PRODUCT MONOGRAPH

[Pr] PARSITAN 50

Ethopropazine Hydrochloride Tablets

Tablet, 50 mg ethopropazine (as ethopropazine hydrochloride), Oral

Manufacturer's Standard

Antiparkinsonian Agent

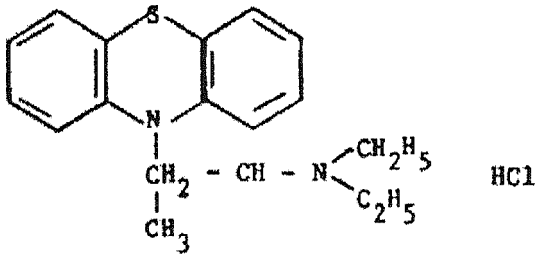
Searchlight Pharma Inc.
1600 Notre-Dame West, Suite 312
Montreal, Quebec
H3J 1M1

Date of Preparation:
OCT 06, 2022

Submission Control No: 267409

STRUCTURAL FORMULA AND CHEMISTRY

Parsitan 50 is 10-2(2-diethylaminopropyl)phenothiazine. Its structural formula may be represented as follows:



Molecular formula: $C_{19}H_{24}N_2S$ HCl
Molecular weight: 348.92
Melting point: 233 - 225°C

It is a fine, white, odorless and non-hygroscopic crystalline powder. It is soluble in absolute alcohol and chloroform, slightly soluble in water at 20°C, very slightly soluble in acetone and insoluble in ether and benzene.

ACTION

Parsitan 50 is an antiparkinsonian agent with potent anticholinergic, para-sympatholytic and antispasmodic activities but with weak adrenolytic and antihistaminic effects. It exerts a strong antagonist action against nicotine-induced convulsions.

INDICATIONS

In the symptomatic treatment of drug-induced extrapyramidal reactions and of the manifestations (rigidity, akinesia, sialorrhea, oculogyric crisis, tremor, etc.) of Parkinson's disease of encephalitic, arteriosclerotic or idiopathic origin.

CONTRAINDICATIONS

Glaucoma and hypersensitivity to phenothiazine drugs are the usual contraindications to the use of Parsitan 50.

WARNING

Because of its anticholinergic effects, administer Parsitan 50 with great caution in patients with prostatic hypertrophy, pyloric stenosis of cardiovascular diseases.

PRECAUTIONS

Parsitan 50 treatment should be instituted in low doses which should be increased progressively until a satisfactory maintenance dosage is obtained. When substituting Parsitan 50 for another antiparkinsonian reduce the dosage of the former drug slowly, while progressively increasing the Parsitan 50 dosage: its dosage should

be reduced gradually.

Phenothiazines may in rare instances cause blood dyscrasias. Even if no such case has been reported with Parsitan 50, it is advisable, during protracted therapy at high dosages, to watch for clinical signs of these disorders and to conduct blood tests at regular intervals. The concomitant administration of drugs such as thiouracil or aminopyrine, which may affect the blood picture, should also be avoided.

ADVERSE REACTIONS

At normal recommended doses, adverse reactions are few and when they do occur they are usually minor and transient. They may be classified as follows :

Central nervous system: Of possible CNS effects, drowsiness and tiredness are the most frequently observed and they usually appear at the beginning of treatment or when the dose has been increased too rapidly; they are sometimes accompanied by dizziness and mild headache which usually subside within a few days.

Rare cases of ataxia or a worsening of parkinsonism have been reported. Prolonged treatment with high doses may produce CNS stimulation characterized by irritability and formication.

Autonomic nervous system: These reactions consist of dryness of the mouth, transient diplopia and paresthesia and are due to the anticholinergic properties of the drug.

Gastrointestinal system: Rare cases of epigastric discomfort.

Cardiovascular system: In rare instances, following large initial doses, tachycardia and orthostatic hypotension.

Toxic or allergic effects: Very few cases of cholestatic jaundice and cutaneous reactions have been observed.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Symptoms: CNS depression or paradoxical stimulation, respiratory depression, cardiovascular collapse and extrapyramidal reactions.

Treatment: Gastric lavage, if performed early after the ingestion of the drug, can remove significant amounts of the product. Otherwise, the treatment is symptomatic.

In cases of lethargy or coma, a CNS stimulant like caffeine can be administered with caution; do not administer a stimulant of the picrotoxin type since it can induce convulsions. In the presence of circulatory collapse, administer dextrose in an infusion solution. If a presser agent is required, use norepinephrine added to the infusion liquid and not epinephrine which could aggravate hypotension. To alleviate agitation or convulsions, administer chloral hydrate, paraldehyde or Gardenal; however, these agents should be used with caution since they can depress respiration.

