PRODUCT MONOGRAPH

[Pr]TEVA-HALOPERIDOL

Haloperidol Tablets
USP

0.5, 1, 2, 5, 10 and 20 mg

Antipsychotic

Teva Canada Limited
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Toronto, Ontario
Canada M1B 2K9
www.tevacanada.com

Date of Revision:
August 26, 2016

Control No.: 196054

ACTION

Haloperidol is a butyrophenone derivative with antipsychotic properties that has been considered particularly effective in the management of hyperactivity, agitation, and mania. Haloperidol is an effective neuroleptic and also possesses antiemetic properties; it has a marked tendency to provoke extrapyramidal effects and has relatively weak alphaadrenolytic properties. It may also exhibit hypothermic and anorexiant effects and potentiates the reaction of barbiturates, general anesthetics and other CNS depressant drugs.

As with other neuroleptics, the mechanism of action of haloperidol has not been entirely elucidated, but has been attributed to the inhibition of the transport mechanism of cerebral monoamines, particularly by blocking the impulse transmission in dopaminergic neurons.

Peak plasma levels of haloperidol occur within 2 to 6 hours of oral dosing and about 20 minutes after intramuscular administration. The mean plasma (terminal elimination) half-life has been determined at 20.7 ± 4.6 (SD) hours, and although excretion begins rapidly, only 24 to 60% of ingested radioactive drug is excreted (mainly as metabolites in urine, some in feces) by the end of the first week, and very small but detectable levels of radioactivity persist in the blood and are excreted for several weeks after dosing. About 1% of the ingested dose is recovered unchanged in the urine.

INDICATIONS AND CLINICAL USES

TEVA-HALOPERIDOL (haloperidol) is indicated in the management of manifestations of acute and chronic psychosis, including schizophrenia and manic states. It may also be of value in the management of aggressive and agitated behavior in patients with chronic brain syndrome and mental retardation and in the symptomatic control of Gilles de la Tourette's syndrome.

CONTRAINDICATIONS

TEVA-HALOPERIDOL (haloperidol) is contraindicated in comatose states and in the presence of CNS depression due to alcohol or other depressant drugs. It is also contraindicated in patients with significant depressive states, previous spastic diseases, and in Parkinson's syndrome, except in the case of dyskinesias due to levodopa treatment. It should not be used in patients shown to be sensitive to the drug, nor in senile patients with pre-existing Parkinson-like symptoms.

Use in Children: Safety and effectiveness in young children have not been established; therefore, haloperidol is contraindicated in this age group.

Use in Pregnancy: Safe use of haloperidol in pregnancy has not been established. It should, therefore, not be used in women of child-bearing potential unless, in the opinion of the physician, the expected benefits of the drug outweigh the potential hazard to the fetus.

WARNINGS AND PRECAUTIONS

TEVA-HALOPERIDOL (haloperidol) prolongs the hypnotic action of barbiturates and may potentiate the effects of alcohol and other central nervous system depressant drugs, such as anesthetics and narcotics; caution should therefore be exercised when it is used with agents of this type and adjustments in its dosage may be required.

Haloperidol may lower the convulsive threshold and has been reported to trigger seizures in previously controlled known epileptics. When instituting haloperidol therapy in these patients, adequate anticonvulsant medication should be maintained concomitantly.

Elderly or debilitated patients receiving the drug should be carefully observed for any evidence of oversedation which might lead to dehydration and reduced pulmonary ventilation and could result in complications, such as terminal bronchopneumonia.

Although haloperidol is a relatively non-sedating neuroleptic, sedation may occur in some patients. Therefore, physicians should be aware of this possibility and caution patients about the danger of participating in activities requiring complete mental alertness, judgment and physical coordination, such as driving and operating dangerous machinery.

Haloperidol has been reported to interfere with the anticoagulant properties of phenindione in an isolated case, and the possibility should be kept in mind of a similar effect occurring when haloperidol is used with other anticoagulants.

Administration to patients with severe cardiac involvement should be guarded, despite the fact that haloperidol is well tolerated by patients with cardiac insufficiency and that it has been used with favorable results to maintain the cardiovascular function of patients with excitive crises. In very rare instances, it has been felt that haloperidol was contributory to the precipitation of attacks in angina-prone patients. Moderate hypotension may occur with parenteral administration or excessive oral doses of haloperidol; however, vertigo and syncope occur only rarely.

Haloperidol has lowered the level of cholesterol in the serum and liver of monkeys. An accumulation of desmosterol has been observed in the serum of rats given repeated high doses (10 mg/kg) of haloperidol. In man, mild transient decreases in serum cholesterol were reported in preliminary studies. However, in a study involving a group of schizophrenic patients on extended medication, significant lowering of serum cholesterol was not observed with haloperidol, and there was no accumulation of desmosterol or 7-dehydrocholesterol. A significant lowering of cholesterol together with an accumulation of another sterol (possibly 7-dehydrocholesterol) has been reported in patients receiving a chemically related drug (trifluperidol), and skin and eye changes (ichthyosis and cataracts) have occurred clinically with another butyrophenone derivative. Skin and eye changes have not been observed in patients receiving haloperidol. However, it is advisable that all patients receiving haloperidol for a prolonged period of time be carefully observed for any changes in the skin and eyes. If such changes are seen, the drug should be discontinued promptly.

