Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Cogentin 1mg/ml Solution for Injection.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sterile injection of 'Cogentin' contains 1.0 mg/ml benzatropine mesilate. (2mg per 2ml ampoule)

For excipients, see 6.1

3 PHARMACEUTICAL FORM

Solution for Injection.
A clear, colourless, sterile solution for injection.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

'Cogentin' is an anti-parkinsonian agent with powerful anticholinergic effects.

It is indicated for symptomatic treatment of all types of 'classical' parkinsonism including arteriosclerotic, post-encephalitic, and idiopathic parkinsonism, and of extrapyramidal reactions induced by phenothiazines or reserpine. It is not recommended for use in tardive dyskinesia

4.2 Posology and method of adminstration

'Cogentin' Injection is only to be used in an emergency or when a patient is unable to swallow tablets.

As 'Cogentin' is cumulative in action, treatment should begin with a low dosage, which can be increased by amounts of 0.5 mg at intervals of five to six days, to the smallest dosage necessary for optimal relief without excessive side-effects. Maximum dosage, 6 mg a day.

'Cogentin' Injection may be used intramuscularly or intravenously in emergencies, or for patients unable to swallow tablets. (As there is no significant difference in time of onset of effect between intramuscular and intravenous administration, the intravenous route is not usually necessary.)

In emergencies, 1-2 ml (1-2 mg) of 'Cogentin' Injection will normally provide quick relief. If signs of parkinsonism begin to return, the dose can be repeated.

'*Classical' parkinsonism: Usual dosage*: 1-2 mg a day, with a range of 0.5-6 mg a day. Dosage must be adjusted on an individual basis, taking into consideration the age and weight of the patient, and the type of parkinsonism. Older patients, thin patients and those with arteriosclerotic parkinsonism usually cannot tolerate large dosages. Most patients with post-encephalitic parkinsonism need and indeed tolerate fairly large dosages. Patients with a poor mental outlook may respond poorly. In arteriosclerotic and idiopathic parkinsonism, therapy may be initiated with a single daily dose of 0.5-1 mg at bedtime. This dosage will be adequate in some patients, whereas 4-6 mg a day may be required by others. In post-encephalitic 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.

Some patients obtain greatest relief by taking the entire dose at bedtime; others react more favourably to divided dosage, two to four times a day. One dose a day frequently is sufficient; divided doses may be unnecessary or even undesirable.

Drug-induced parkinsonism: Usual dosage range: 1-4 mg once or twice a day.

Acute dystonic reactions: 1-2 ml (1-2 mg) by intravenous injection followed usually by 1-2 mg orally twice a day.

Extrapyramidal reactions appearing soon after starting phenothiazine or reserpine therapy are likely to be temporary, and are usually controlled in one or two days by 1-2 mg of 'Cogentin' two or three times a day. 'Cogentin' should be withdrawn after one or two weeks to determine if it is still needed. It can be reinstated if necessary.

Certain extrapyramidal reactions which develop slowly (e.g. tardive dyskinesia) do not usually respond to 'Cogentin'.

Paediatric use: Use with caution in children over 3 years old (see section 4.3 'Contra-indications').

Use in the elderly: As with younger patients, dosage should be the smallest possible for optimum relief of symptoms. Initial dosage should be 0.5-1 mg preferably at night, increasing until optimum effect is seen. Older patients usually cannot tolerate large doses.

4.3 Contraindications

Because of the atropine-like side effects, 'Cogentin' is contra-indicated in children under 3 years old and should be used with caution in older children. 'Cogentin' is contra-indicated in patients who are hypersensitive to this product or who have prostatic hypertrophy, pyloric stenosis, paralytic ileus or closed angle glaucoma.

4.4 Special warnings and special precautions for use

Continued supervision of patients is recommended as 'Cogentin' has a cumulative action. Patients with a tendency towards tachycardia and those with prostatic hypertrophy, should be closely observed.

Patients with mental disorders should be carefully supervised when 'Cogentin' is used to control drug-induced extrapyramidal reactions, especially when therapy is started or the dosage of 'Cogentin' is increased. Intensification of mental symptoms may occasionally occur. 'Cogentin' should be temporarily withdrawn if the reactions are severe.

