**METOPROLOL TARTRATE INJECTION, USP**

**INDICATIONS AND USAGE**

**Angina Pectoris**

In a large (1,395 patients randomized), double-blind, placebo-controlled clinical study, metoprolol was shown to reduce 3-month mortality by 36% in patients with unstable angina who were treated within 72 hours of onset of symptoms. The median delay from the onset of symptoms to the initiation of therapy was 8 hours in both the metoprolol- and placebo-treatment groups. Among patients treated with metoprolol, reductions in the incidence of ventricular fibrillation and in chest pain following initial intravenous therapy were also observed with metoprolol and were independent of the baseline heart rate. Reductions in the incidence of ventricular fibrillation were also observed in the placebo group, but were relatively small. The results indicate that metoprolol may reduce the need for emergency procedures such as coronary bypass surgery or angioplasty, which are performed to prevent sudden cardiac death associated with ventricular fibrillation. Metoprolol may reduce the need for such procedures in patients who are at high risk for sudden cardiac death following the onset of unstable angina.

**Heart Failure**

Metoprolol has been shown to reduce the need for hospitalization in patients with chronic heart failure. The benefit is independent of baseline heart rate or the presence of concomitant digitalis therapy. The mechanism by which metoprolol reduces the need for hospitalization involves slowing of the heart rate and, possibly, a reduction in the ventricular volume during diastole.

**Ischemic Heart Disease**

In a retrospective analysis of pooled data from controlled, randomized studies of patients with coronary artery disease, metoprolol has been shown to reduce the need for emergency procedures such as coronary bypass surgery or angioplasty, which are performed to prevent sudden cardiac death associated with ventricular fibrillation. Metoprolol may reduce the need for such procedures in patients who are at high risk for sudden cardiac death following the onset of unstable angina.

**Hypertension**

Metoprolol is effective in the treatment of mild to moderate hypertension when used alone or in combination with diuretics. In controlled, comparative, clinical studies, metoprolol has been shown to be as effective an antihypertensive agent as thiazide diuretics when used alone or in combination with other antihypertensive agents. The combination of metoprolol and a diuretic is typically recommended for initial therapy in older patients who have a tendency to develop postural hypotension.

**Prevention of Hypertrophy in Hypertensive Patients**

In a randomized, double-blind clinical trial of metoprolol versus placebo in hypertensive patients with electrocardiographic evidence of left ventricular hypertrophy, metoprolol (100 mg daily) was shown to reduce blood pressure more effectively than placebo (7.2 mm Hg vs. 2.2 mm Hg, respectively). In addition, metoprolol produced a reduction in left ventricular mass index (10.3 g/m² vs. 1.8 g/m², respectively).

**CONTRAINDICATIONS**

Hypersensitivity to metoprolol and related derivatives, or to any of the excipients; hypersensitivity to other beta blockers (cross sensitivity between beta blockers can be expected). Metoprolol is contraindicated in patients with a heart rate < 50 bpm, systolic blood pressure < 100 mmHg; or moderate-to-severe cardiac failure (see WARNINGS).

**WARNINGS**

See PRECAUTIONS (15.1, 15.2, 15.3, 15.4, 15.5).

**ADVERSE REACTIONS**

**A. Cardiac**

Bradycardia

SOS: Bradycardia: 1.2% of patients treated with metoprolol; 2.5% of patients treated with placebo. 

The incidence of heart block is increased in patients with intrinsic heart block or with second or third degree atrioventricular block at baseline.

**B. Respiratory**

Respiratory symptoms: 1.5% of patients treated with metoprolol; 2.0% of patients treated with placebo.

**C. Other**

Gastrointestinal: Nausea, vomiting, diarrhea, constipation, dry mouth, flatulence, indigestion, and abdominal pain. 

Liver: Transaminitis, hepatitis.

**DIAGNOSIS AND DISCHARGE**

**ADVERSE REACTIONS**

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Liver: Transaminitis, hepatitis.

**PRECAUTIONS**

**A. Administration of Beta-Blocking Drugs**

Patients should be warned against interruption or discontinuation of therapy, particularly during periods of stress, such as during surgery or during periods of infection. If a reduction of dosage has been necessary before surgery, it should be continued following surgery. Discontinuation of metoprolol during periods of stress or infection may be life-threatening. Metoprolol is a beta blocker and should not be used to treat acute tachyarrhythmias.

**B. Cardiovascular**

Bradycardia

SOS: Bradycardia: 1.2% of patients treated with metoprolol; 2.5% of patients treated with placebo. 

The incidence of heart block is increased in patients with intrinsic heart block or with second or third degree atrioventricular block at baseline.

**C. Gastrointestinal**

Gastrointestinal: Nausea, vomiting, diarrhea, constipation, dry mouth, flatulence, indigestion, and abdominal pain.

Liver: Transaminitis, hepatitis.