Tardive dyskinesias are known to occur in patients on long-term antipsychotic therapy, including haloperidol (see ADVERSE REACTIONS). This should be borne in mind when using

neuroleptics, and if possible, the dosage should be reduced or the drug discontinued when manifestations of this syndrome are detected.

The antiemetic action of haloperidol may obscure signs of toxicity due to overdosage of other drugs or mask the symptoms of some organic diseases, such as brain tumor or intestinal obstructions.

If an antiparkinson agent is used concomitantly with haloperidol, both drugs should not be discontinued simultaneously, since extrapyramidal symptoms may occur due to the slower excretion rate of haloperidol.

Neuroleptic drugs elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent *in vitro*, a factor of potential importance if the prescription of these drugs is contemplated in a patient with a previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia and impotence have been reported, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms has been found in rodents after chronic administration of neuroleptic drugs. Neither clinical studies nor epidemiologic studies conducted to date, however have shown an association between chronic administration of these drugs and mammary tumorigenesis; the available evidence is considered to be too limited to be conclusive at this time.

Neutropenia, granulocytopenia and agranulocytosis have been reported during antipsychotic use. Therefore, it is recommended that patients have their complete blood count (CBC) tested prior to starting TEVA-HALOPERIDOL and then periodically throughout treatment.

Withdrawal Emergent Neurological Signs: Abrupt withdrawal after short-term administration of antipsychotic drugs does not generally pose problems. However, transient dyskinetic signs are experienced by some patients on maintenance therapy after abrupt withdrawal. The signs are very similar to those described under Tardive Dyskinesia, except for duration. Although it is not known whether gradual withdrawal of antipsychotic drugs will decrease the incidence of withdrawal emergent neurological signs, gradual withdrawal would appear to be advisable.

Endocrine and Metabolism:

Hyperglycemia:

Diabetic ketoacidosis (DKA) has occurred in patients with no reported history of hyperglycemia. Patients should have baseline and periodic monitoring of blood glucose and body weight.

Hyperprolactinemia:

Long-standing hyperprolactinemia when associated with hypogonadism may lead to decreased bone mineral density in both female and male subjects.

Genitourinary

Rare cases of priapism have been reported with antipsychotic use, such as haloperidol.

This adverse reaction, as with other psychotropic drugs, did not appear to be dose-dependent and did not correlate with the duration of treatment.

Special Populations, Pregnant Women:

Non-Teratogenic Effects

Neonates exposed to antipsychotic drugs (including haloperidol) during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms following delivery. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress and feeding disorder in these neonates. These complications have varied in severity; while in some cases symptoms have been self-limited, in other cases neonates have required intensive care unit support and prolonged hospitalization.

TEVA-HALOPERIDOL should not be used during pregnancy unless the expected benefits to the mother markedly outweigh the potential risks to the fetus.

Hematologic:

Venous Thromboembolism:

Venous thromboembolism (VTE), including fatal pulmonary embolism, has been reported with antipsychotic drugs, including Haloperidol Decanoate, in case reports and/or observational studies. When prescribing Haloperidol Decanoate all potential risk factors for VTE should be identified and preventative measures undertaken.

ADVERSE REACTIONS

Neurological: Neuromuscular (extrapyramidal) effects such as Parkinson-like symptoms, akathisia, dyskinesia, dystonia, hyper-reflexia, rigidity, opisthotonas and occasionally, oculogyric crisis are the most frequently reported side effects associated with the administration of haloperidol. Headache, vertigo and cerebral seizures have also been reported. The extrapyramidal reactions are usually dose-related in occurrence and severity and as a rule, tend to subside when the dose is reduced or the drug is temporarily discontinued. However, considerable inter-patient variability exists and although some individuals may tolerate higher than average doses of haloperidol, severe extrapyramidal reactions, necessitating discontinuation of the drug, may occur at relatively low doses. Administration of an anti-Parkinson agent is usually, but not always, effective in preventing or reversing neuromuscular reactions associated with haloperidol.

Tardive Dyskinesias: As with all antipsychotic agents, tardive dyskinesia may appear in some patients on long-term therapy or may appear after drug therapy has been discontinued. The risk appears to be greater in elderly patients on high dose therapy, especially females. The symptoms are persistent and in some patients appear to be irreversible. The syndrome is characterized by rhythmical involuntary movements of the tongue, face, mouth or jaw (e.g. protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes they may be accompanied by involuntary movements of extremities.

