**ZIACT™ (Bisoprolol Fumarate and Hydrochlorothiazide) Tablets**

<table>
<thead>
<tr>
<th>Body System/Adverse Experience</th>
<th>All Patients N=543</th>
<th>Drug-related Adverse Experience N=536</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiovascular</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bradycardia</td>
<td>0.7%</td>
<td>0.7%</td>
</tr>
<tr>
<td>arrhythmia</td>
<td>1.1%</td>
<td>0.9%</td>
</tr>
<tr>
<td>pericarditis</td>
<td>0.4%</td>
<td>0.0%</td>
</tr>
<tr>
<td>chest pain</td>
<td>0.7%</td>
<td>0.7%</td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bronchospasm</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>cough</td>
<td>1.1%</td>
<td>0.7%</td>
</tr>
<tr>
<td><strong>Body as a Whole</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>asthenia</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>tachycardia</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>peripheral edema</td>
<td>0.1%</td>
<td>0.7%</td>
</tr>
<tr>
<td><strong>Central Nervous System</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>dizziness</td>
<td>1.8%</td>
<td>5.1%</td>
</tr>
<tr>
<td>headache</td>
<td>4.7%</td>
<td>2.7%</td>
</tr>
<tr>
<td><strong>Musculoskeletal</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>muscle cramps</td>
<td>1.2%</td>
<td>0.7%</td>
</tr>
<tr>
<td>pain</td>
<td>0.1%</td>
<td>0.9%</td>
</tr>
<tr>
<td><strong>Psychiatric</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>insomnia</td>
<td>2.4%</td>
<td>1.7%</td>
</tr>
<tr>
<td>somnolence</td>
<td>1.1%</td>
<td>1.1%</td>
</tr>
<tr>
<td>loss of libido</td>
<td>0.1%</td>
<td>0.4%</td>
</tr>
<tr>
<td><strong>Gastrointestinal</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>diarrhea</td>
<td>1.4%</td>
<td>1.2%</td>
</tr>
<tr>
<td>nausea</td>
<td>0.9%</td>
<td>1.1%</td>
</tr>
<tr>
<td>dyspepsia</td>
<td>1.2%</td>
<td>0.7%</td>
</tr>
</tbody>
</table>

*Adverse events are adjusted to combine across studies. T=Combined across studies.

**PRECAUTIONS**

**General:** Electrolyte and Fluid Balance Status: Periodic determination of serum electrolytes should be performed, and patients treated with bisoprolol or furosemide should be evaluated for fluid or electrolyte disturbances. Thiazide diuretics have been shown to increase the urinary excretion of magnesium; this may result in hypomagnesemia. Hypokalemia may develop. Hypokalemia and hypomagnesemia can produce ventricular arrhythmias or syncope and may exaggerate the toxicity of digitalis. Therefore, hypokalemia may occur in elderly patients, even under the most favorable circumstances. Hypokalemia may be exacerbated by certain drugs, including digitalis. In addition, hypokalemia may also result from an imbalance between the dietary intake of potassium and the potassium loss associated with diuretic therapy. Hyperkalemia or acute or chronic hypoproteinemia may precipitate cardiac arrest. Congestive heart failure or severe left ventricular dysfunction will enhance potassium retention. Therefore, potassium depletion should be corrected before initiating therapy with this combination.

**Respiratory:** The following adverse events have been reported with bisoprolol and furosemide. Many of them are dose-related and can be managed by dose reduction. The most common side effects of bisoprolol fumarate are bradycardia, hypotension, and heart failure. The most common side effects of furosemide are hypokalemia, hyperkalemia, and hypernatremia. The combination of these drugs may increase the risk of these side effects. Therefore, careful monitoring of these parameters is recommended.

**Drug Interactions:** The following drugs may interact with thiazides:

- Anticoagulants: Concurrent use of warfarin may increase the anticoagulant effect of warfarin.
- Beta-blockers: Concurrent use of bisoprolol fumarate may increase the hypotensive effect of bisoprolol.
- Calcium channel blockers: Concurrent use of a calcium channel blocker may increase the hypotensive effect of thiazides.
- Diuretics: Concurrent use of furosemide may increase the diuretic effect of thiazides.
- Nonsteroidal anti-inflammatory drugs: Concurrent use of nonsteroidal anti-inflammatory drugs may increase the risk of renal toxicity.
- Thyroid hormones: Concurrent use of thyroid hormones may increase the risk of hyperglycemia.
- Oral hypoglycemics: Concurrent use of oral hypoglycemics may increase the risk of hypoglycemia.

**ADVERSE REACTIONS**

Bisoprolol fumarate has been shown to induce bradycardia, hypotension, and heart failure. However, the risk of these side effects is low compared to other beta-blockers. Furosemide has been shown to cause dehydration, hypovolemia, and hypokalemia. The combination of these drugs may increase the risk of these side effects. Therefore, careful monitoring of these parameters is recommended.

**Laboratory Abnormalities:** The following laboratory abnormalities have been reported with bisoprolol and furosemide:

- **Gastrointestinal:** Anorexia, nausea, vomiting, decreased appetite, anorexia, and weight loss.
- **Respiratory:** Dyspnea, cough, wheezing, and respiratory distress.
- **Skin:** Rash, pruritus, urticaria, and pruritic dermatitis.
- **Laboratory Tests:** Anemia, leukopenia, and thrombocytopenia.

**Proper Use of the Drug:** The drug should be used according to the specified dosage instructions. Patients should be monitored for adverse reactions, and the dosage should be adjusted as necessary. Patients should be advised to report any symptoms of adverse reactions to their healthcare provider.

**References:**


May 1994

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