HOW SUPPLIED: Loxapine Capsules, USP are available containing loxapine succinate, USP 5 mg, 10 mg, 25 mg, and 50 mg* each.

Each capsule for oral administration, contains loxapine succinate, USP 5 mg, 10 mg, 25 mg or 50 mg equivalent to 5 mg, 10 mg, 25 mg or 50 mg of loxapine base, respectively.

Initial dosage of 10 mg twice daily is recommended, although in severely disturbed patients initial dosage up to a total of 50 mg daily may be required. Dosage should then be increased fairly rapidly over the first 7 to 10 days until there is effective control of psychosis. The target therapeutic maintenance level and maintenance range is 60 mg to 100 mg daily. However, as with all drugs used to treat schizophrenia, some patients respond to lower dosages and others require higher dosage for optimal benefit. Daily dosage higher than 350 mg is not recommended.

Maintenance Therapy: For maintenance therapy dosage should be reduced to the lowest level compatible with symptom control. Many patients have been maintained satisfactorily at dosages in the range of 20 mg to 60 mg daily.

Absorption, Distribution, Metabolism, and Excretion: Absorption of loxapine following oral or parenteral administration is virtually complete. The drug is removed rapidly from the plasma and distributed in tissues. Animal studies suggest an initial preferential distribution in lungs, brain, spleen, heart, and kidney. Loxapine is metabolized extensively and is excreted mainly in the first 24 hours. Metabolites are excreted in the urine in the form of conjugates and in the feces unconjugated.

Indications and Usage: Loxapine capsules are indicated for the treatment of schizophrenia. The efficacy of loxapine capsules in schizophrenia was established in clinical trials which employed institutionalized and chronically hospitalized acutely ill schizophrenic patients as subjects.

Contraindications: Loxapine capsules are contraindicated in comatose or severe drug-induced depressed states (alcohol, barbiturates, narcotics, etc.). Loxapine is contraindicated in individuals with known hypersensitivity to dibenzoxepines.

Warnings: Loxapine increases the risk of death in drug-treated patients of between 1.6 to 1.7 times the risk in placebo-treated patients. Loxapine should be used cautiously in patients with cardiovascular disease. Loxapine should be used with caution in patients with a history of urinary tract obstruction.

The 50 mg capsules have a brown opaque cap and a light blue opaque body printed with MYLAN over 7650 in black ink on both the cap and body. The capsule is filled with white to off-white powder. They are available as follows:

NDC 51079-901-20 - Unit dose blister packages of 100 (10 cards of 10 capsules each).

The 25 mg capsules have a brown opaque cap and a light green opaque body printed with MYLAN over 7625 in black ink on both the cap and body. The capsule is filled with white to off-white powder. They are available as follows:

NDC 51079-902-20 - Unit dose blister packages of 100 (10 cards of 10 capsules each).

The 10 mg capsules have a brown gelatin capsule with an olive opaque cap and a light green opaque body printed with MYLAN over 7610 in black ink on both the cap and body. The capsule is filled with white to off-white powder. They are available as follows:

NDC 51079-903-20 - Unit dose blister packages of 100 (10 cards of 10 capsules each).

Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]
Symptoms of dystonia, prolonged abnormal movements, mental status changes, acute dystonic reactions, and neuroleptic malignant syndrome (NMS) may occur at the beginning of therapy or when dosage is increased. They are associated with the use of antipsychotic drugs and may occur at doses that are considered to be therapeutic. The risk of these symptoms can be minimized by careful observation and use of antiparkinson drugs in the management of these conditions. The effects of antiparkinson agents in these conditions have not been established; therefore, their use in the treatment of antipsychotic-induced extrapyramidal symptoms is not recommended. The management of antipsychotic-induced extrapyramidal symptoms should be empiric, and the use of antiparkinson drugs should be continued until the symptoms subside. If symptoms do not respond to antiparkinson drugs, they may be resolved by decreasing the dose of loxapine or discontinuing it.

NEUROLEPTIC MALIGNANT SYNDROME (NMS): A potentially fatal syndrome sometimes referred to as Neuroleptic Malignant Syndrome (NMS) may occur in patients receiving antipsychotic drugs. The syndrome, which is usually not severe and can be controlled by reduction of drug dosage or by administration of antiparkinson drugs, has been observed in patients who do not receive antiparkinson drugs.

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OVERDOSAGE: In the event of an overdose, supportive and symptomatic treatment should be initiated. If necessary, activated charcoal and/or hemodialysis may be of benefit. The mortality rate associated with an overdose of loxapine is low, but patients should be observed for at least 48 hours after treatment because of the possibility of a delayed reaction. If death occurs, it is likely to be delayed for several days. Although plasma levels of loxapine are not a reliable index of the time and extent of toxic effects, plasma levels above 1 μg/mL have been associated with toxicity. The toxic dose is dependent on the amount ingested and individual patient tolerance. As would be expected from the pharmacologic actions of the drug, the clinical findings will vary with the amount ingested and individual patient tolerance. The clinical findings will vary with the amount ingested and individual patient tolerance. However, the most common symptoms will be those associated with an antipsychotic agent, the syndrome may be masked. It has been suggested that the syndrome may be masked by antiparkinson drugs. It has been suggested that the syndrome may be masked by antiparkinson drugs.

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**DESCRIPTION:** Loxapine, a dibenzoxepine compound, represents a subclass of tricyclic antipsychotics. Loxapine is closely related to the thioxanthenes, butyrophenones, and phenothiazines. Chemically, it is 2-Chloro-11H-methyl-5,7-piperazino[benzil]triazol-1H,11H-oxazine and is present as the succinate salt.

**Absorption, Distribution, Metabolism, and Excretion:**

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**INDICATIONS AND USAGE:** Loxapine capsules are indicated for the treatment of schizophrenia. The efficacy of loxapine capsules in schizophrenia was established in clinical investigations which involved hospitalized and chronically hospitalized acutely ill schizophrenic patients as subjects.

**CONTRAINDICATIONS:** Loxapine capsules are contraindicated in comatose or severe drug-induced depressed states (alcohol, barbiturates, narcotics, etc.). Loxapine is contraindicated in individuals with known hypersensitivity to loxapine or any of its excipients.

**WARNINGS:**

**Increased Mortality in Elderly Patients with Dementia-Related Psychosis:** Elderly patients with dementia-related psychotic behavior treated with antipsychotic drugs are at an increased risk of death. Analyses of seventeen placebo-controlled trials (median duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group, although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotics may also increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. Loxapine succinate is not approved for the treatment of patients with dementia-related psychosis (see WARNINGS).

**Tardive Dyskinesia:** Tardive dyskinesia: Tardive dyskinesia is a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements that may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown. Both the risk of developing the syndrome and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient is increased; however, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment itself,