There is no known effective treatment for tardive dyskinesia; anti-Parkinsonism agents usually do not alleviate the symptoms of this syndrome. It is suggested that all antipsychotic agents be discontinued if these symptoms appear. Should it be necessary to reinstitute treatment or increase the dosage of the agent, or switch to a different antipsychotic agent, the syndrome may be masked. The physician may be able to reduce the risk of this syndrome by minimizing the unnecessary use of neuroleptic drugs and reducing the dose or discontinuing the drug if possible, when manifestations of this syndrome are recognized particularly in patients over the age of 50. It has been reported that fine vermicular movements of the tongue may be an early sign of the syndrome and if the medication is stopped at that time the syndrome may not develop.

Behavioral: Insomnia, depressive reactions, and toxic confusional states are the more common effects encountered. Drowsiness, lethargy, stupor and catalepsy, confusion, restlessness, agitation, anxiety, euphoria, and exacerbation of psychotic symptoms, including hallucinations, have also been reported.

Cardiovascular: Tachycardia and hypotension have occurred but severe orthostatic hypotension has not been reported. However, should it occur, supportive measures, including intravenous vasopressors such as norepinephrine may be required. EPINEPHRINE SHOULD NOT BE USED, since haloperidol may block the vasoconstrictor effects of this drug.

Autonomic: Dry mouth, blurred vision, urinary retention and incontinence have been reported.

Allergic and Toxic: The overall incidence of significant hematologic changes in patients on haloperidol has been low. Occasionally, there have been reports of mild and usually transient leukopenia and leukocytosis, decreases in blood cell counts, anemia, and a tendency toward lymphomonocytosis. Agranulocytosis has rarely been reported with the use of haloperidol, and then only in associated with other medication. Impairment of liver function (jaundice or hepatitis) has been reported rarely. One case of photosensitization is known and isolated cases of idiosyncratic cutaneous involvement have been observed.

Endocrine: Lactation, breast engorgement, mastalgia, menstrual irregularities, gynecomastia, impotence, increased libido and changes in blood sugar levels have been reported.

Gastrointestinal: Heartburn, nausea, vomiting, anorexia, weight loss, constipation, diarrhea and hypersalivation have been reported.

Miscellaneous: Other untoward effects encountered include peripheral edema, hypocholesterolemia, hyperpyrexia, alopecia, laryngospasm, bronchospasm and increased depth of respiration, stasis pneumonia, and a syndrome characterized by perspiration, dehydration, hyperthermia and a dazed state of mind (if this occurs the drug should be discontinued).

Patients should be advised of the risk of severe constipation during TEVA-HALOPERIDOL treatment, and should tell their doctor if constipation occurs or worsens, as they may need laxatives.

SYMPTOMS AND TREATMENT OF OVERDOSAGE:

For management of a suspected drug overdose, contact your regional Poison Control Centre.

In general, the symptoms of overdosage would be an exaggeration of known pharmacologic effects and adverse reactions, the most prominent of which would be 1) severe extrapyramidal reactions, 2) hypotension, or 3) sedation. The patient would appear comatose with respiratory depression and hypotension which could be severe enough to produce a shock-like state. The extrapyramidal reaction would be manifested by muscular weakness or rigidity and a generalized or localized tremor as demonstrated by the akinetic or agitans types, respectively.

Gastric lavage or induction of emesis should be carried out immediately followed by administration of the universal antidote. Since there is no specific antidote, treatment is primarily supportive. A patent airway must be established by use of an oropharyngeal airway or endotracheal tube or in prolonged cases of coma, by tracheotomy. Respiratory depression may be counteracted by artificial respiration and mechanical respirators. Hypotension and circulatory collapse may be counteracted by use of intravenous fluids, plasma, or concentrated albumin, and vasopressor agents such as norepinephrine. Epinephrine should not be used. In case of severe extrapyramidal reactions, antiparkinson medication should be administered.

DOSAGE AND ADMINISTRATION

Initial dosage should be individualized through consideration of severity of symptoms, age, weight, health, previous response to neuroleptic drugs and concomitant disease states. It is important initially to increase dosage adequately until symptoms are controlled or side effects requiring lowering the dosage or discontinuing the drug are encountered, when a satisfactory therapeutic response is achieved, dosage should then be reduced gradually to the lowest effective maintenance level.

Patients with previous adverse responses to other neuroleptic drugs, children and the elderly or debilitated may require less haloperidol. The optimal response in such patients is best obtained if therapy is initiated at a lower dosage level and titration is more gradual.

Initially, oral dosages of 1-2 mg, b.i.d. or t.i.d. are usually employed, followed by upward adjustment as tolerated until the desired effect is achieved or limiting side effects appear. Clinical experience has shown that it is seldom necessary to employ dosages greater than 4-6 mg t.i.d. However, 30-40 mg daily may be required in severely disturbed patients who remain inadequately controlled by lower doses and up to 100 mg daily has been used occasionally in particularly resistant patients. Nevertheless, the safety of prolonged administration of the higher doses has not been established. After a therapeutic response has been achieved, dosages should be gradually adjusted downwards until a schedule providing adequate maintenance is reached. Maintenance dosages are commonly in the range of 1-2 mg t.i.d. or q.i.d.