Keep the respiratory tract free and allow for sufficient oxygenation. Wide spectrum antibiotics may prevent risks of pulmonary infection.

PHARMACOLOGY

Ethopropazine possesses a potent spasmolytic action as measured *in vitro* on the spasm induced by acetylcholine and barium chloride on the isolated rabbit intestine.

In vivo, ethopropazine exerts a potent parasympathetic activity: it diminishes salivation and abolishes the hyperistalsis produced by acetylcholine on the small intestine. Furthermore, Parsitan 50 is twice as efficient as diethazine in reversing hypotension and reflex bradycardia caused by electrical stimulation of the peripheral and of the vagus nerve.

Parsitan 50 is a strong antagonis of nicotine-induced convulsions in the rabbits; it has but little adenolytic and antihistaminic activity.

In the dog and in the rabbit, after the injection of a single 250 mg/Kg s.c. dose, Parsitan 50 is found in the blood mainly in the unconjugated form; two hours after the injection, the concentration does not exceed 9% of the administered dose and only traces are still detectable after24 hours. Only 3 to 4% of the injected material is recovered from the urine, primarily in the conjugated form.

TOXICITY

The LD_{50}'s of Parsitan 50 are 650 mg/Kg p.o., 500 mg/Kg s.c. and 40 to 45 mg/Kg i.v. in the mouse and 250 mg/Kg s.c. and 15 mg/Kg i.v. in the rabbit.

DOSAGE AND ADMINISTRATION

The dosage must be adapted to each individual. In drug induced extrapyramidal reactions 100 mg b.i.d. usually bring about good control of symptoms.

In post-encephalitic, arterioscleroticor idiopathic parkinsonism, initiate treatment of a low dose of 50 mg three times a day and increase from 50 to 100 mg daily every 2 or 3 days until the optimum effect is obtained or the limit of tolerance is attained. Drowsiness and anticholinergic effects which may appear at the beginning of treatment generally subside after a few days. The normal daily dose usually ranges between 100 and 500 mg but it may reach l g or more per day in certain patients.

DOSAGE FORMS

Tablets of 50 mg, bottles of 100.

REFERENCES

SIGWALD, J. :
Un nouveau médicament symptomatique des syndromes parkinsoniens: le chlorhydrate de (diethylamino- 2'methyl 2') ethyl l' N-dibenzo-parathiazine.
Preliminary Information for Clinical Investigators on "Lysivane" brand of N-(2-diethylamino-n-propyl) phenothiazine hydrochloride. MAY &BAKER, July 1949.

LEBLOND, S and PICHETTE, R. :
Tentatives de traitement de la maladie de Parkinson. Laval Med., 156, February 1951.

MAROTTA, M. and BOVET, D. :
Action sur1'ulcere gastrique experimental du rat, des dérivés de la phenothiazine et en particulier du Diparcol, du Parsidol et du Phenergan.
Arch. Int. Phannacodyn., LXXXVI, (II), April 1si, 1951.

GILLHESPY, R.0. :
Lysivane in the treatment of parkinsonism. Brit. Med. J., 301, August 4, 1951.

PERREAU, P., FRESNEAU, M. and PASQUIER, C. :
Chorée aigue rhumatismale résistant aux traitements classiques et a l'ACTH. Guérison par un antiparkinsonien de synthèse. Ouest Med., 3, 58-59, 1953.

DOSHAY, L.J., CONSTABLE Kate and AGATE, F.J.:
Ethopropazine (Parsidol) hydrochloride in treatment of paralysis agitans.
J.A.M.A., 160, 348-351, February 1956.

ST-JEAN, A., DONALD, M. and BAN, T.A.:
Interchangeability of antipark:isonian medication. Am. J. Psychiat., 120, 1189-1190, June 1964.

RICHARDSON, J.C. and LEE, R.G. :
Drugs of parkinsonism.
Can. Med. Assoc. J., 92, 17, 928-929, April 1965.

KRUSE, W.:
Treatment of drug-induced extrapyramidal symptoms (A comparative study of three antiparkinson agents). Diseases Nervous System, 79-81, February 1960.

ELIE, R., MORIN, L. and TETREAULT, L.:
Effets de l'othopropazine et du trihexyphénidyle sur quelques paramètres du syndrome neuroleptique. (Submitted for publication).