'Cogentin' has anticholinergic effects, and glaucoma is a possibility. Although 'Cogentin' does not appear to have any adverse effect on simple glaucoma, its use is probably not advisable in narrow-angle glaucoma. It may cause anhidrosis; this should be borne in mind, particularly in hot weather, especially when given concomitantly with other atropine-like drugs to the chronically ill, alcoholics, or patients with a central nervous system disease and those who do manual labour in a hot environment. 'Cogentin' should be used cautiously in patients with or prone to abnormalities of sweating.

If there is evidence of anhidrosis, the possibility of hyperthermia should be considered. Dosage should be decreased as necessary to maintain body heat equilibrium by the action of perspiration. Severe anhidrosis and fatal hyperthermia have occurred.

4.5 Interaction with other medicinal products and other forms of interaction

The anticholinergic effects of this product are likely to be increased by concomitant use of amantadine, anti-histamines, phenothiazines, butyrophenones, tricyclic anti-depressants and other drugs with anticholinergic or antidopaminergic effects. Extra care should be taken when 'Cogentin' is given concomitantly with these medications. Patients should be advised to report gastro-intestinal complaints, fever or heat intolerance promptly.

Paralytic ileus, sometimes fatal, has occurred in patients taking anticholinergic-type anti-parkinsonian drugs, including 'Cogentin', in combination with phenothiazines and/or tricyclic antidepressants.

Tardive dyskinesia may appear in some patients on long-term therapy with phenothiazines or related agents, after discontinuation of such therapy. Anti-parkinsonian agents do not usually alleviate symptoms of tardive dyskinesia, and in some cases may aggravate or unmask them. 'Cogentin' is not recommended in tardive dyskinesia.

4.6 Pregnancy and lactation

It is not known whether 'Cogentin' can cause foetal harm when administered to a pregnant woman or can affect reproductive capacity. 'Cogentin' should be given to a pregnant woman only if clearly needed.

Breast-feeding mothers: it is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when 'Cogentin' is administered to a breast-feeding mother.

4.7 Effects on ability to drive and use machines

'Cogentin' may impair the mental alertness and physical ability required for the performance of such hazardous tasks as driving a car or operating machinery.

4.8 Undesirable effects

Side effects, 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.

If dry mouth is so severe that there is difficulty in swallowing or speaking, or loss of appetite and weight occur, reduce dosage, or discontinue the drug temporarily.

Slight reduction in dosage may control 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. If this cannot be controlled by dosage reduction, the medication should be discontinued.

Other
Heat stroke, hyperthermia, fever

4.9 Overdose

Symptoms may be any of those seen in atropine poisoning or antihistamine overdosage: Central nervous system (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 neuroleptic drugs (e.g. phenothiazines); hallucinations (especially visual); dizziness; muscle weakness; ataxia; dry mouth; mydriasis; blurred vision; palpitations; tachycardia; 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.

Physostigmine salicylate (1-2 mg, subcutaneously or intravenously) is reported to reverse symptoms of anticholinergic intoxication. A second injection may be given after two hours if needed. Otherwise, treatment is symptomatic and supportive.

A short-acting barbiturate may be used for CNS excitement, but with caution to avoid subsequent depression. Supportive care for CNS depression may be required (such convulsant stimulants as picrotoxin, leptazol or bemegride should be avoided). In severe respiratory depression, artificial respiration may be required. Also needed may be 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, and a darkened room for photophobia.

Data on the metabolism of benzatropine maleate are not available at present; but a death was recorded 1½ hours after ingestion.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Anticholinergic drugs exert their anti-parkinsonian effect by correcting the relating cholinergic excess which is thought to occur in parkinsonism as a result of dopamine deficiency.

The deficiency of dopamine in the striatum of patients with parkinsonism intensifies the excitatory effects of the cholinergic system within the striatum. Anticholinergics aid such patients by blunting this component of the nigrostriated pathway.

5.2 Pharmacokinetic properties

Following i.m. injection, the clinical effects of benzatropine are apparent within 10 minutes and the maximum effect is seen within 30 minutes.

Benzatropine has a cumulative effect and a prolonged duration of action when compared with other anticholinergic agents used in the treatment of Parkinson’s it may take up to seven days before all evidence of drug-related effects have ceased.

5.3 Preclinical safety data

No relevant information.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Water for injections

6.2 Incompatibilities

None known.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 25°C. Do not freeze.

Keep the vial in the outer carton.

6.5 Nature and contents of container

Type I glass ampoules containing 2mls of solution.

6.6 Instructions for use and handling

For single use only. Discard any unused contents.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER

PA 35/46/2

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