Children (6 years or over, and able to swallow the tablets) and Elderly or Debilitated Patients:
Lower doses are recommended in these patients since they may be more sensitive to the drug.

Initial daily doses ranging from 0.5 to 1.5 mg (0.25* to 0.5 mg, 2 or 3 times a day) should be employed. Upward adjustment of these doses should be made gradually maximum and maintenance doses should be individualized and are generally lower in this type of patient.
*Please note that Teva does not hold a liquid dosage form to reach the 0.25mg dose, and the 0.5mg tablets cannot be split in halves.

AVAILABILITY

TEVA-HALOPERIDOL (haloperidol) tablets are supplied as:

0.5 mg: Small, white, round, flat-faced, bevel-edged, compressed tablets, engraved **0.5** between vertical broken bisect on one side and **novo** on the reverse. Bottles of 100 tablets.

1.0 mg: Small, yellow coloured, round, flat-faced, bevel-edged, compressed tablets, engraved **1** between broken bisect on one side and stylized **N** on the reverse. Bottles of 100 tablets.

2.0 mg: Pink coloured, round, flat-faced, bevel-edged, compressed tablets, engraved **2** between broken horizontal bisect on one side and stylized **N** on the reverse. Bottles of 100 tablets.

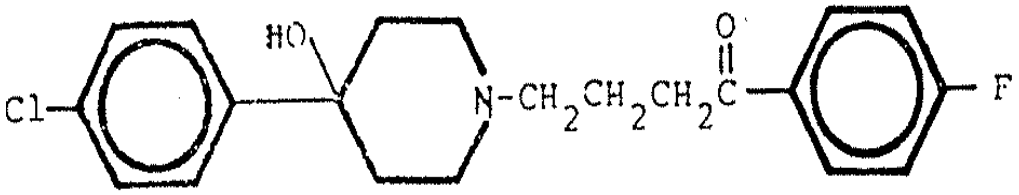
5.0 mg: Small, green coloured, round, flat with bevelled-edge, compressed tablets, engraved **N** over **5** on one side and plain on the reverse. Bottles of 100 tablets.

10.0 mg: Small, aqua-marine coloured, round, flat with bevelled-edged, compressed tablets, engraved **10** between broken vertical bisect on one side and stylized **N** on the reverse. Bottles of 100 tablets.

20.0 mg: Salmon coloured, round, flat with bevelled-edged, compressed tablets, engraved **20** between broken vertical bisect on one side and stylized **N** on the reverse. Bottles of 100 tablets.

PHARMACOLOGY

Haloperidol is an antipsychotic drug with the chemical name 4-[4-(p-chlorophenyl)-4-hydroxypiperidino]-4,-fluorobutyrophenone. Its chemical structure is as follows:



Molecular Formula: $C_{21}H_{23}ClFNO_2$ Molecular Weight: 375.87

The pharmacological profile of haloperidol in laboratory animals resembles that of the phenothiazine antipsychotics. As with other neuroleptics, it reduces locomotor and exploratory behaviour (ambulation and "emotional" defecation) in rats at low doses and induces cataleptic immobility and palpebral ptosis at higher doses. Haloperidol is more potent than chlorpromazine in abolishing the righting reflex in mice (milligram potency 2 times that of chlorpromazine). It also depresses food consumption and weight increase in laboratory animals and has an epileptogenic effect at subtoxic dose levels. Haloperidol suppresses the conditioned avoidance response in the jumping box test (milligram potency 16 times that of chlorpromazine in rats). It blocks amphetamine-induced activity in rats and apomorphine-induced emesis in dogs (milligram potency 50 times that of chlorpromazine), but it is weaker than chlorpromazine in prolonging barbiturate sleeping time. It has relatively weak adrenolytic properties. Equal doses of haloperidol and chlorpromazine are required to produce significant hypotension in the cat and hypothermia in the rat. In dogs and cats, it decreases the epinephrine-induced contractions of the nictitating membrane, but is less effective against norepinephrine. It would appear from studies in the rabbit that the decreased responsiveness of the reticular formation produced by the drug may be more marked in the caudal portion of that area. Changes in the EEG activity produced by haloperidol are similar to those seen with phenothiazine derivatives. In animals and in humans haloperidol is rapidly absorbed following oral administration and peak plasma levels are reached in 2 to 6 hours. Excretion begins promptly, but proceeds slowly and in isotope studies small amounts of radioactivity are excreted or can be detected in the plasma several weeks after ingestion of the drug. This may be related to a high degree of plasma protein binding which in one study was observed to the extent of 92%.

TOXICOLOGY

TABLE 1: LD_{50} (mg/kg by ROUTE OF ADMINISTRATION).