**REFERENCES**

1. Theophylline: Metoprolol is not effective in the treatment of chronic obstructive pulmonary disease. However, in patients with chronic bronchitis, metoprolol may reduce the frequency of exacerbations.

2. Angina Pectoris: Metoprolol is not effective in the treatment of chronic obstructive pulmonary disease. However, in patients with chronic bronchitis, metoprolol may reduce the frequency of exacerbations.

3. Diuretics: Metoprolol is not effective in the treatment of chronic obstructive pulmonary disease. However, in patients with chronic bronchitis, metoprolol may reduce the frequency of exacerbations.

4. Hypertension: Metoprolol is not effective in the treatment of chronic obstructive pulmonary disease. However, in patients with chronic bronchitis, metoprolol may reduce the frequency of exacerbations.
Alcoholism: Consider the advisability of giving the agent to patients who are alcoholics or recovering alcoholics as there is a possibility that the appetite and weight may increase and the patient may have to be closely monitored.

Hypersensitivity: In case of sensitivity to the agent, discontinue its use and replace with one of the alternative agents.

Cardiovascular: In patients with hypertension, a beta-blocker such as metoprolol can be used in doses of 50-100 mg three times daily or higher, depending on the degree of hypertension and the effectiveness of the drug in individual patients.

Renal impairment: In patients with renal impairment, the dose of metoprolol should be reduced or the interval between doses increased, depending on the degree of impairment.

Pediatric patients: The safety and effectiveness of metoprolol in pediatric patients have not been established.

ADVERSE REACTIONS

Reproductive System: Agranulocytosis and agranulocytosis have been reported in patients taking metoprolol. These adverse reactions were reported from treatment regimens where intravenous metoprolol was administered, when tolerated.

Myocardial Infarction: There have been rare reports of reversible alopecia, agranulocytosis, and dry eyes. Discontinuation of the drug should be considered if any such reaction is not otherwise explainable.

Gastrointestinal: Diarrhea and blood dyscrasias have been reported. The diarrhea usually occurs within the first 2 weeks of treatment and is self-limiting.

Respiratory: Wheezing (bronchospasm) and dyspnea have been reported in about 1 of 100 patients. These adverse reactions are usually dose-dependent and may occur at any time during treatment. In patients with asthma or other similar conditions, a beta-blocker should be chosen with caution. Metoprolol should always be discontinued immediately if these adverse reactions develop.

Cardiovascular: Hypertension, bradycardia, and heart failure have been reported in patients taking metoprolol. These adverse reactions are usually dose-dependent and may occur at any time during treatment. In patients with hypertension, a beta-blocker such as metoprolol can be used in doses of 50-100 mg three times daily or higher, depending on the degree of hypertension and the effectiveness of the drug in individual patients.

Central nervous system: Dizziness, somnolence, fatigue, lightheadedness, nervousness, anxiety, depression, and insomnia have been reported. These adverse reactions are usually dose-dependent and may occur at any time during treatment. In patients with pre-existing central nervous system disorders, a beta-blocker should be chosen with caution.

Musculoskeletal: Myalgia, arthralgia, and joint pain have been reported in patients taking metoprolol. These adverse reactions are usually dose-dependent and may occur at any time during treatment. In patients with pre-existing musculoskeletal disorders, a beta-blocker should be chosen with caution.

Endocrine: Gynecomastia, impotence, and sexual dysfunction have been reported in patients taking metoprolol. These adverse reactions are usually dose-dependent and may occur at any time during treatment. In patients with pre-existing endocrine disorders, a beta-blocker should be chosen with caution.

Skin: Rash, pruritus, urticaria, and angioedema have been reported in patients taking metoprolol. These adverse reactions are usually dose-dependent and may occur at any time during treatment. In patients with pre-existing skin disorders, a beta-blocker should be chosen with caution.

Other: Pulmonary edema, hypotension, and bradycardia have been reported in patients taking metoprolol. These adverse reactions are usually dose-dependent and may occur at any time during treatment. In patients with pre-existing pulmonary or cardiovascular disorders, a beta-blocker should be chosen with caution.

Adverse Reactions Commonly Associated with Metoprolol: Hypotension, bradycardia, and heart failure have been reported in patients taking metoprolol. These adverse reactions are usually dose-dependent and may occur at any time during treatment. In patients with hypertension, a beta-blocker such as metoprolol can be used in doses of 50-100 mg three times daily or higher, depending on the degree of hypertension and the effectiveness of the drug in individual patients.

ADVERSE REACTIONS

Hematologic: Blood dyscrasias and anemia have been reported in patients taking metoprolol. These adverse reactions are usually dose-dependent and may occur at any time during treatment. In patients with pre-existing hematologic disorders, a beta-blocker should be chosen with caution.

Gastrointestinal: Diarrhea and blood dyscrasias have been reported. The diarrhea usually occurs within the first 2 weeks of treatment and is self-limiting. In patients with pre-existing gastrointestinal disorders, a beta-blocker should be chosen with caution.

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