 to 2 mg, with a range of 0.5 to 6 mg.

Dosage must be individualised. In determining the dosage, the age and weight of the patient and the type of parkinsonism must be taken into consideration. Older patients, thin patients, and patients with arteriosclerotic parkinsonism generally cannot tolerate large doses. However, most patients with postencephalitic parkinsonism require and indeed, tolerate fairly large doses. Patients with a poor mental outlook are usually poor candidates for therapy.

In arteriosclerotic and idiopathic parkinsonism, therapy may be initiated with a single daily dose of 0.5 to 1 mg at bedtime. This dosage will be adequate in some patients, whereas 4 mg to 6 mg a day may be required by others.

In postencephalitic parkinsonism, therapy may be initiated in most patients with 2 mg a day in one or more doses. In highly sensitive individuals, therapy may be initiated with 0.5 mg at bedtime and increased as necessary.

**Medicine-Induced Parkinsonism**

When treating extrapyramidal disorders due to central nervous system medicines such as phenothiazine or reserpine, a dosage of 1 to 4 mg once or twice a day orally is recommended. Dosage should be varied to suit the needs of the patient. After one or two weeks of administration, Benztropine Omega should be withdrawn to determine the continued need for medication. If parkinsonism recurs, Benztropine Omega can be reinstituted.

Usually the injection of 1 to 2 mL of Benztropine Omega quickly relieves acute dystonic reactions, after which benztropine tablets, 1 to 2 mg twice a day, usually prevent recurrence.

### 4.3 Contraindications

Because of the atropine-like adverse effects, Benztropine Omega is contraindicated in children under three years of age, and should be used with caution in older children.

Benztropine Omega is contraindicated in patients who are hypersensitive to any component of this product.

Benztropine Omega is contraindicated in patients with tardive dyskinesia, narrow angle glaucoma (see section 4.4), dementia or prostatism.
4.4 Special warnings and precautions for use

Since Benztropine Omega has cumulative action, continued supervision is advisable.

Patients with a tendency to tachycardia, and patients with prostatic hypertrophy, should be closely observed during treatment.

In large doses, the medicine may cause complaints of weakness and inability to move particular muscle groups. For example, if the neck has been rigid and suddenly relaxes, it may feel weak, causing some concern. In this event, dosage adjustment is required.

Mental confusion and excitement may occur with large doses, or in susceptible patients. Visual hallucinations have been reported occasionally. Furthermore, in the treatment of extrapyramidal symptoms due to central nervous system medicines, such as phenothiazines, and reserpine in patients with a mental disorder, occasionally there may be intensification of mental disorders. In such cases, antiparkinsonian medicines can precipitate a toxic psychosis. Patients with mental disorders should be kept under careful observation, especially at the beginning of treatment or if dosage is increased.

Tardive dyskinesia may appear in some patients on long-term therapy with phenothiazines and related agents, or may occur after therapy when these medicines have been discontinued. Antiparkinsonism agents usually do not alleviate the symptoms of tardive dyskinesia, and in some instances may aggravate or unmask such symptoms. Benztropine Omega is not recommended in tardive dyskinesia (see section 4.3).

Since benztropine mesylate contains structural features of atropine, it may produce anhidrosis. For this reason, it should be given with caution during hot weather, especially when given concomitantly with other atropine-like medicines to the chronically ill, the alcoholic, those who have central nervous system disease and those who do manual labour in a hot environment. Anhidrosis may occur more readily when some disturbance of sweating already exists.

If there is evidence of anhidrosis, the possibility of hyperthermia should be considered. Dosage should be decreased at the discretion of the physician so that the ability to maintain body heat equilibrium by perspiration is not impaired. Severe anhidrosis and fatal hyperthermia have occurred.

The physician should be aware of the possible occurrence of glaucoma. Although the medicine does not appear to have any adverse effect on simple glaucoma, Benztropine Omega should not be used in narrow-angle glaucoma (see section 4.3).

Benztropine Omega should also be used with caution in patients with urinary retention, cardiovascular disease and hepatic or renal impairment.

4.5 Interaction with other medicinal products and other forms of interaction

When Benztropine Omega is given concomitantly with phenothiazines, haloperidol or other medicines with anticholinergic or antidopaminergic activity, patients should be advised to report gastrointestinal complaints fever or heat intolerance promptly. Paralytic ileus, sometimes fatal, has occurred in patients taking anticholinergic-type antiparkinsonism medicines, including Benztropine Omega, in combination with phenothiazines and/or tricyclic antidepressants.

4.6 Fertility, pregnancy and lactation

Pregnancy: The safe use of this medicine in pregnancy has not been established.

Nursing Mothers: It is not known whether this medicine is excreted in human milk. Because many medicines are excreted in human milk, caution should be exercised when Benztropine Omega is administered to a nursing mother.
4.7 Effects on ability to drive and use machines

**Occupational Hazards:** Benztropine mesylate may impair mental and/or physical abilities required for performance of hazardous tasks, such as operating machinery or driving a motor vehicle.