Species	i.v.	s.c.	oral
Mice	13	54	144 mg/kg
Rats	22	63	850 mg/kg
Hamsters	-	-	405 mg/kg
Rabbits	8	-	-
Dogs	18	80	90 mg/kg

During an 18 month evaluation in rats haloperidol was mixed with the animals normal daily diet and consumed in amounts that averaged 33.0, 14.5, 6.5 and 3.5 mg/kg/day. None of these amounts of haloperidol caused abnormalities as evidenced by repeated urinalyses, hematologic studies (CBC and blood chemistries), and gross and/or microscopic observations. At the end of the evaluation, however, mean body weights and food consumption were lower in the treated animals than in the untreated controls. The lesser gain in body weight may be attributed to the decreased food consumption; the latter was presumably caused by the drug's tranquilizing action.

Two safety evaluations of haloperidol were conducted in dogs. In one evaluation, 3 groups of 6 animals each received either 2.0, 0.5, or 0 mg/kg/day for 6 months; in the other evaluation, 4 groups of 8 animals each received either 12.0, 6.0, 2.0 or 0 mg/kg/day for 12 months.

No fatalities occurred in either evaluation and none of the dogs in the 6-month evaluation exhibited any drug-related toxic effects (gross or microscopic). In the 12-month study, decreased weight gain was observed in dogs at the mid- and high-dose levels and dogs on the highest dose showed convulsions, tremors, and emesis. Transient breast engorgement and lactation occurred in 6 to 12 female dogs between the 3rd and 8th weeks of the evaluation, but were not dose-related. Liver toxicity was dose-related with hepatocellular changes seen in dogs on the two highest doses and possibly at all dose levels.

SGPT changes (increase) were reversible since they returned to normal in animals studied for one month after termination of dosing; liver sections from animals sacrificed at this time also indicated that cellular changes had returned toward normal.

When haloperidol was administered to rats (0.6-3.0 mg/kg), rabbits (1.0 and 6.0 mg/kg) and dogs (1.0-4.0 mg/kg), the offspring of each of these species did not exhibit a greater incidence of teratologic effects than was observed in the respective control groups. In rats receiving amounts of the drug (4.0 mg/kg) large enough to produce marked CNS depression, increased delivery time was noted. Available data suggest that, in rats, large oral doses (1.9 mg/kg) may reduce libido, and that larger i.v. doses (3.0 mg/kg) may decrease implantation. An increased incidence of fetal resorptions was observed in rabbits receiving 6.0 mg/kg orally; however, at 1.0 mg/kg orally this effect was not observed.

BIBLIOGRAPHY

PRE-CLINICAL

1. Cressman, W.A., Bianchine, J.R., Slotnick, V.B., Johnson, P.C. and Plostnieks, J. Plasma Level Profile of Haloperidol in Man Following Intramuscular Administration. Europ. J. Clin. Pharm. 7:99, 1974.

2. Forsman, A. and Ohman, R.: On the Pharmacokinetics of Haloperidol. Nord. Psyk. Tidsskr. 28:441, 1974.

3. Di Mascio, A.: The Butyrophenones: An Overview of Their Pharmacologic and Metabolic Properties. In: Di Mascio, A. and Shader, R.I. (eds): Butyrophenones in Psychiatry. New York, Raven Press, 1972, pp. 11-23.

4. Snyder, S.H., Taylor K.M., Coyle, J.T. and Myerhoff, J.L.: The Role of Brain Dopamine in Behavioral Regulation and the Actions of Psychotropic Drugs. Amer. J. Psychiat. 127(2):199, 1970.

5. Simpson, G.M., Cooper, T.B. and Braun, G.A.: Further Studies on the Effects of Buturophenones on Cholesterol Synthesis in Humans. Curro Ther. Res. 9(8):413, 1967.

6. Janssen, P.A.J.: The Pharmacology of Haloperidol. Int J. Neuropsychiatry, Supple 1, 3:S10, 1967.

7. Dunlop, E.: Clinical Pharmacological Studies in Haloperidol. J. New Drugs, 6:243, 1966.

CLINICAL

1. Sellers, E.M. and Kalant, H.: Alcohol Intoxication and Withdrawal. New Engl. J. Med. 294(14):757, 1976.

2. Haloperidol in Psychiatry. The Medical Letter 17(3): Jan. 31, 1975.

3. Ban, T.A.: Haloperidol and the Butyrophenones. Psychosomatics 14(5):286, 1973.

4. Ayd, F.J.: Haloperidol: Fifteen Years of Clinical Experience. Dis. Nerv. Syst. 33(7):459, 1972.

5. Stotsky, B.A.: Haloperidol in the Treatment of Geriatric Patients. In: Di Mascio, A. and Shader, R.I. (eds.): Butyrophenones in Psychiatry. New York, Raven Press, 1972, p. 71.

6. Shapiro, A.K., Shapiro, E., Wayne, H. and Clarkin, J.: Psychopathology of Gilles de la Tourette's Syndrome. Amer J. Psychiatry, 129(3):427, Oct. 1972.

7. Klett, C.J. and Caffey, E.M.: Evaluating Long-Term Need for Antiparkinson Drugs by Chronic Schizophrenics. Veterans Administration Cooperative Studies in Psychiatry. Prepublication Report No. 87, May 1972.

8. Greenblatt, D.J., Shader, R.I. and Di Mascio, A.: Extrapyramidal Effects In: Shader, R.I. and Di Mascio, A. (eds.): Psychotropic Drug Side Effects. Baltimore, The Williams & Wilkins Co. 1970, pp. 92-106.

9. Ucer, E. and Kreger, K.C.: A Double-blind Study Comparing Haloperidol with Thioridazine in Emotionally Disturbed Mentally Retarded Children. Curro Ther. Res. 11(5):278, 1969.

10. Le Vann, L.J.: Haloperidol in the Treatment of Behavioral Disorders in Children and Adolescents Can. Psy. Ass. J. 14(2):217, 1969.

11. Burk, H.W. and Menolascino, F.J.: Haloperidol in Emotionally Disturbed Mentally Retarded Individuals. Amer. J. Psychiat. 124:1589, 1968.

12. Connell, P.H., Corbett, J.A.' Horne, J.D. and Mathews, A.M.: Drug Treatment of Adolescent Tiqueurs. Brit. J. Psychiat. 113:375, 1967.

13. Crane, G.E.: A Review of Clinical Literature on Haloperidol. Int. J. Neuropsychiatry, Supple 1, 3:S111, 1967.

14. Simpson, G.M.: Prospective Clinical Applications of Haloperidol. Int. J. Neuropsychiatry, 3:533, 1967.

15. Goldstein, B.J.: Haloperidol in Controlling the Symptoms of Acute Psychoses. Part 1. A Preliminary Investigation. Curro Ther. Res. 8:232, 1966.

16. Goldstein, B.J. and Clyde, D.J.: Haloperidol in Controlling the Symptoms of Acute Psychoses Part 2: A Double-Blind Evaluation of Haloperidol and Trifluoperazine. Curr. Ther. Res. 8:236, 1966.

17. Rogers, W.J.B.: Use of Haloperidol in Children's Psychiatric Disorders. Clin. Trials UJ. 2:162, May 1965.

18. Holstein, A.P. and Chen, C.H.: Haloperidol - A Preliminary Clinical Study. Amer. J. Psychiat. 122:462, 1965.

19. Chapel, J.L., Brown, N. and Jenkins R.L.: Tourette's Disease: Symptomatic Relief with Haloperidol. Amer. J. Psychiat. 121:608, 1964.

20. Pratt, J. Bishop, M. and Gallant, D.: Comparison of Haloperidol in the Psychiatric Disorders of Old Age. Amer. J. Psychiat. 120(12):1190, 1964.

21. Sugerman, A.A. Williams, B.H. and Adlerstein, A.M.: Haloperidol in the Psychiatric Disorders of Old Age. Amer. J. Psychiat. 120(12):1190, 1964.

22. Haward, L.R.: Differential Inter-Drug Analysis - A Preliminary Study, Brit. J. Psychiat. 110:514, July 1964.

23. Lawson, J.I.M. and McGowan, S.W.: Haloperidol in Obstetrics, A Clinical Trial in 350 Women in Labor. Lancet 1:1205, 1962.

24. HALDOL Product Monograph, McNeil Pharmaceutical (Canada) Ltd. Date of revision: November 28, 1983.

25. Apo-Haloperidol Tablets Product Monograph, Apotex Inc., Canada. Date of revision: January 28, 2013, Control No. 160968.

PART III: CONSUMER INFORMATION

PrTEVA-HALOPERIDOL
Haloperidol Tablets USP

This leaflet is part III of a three-part "Product Monograph" published when TEVA-HALOPERIDOL was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about TEVA-HALOPERIDOL. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

This medication is used for the management of manifestations of chronic schizophrenia.

What it does:

TEVA-HALOPERIDOL is an antipsychotic medication which affects chemicals in the brain that allow communication between nerve cells (neurotransmitters). These chemicals are called dopamine and serotonin. Exactly how TEVA-HALOPERIDOL works is unknown. However, it seems to readjust the balance of dopamine and serotonin.

When it should not be used:

You should not use TEVA-HALOPERIDOL if you have:

- An allergy to haloperidol, to any of its ingredients or to phenothiazines
- A medical condition known as pheochromocytoma (a tumor of the adrenal gland)
- A severe heart or blood vessel disorder
- Severe kidney problems
- Had brain damage
- Liver disease
- A blood cell disorder such as anemia, low white blood cell counts, or low platelets
- Drowsiness, slow breathing, weak pulse
- Decreased alertness caused by taking certain medications or drinking alcohol
- You are going to receive anesthesia in the spine or for a region (such as an arm, leg or the lower part of your body)

What the medicinal ingredient is:

Haloperidol

What the nonmedicinal ingredients are:

The TEVA-HALOPERIDOL tablets contain sodium starch glycolate, dibasic calcium phosphate (dehydrates), microcrystalline cellulose, sodium lauryl sulfate, colloidal silicon dioxide and magnesium stearate.