4.8 Undesirable effects

Adverse reactions most of which are anticholinergic or antihistaminic in nature, are listed below by body system in order of decreasing severity:

**Cardiovascular**
Tachycardia.

**Digestive**
Constipation, dry mouth, nausea, vomiting.

Adjustment of dosage or time of administration sometimes helps to control these reactions. If dry mouth is so severe that there is difficulty in swallowing or speaking, or loss of appetite and weight, reduce dosage, or discontinue the medicine temporarily.

Nausea unaccompanied by vomiting usually can be disregarded. Slight reduction in dosage may control the nausea and still give sufficient relief of symptoms. Vomiting may be controlled by temporary discontinuation, followed by resumption at a lower dosage.

**Nervous system**
Toxic psychosis including confusion, disorientation, memory impairment, visual hallucinations; exacerbation of pre-existing psychotic symptoms; nervousness; depression; listlessness; numbness of fingers.

**Special Senses**
Blurred vision, dilated pupils.

**Urogenital**
Urinary retention, dysuria.

**Metabolic/Immune and Skin**
Occasionally, an allergic reaction, e.g. skin rash, develops. Sometimes this can be controlled by reducing dosage, but occasionally benztropine mesylate has to be discontinued.

**Other**
Heart stroke, hyperthermia, fever.

4.9 Overdose

**Manifestations:** May be any of those seen in atropine poisoning or antihistamine overdosage: CNS depression, preceded or followed by stimulation; confusion; nervousness; listlessness; intensification of mental symptoms or toxic psychosis in patients with mental illness being treated with phenothiazine derivatives or reserpine; hallucinations (especially visual); dizziness; muscle weakness; ataxia; dry mouth; mydriasis; blurred vision; palpitations; nausea; vomiting; dysuria; numbness of fingers; dysphagia; allergic reactions, e.g., skin rash;
headache; hot, dry, flushed skin; delirium; coma; shock; convulsions; respiratory arrest; anhidrosis; hyperthermia; glaucoma; constipation.

**Treatment:** Physostigmine salicylate, 1 to 2 mg, s.c. or i.v., reportedly will reverse symptoms of anticholinergic intoxication (Duvoisin, R.C., Katz R., J. Amer. Med. Ass. 1968, 206: 1963-1965). A second injection may be given after 2 hours if required. Otherwise treatment is symptomatic and supportive. Induce emesis or perform gastric lavage (contraindicated in precomatose, convulsive, or psychotic states). Maintain respiration. A short-acting barbiturate may be used for CNS excitement, but with caution to avoid subsequent depression; supportive care for depression (avoid convulsant stimulants such as picrotoxin, pentylenetetrazol, or bemegride); artificial respiration for severe respiratory depression; a local miotic for mydriasis and cycloplegia; ice bags or other cold applications and alcohol sponges for hyperpyrexia, a vasopressor and fluids for circulatory collapse. Darken room for photophobia.

For advice on the management of overdose please contact with National Poisons Centre on 0800 POISON (0800 764766).

5 **PHARMACOLOGICAL PROPERTIES**

5.1 **Pharmacodynamic properties**

Pharmacotherapeutic group: Anticholinergic; ATC code: N04AC01

Benztropine Omega is a synthetic compound resulting from the combination of the active portions of atropine and diphenhydramine. Benztropine possesses both anticholinergic and antihistaminic effects, although only the former have been established as therapeutically significant in the management of parkinsonism.

Benztropine antagonizes the effect of acetylcholine. This decreases the imbalance between the neurotransmitters, acetylcholine and dopamine, which may improve the symptoms of early Parkinson’s disease.

This medicine has been granted a provisional consent under Section 23 of the Act. This means that further evidence on this medicine is awaited or that there are specific conditions of use. The provisional consent has been granted for two years to address an urgent shortage in the market.

5.2 **Pharmacokinetic properties**

In a clinical study measuring serum levels of neuroleptics and anticholinergics via radioreceptor assay, the correlation between total daily dose of benztropine and serum concentration was extremely poor ($r=0.281$). Serum concentrations varied nearly 100-fold with given doses between 2 and 6 mg/day. A markedly non-linear relationship between daily dose and serum anticholinergic medicine levels was observed with an increasing oral dosage of benztropine. In most cases, 2 mg increments in oral dose were associated with several-fold increases in the serum level of anticholinergic activity.

It has been reported that the duration of action for benztropine may persist for up to 24 to 48 hours following a single 2 mg IM injection. Benztropine binds extensively, approximately 95%, with serum proteins. Benztropine crosses the blood-brain barrier.

5.3 **Preclinical safety data**

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.
6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Sodium Chloride
Sodium hydroxide (for pH adjustment)
Water for Injections

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 months

6.4 Special precautions for storage
Do not store above 30°C. Protect from freezing.

6.5 Nature and contents of container
Benztropine Omega is supplied in glass vials of 2mL, contained within a carton pack of 10 vials.

6.6 Special precautions for disposal and other handling
Single use vial. Discard unused portion.

7 MEDICINE SCHEDULE
Prescription Medicine.

8 SPONSOR
A. Menarini New Zealand Pty Ltd
P O Box 90296,
Victoria Street West
Auckland 1142

Phone: 0800 102 349

9 DATE OF FIRST APPROVAL
22 June 2017

10 DATE OF REVISION OF THE TEXT
22 June 2017

Benztropine Omega data sheet dated 22 June 2017