Additionally the 1 mg, 2 mg, 5 mg, 10 mg and 20 mg tablets contain as follows:

- 1 mg: FD&C Yellow #6 aluminum lake and D&C Yellow #10 aluminum lake
- 2 mg: FD&C Red #3 lake
- 5 mg: FD&C Yellow #6 aluminum lake, D&C Yellow #10 aluminum lake and FD & C Blue #1 aluminum lake
- 10 mg: FD & C Blue #1 aluminum lake and D&C Yellow #10 aluminum lake
- 20 mg: FD&C Yellow #6 aluminum lake, FD&C Red #3 lake and FD & C Blue #1 aluminum lake

What dosage forms it comes in:

TEVA-HALOPERIDOL is available in 0.5 mg, 1 mg, 2 mg, 5 mg, 10 mg and 20 mg tablets.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Studies with various medicines of the group to which TEVA-HALOPERIDOL belongs, when used in the elderly patients with dementia, have been associated with an increased rate of death. TEVA-HALOPERIDOL is not indicated in elderly patients with dementia.

BEFORE you use TEVA-HALOPERIDOL talk to your doctor or pharmacist if:

- You have heart disease, glaucoma or prostatic hypertrophy
- You are addicted to alcohol. You should not take TEVA-HALOPERIDOL if you are under the effects of alcohol.
- You are pregnant. TEVA-HALOPERIDOL should not be used during pregnancy unless your doctor considers the benefits to you markedly outweigh the potential risks to the fetus
- You are taking barbiturates, painkillers, narcotics or, antihistamines or other drugs that make you drowsy.
- You have any allergies to this drug or its ingredients
- You have or ever had a blackout or seizure
- You are breast feeding.
- You have risk factors for developing blood clots such as: a family history of blood clots, age over 65, smoking, obesity, recent major surgery (such as hip or knee replacement), immobility due to air travel or other reason, or take oral contraceptives (“The Pill”).

TEVA-HALOPERIDOL may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery, especially during the first few days of therapy. You should be cautious when performing potentially hazardous tasks.

Effects on Newborns:
In some cases babies born to a mother taking TEVA-HALOPERIDOL during pregnancy have experienced symptoms that are severe and require the newborn to be hospitalized. Sometimes, the symptoms may resolve on their own. Be prepared to seek immediate emergency medical attention for your newborn if they have difficulty breathing, are overly sleepy, have muscle stiffness, or floppy muscles (like a rag doll), are shaking, or are having difficulty feeding.

People who take TEVA-HALOPERIDOL are cautioned:

- Against exposure to extreme heat
- That drugs such as TEVA-HALOPERIDOL increase the toxicity of certain types of insecticides ("organophosphorous" insecticides) including insecticides for agriculture (farming), treating animals (flea and tick control) and for treating pests around the house and garden. Be cautious if you must use these products while taking TEVA-HALOPERIDOL.

INTERACTIONS WITH THIS MEDICATION

TEVA-HALOPERIDOL can add to the effects of alcohol. You should avoid consuming alcoholic beverages while on TEVA-HALOPERIDOL therapy.

Tell your doctor about all your prescription and over-the-counter medications, vitamins, minerals, herbal products (such as St. John's Wort), and drugs prescribed by other doctors. Do not start a new medication without telling your doctor.

Before using TEVA-HALOPERIDOL, tell your doctor if you regularly use other medicines that make you sleepy (such as cold or allergy medicine, narcotic pain medicine, sleeping pills, muscle relaxants, and medicine for seizures, depression, or anxiety). You should not take TEVA-HALOPERIDOL if you have drowsiness caused by other medications.

Drugs that may interact with TEVA-HALOPERIDOL include:
anti-anxiety agents, antidepressants, muscle relaxants, anti-seizure medicine, high blood pressure medicine, cabergoline, metrizamide, guanethidine, guanadrel, grepafloxacin, sparfloxacin, lithium, cisapride, atropine-like drugs, narcotic pain relievers (e.g., codeine), drugs used to aid sleep, drowsiness-causing antihistamines (e.g., diphenhydramine), other drugs that may make you drowsy.

Many cough-and-cold products contain ingredients that may add a drowsiness effect. Before using cough-and-cold medications, ask your doctor or pharmacist about the safe use of those products. Do not start or stop any medicine without doctor or pharmacist approval.

This list is not complete and there may be other drugs that can interact with TEVA-HALOPERIDOL.

PROPER USE OF THIS MEDICATION

Take this medication by mouth exactly as prescribed. During the first few days your doctor may gradually increase your dose to allow your body to adjust to the medication. Do not take this more often or increase your dose without consulting your doctor. Your condition will not improve any faster but the risk of serious side effects will be increased. Do not stop taking this drug suddenly without your doctor's approval.

Your doctor will decide which dose is best for you.

Usual dose:

Dose is individualized based on the severity of your symptoms, your age, weight, health, other diseases you may have, and previous response to drugs similar to haloperidol.

The initial dose is 1-2 mg twice or three times a day.

Some patients may require doses of 4-6 mg three times a day. For some patients doses as high as 30-40 mg a day have been used.
Rarely doses of 100 mg per day have been used.

The maintenance dose is commonly in the range of 1-2 mg three to four times a day.

Lower doses are recommended for children and elderly or debilitated patients as they may be more sensitive to the drug.

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Overdose symptoms may include agitation, and confusion, drowsiness, dizziness, muscle stiffness or twitching, increased salivation, trouble swallowing, weakness, loss of balance or coordination, and fainting.

Missed Dose:

Take the missed dose as soon as you remember. If it is almost time for your next dose, wait until then to take the medicine and skip the missed dose. Do not double your dose to make up the missed dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like other medications, TEVA-HALOPERIDOL may cause some side effects. These side effects may be minor and temporary. However, some may be serious and need medical attention.

Side effects may include: sweating, urinary incontinence, dizziness, drowsiness, dry mouth, nasal congestion, nausea and vomiting, headache, menstrual changes, change in libido, swelling of the breasts and milk production in both men and women, weight changes and blurred vision.

If any of these affects you severely, tell your doctor.

Your doctor should check your body weight before starting TEVA-HALOPERIDOL and continue to monitor it for as long as you are being treated.

Your doctor should take blood tests before starting TEVA-HALOPERIDOL. They will monitor blood sugar, and the number of infection fighting white blood cells. Your doctor should continue to monitor your blood for as long as you are being treated.

If you have high levels of prolactin (measured with a blood test) and a condition called hypogonadism, you may be at increased risk of breaking a bone due to osteoporosis. This occurs in both men and women.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate emergency medical attention
		Only if severe	In all cases	
Unknown	**Allergic Reaction:** rash, hives, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing			✓

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate emergency medical attention
		Only if severe	In all cases	
	Neuroleptic Malignant Syndrome: any group of symptoms which may include high fever, sweating, stiff muscles, fast heartbeat, fast breathing and feeling confused, drowsy or agitated			✓
	Extrapyramidal Symptoms: muscle stiffness, body spasms, upward eye rolling, exaggeration of reflexes, drooling, difficulty moving how and when you want.			✓
	Fast or irregular heartbeat		✓	
	Seizures or fits			✓
	Long-lasting (greater than 4 hours in duration) and painful erection of penis			✓
	Tardive Dyskinesia: uncontrollable movements or twitches of the body, face, eyes or tongue, stretching the neck and body		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate emergency medical attention
		Only if severe	In all cases	
	Low Blood Pressure: feeling of lightheadedness or fainting especially when getting up from a lying or sitting position		✓	
	High Blood Pressure: headaches, vision disorders, nausea and vomiting		✓	
	Decreased sweating		✓	
	Jaundice: yellow colour to skin and eyes, dark urine		✓	
	Respiratory Infection: fever, flu-like symptoms, coughing, difficult or fast breathing		✓	
	New or worsening constipation		✓	
	Akathisia: a feeling of restlessness, inability to remain motionless		✓	
	Vision Changes: blurred vision, glaucoma or other eye disorder		✓	
	Increased Blood Sugar: frequent urination, thirst and hunger	✓		

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate emergency medical attention
		Only if severe	In all cases	
Uncommon	**Blood clots:** swelling pain and redness in an arm or leg that can be warm to touch. You may develop sudden chest pain, difficulty breathing and heart palpitations		✓	

This is not a complete list of side effects. For any unexpected effects while taking TEVA-HALOPERIDOL, contact your doctor or pharmacist.

HOW TO STORE IT

Store at controlled room temperature (15º-30ºC).

Keep this and all medications out of the reach and sight of children.

Reporting Side Effects

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at MedEffect (http://hc-sc.gc.ca/dhp-mps/medeff/index-eng.php);
- By calling 1-866-234-2345 (toll-free);
- By completing a Consumer Side Effect Reporting Form and sending it by:
  - Fax to 1-866-678-6789 (toll-free), or
  - Mail to: Canada Vigilance Program
    Health Canada
    Postal Locator 0701E
    Ottawa, ON
    K1A 0K9

Postage paid labels and the Consumer Side Effect Reporting Form are available at MedEffect (http://hc-sc.gc.ca/dhp-mps/medeff/index-eng.php).

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Last revised: August 26, 2016

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found by contacting Teva Canada Limited at:
Phone: 1-800-268-4127 ext. 3;
Email: druginfo@tevacanada.com; or
Fax: 1-416-335-4472

Reporting Side Effects to Teva Canada Limited:
Phone: 1-800-268-4127 ext. 3;
Email: PhV@tevacanada.com; or
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