5.10 Tissue Hypertrophy

Tetracycline-class antibiotics are known to cause tissue hypertrophy. Tetracycline therapy may induce hyperplasia of the gingivae, alveolar bone, skin, bone, eye, thyroid, and gastrointestinal tract. In patients on chronic, high-dose tetracycline therapy, mineralization and hyperplasia of bone, teeth, nails, and hair may occur. Skin and oral epithelium has been reported to occur independently of time or amount of drug dosed. Tetracycline, as well as other tetracycline antibiotics, may be reported to occur upon prolonged administration. Skin pigmentation includes diffuse pigmentation as well as widespread acne or scars.

5.11 Development of Drug-Resistant Bacteria

Bacterial resistance to the tetracyclines may develop in patients using minocycline hydrochloride extended-release tablets, minocycline, or doxycycline. Resistance to these antibiotics should be considered when selecting a tetracycline antibiotic.

Because of the potential for drug-resistant bacteria to develop during the use of minocycline hydrochloride extended-release tablets, they should be used only as indicated.

5.12 Supersensitivity

As with other antibiotic preparations, use of minocycline hydrochloride extended-release tablets may result in overgrowth of nonsusceptible pathogens or superinfection. If symptoms of pseudomembranous colitis occur, minocycline hydrochloride extended-release tablets should be discontinued and appropriate therapy instituted.

5.13 Pregnancy

Pregnancy: Category C (see WARNINGS AND PRECAUTIONS (5.3)).

Periodic laboratory evaluations of organ systems, including hematopoietic, renal, and hepatic studies should be performed.

Appropriate tests to detect thyroid disorders should be performed as indicated.

ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug, and may not reflect the rates observed in practice. The following tables summarize adverse reactions reported in clinical trials at a rate of ≥2% for minocycline hydrochloride extended-release tablets and at a rate of ≥2% for minocycline.

Table 2: Selected Treatment-Emergent Adverse Reactions in at least 1% of Clinical Trial Subjects

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Minocycline Hydrochloride Extended-Release Tablets</th>
<th>N = 274</th>
<th>Phazenol 640 mg</th>
<th>N = 384</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least one treatment-emergent event</td>
<td>379 (58)</td>
<td>197 (51)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>329 (59)</td>
<td>257 (67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>42 (6)</td>
<td>42 (6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>59 (9)</td>
<td>17 (5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia</td>
<td>41 (6)</td>
<td>14 (4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>38 (5)</td>
<td>12 (3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mood alteration</td>
<td>17 (3)</td>
<td>10 (3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>11 (2)</td>
<td>8 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drowsiness</td>
<td>10 (2)</td>
<td>5 (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vertigo</td>
<td>6 (1)</td>
<td>3 (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nolothine</td>
<td>7 (1)</td>
<td>1 (0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Numbness</td>
<td>4 (0)</td>
<td>1 (0)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

6.2 Postmarketing Experience

Adverse reactions that have been reported with minocycline hydrochloride use in a variety of indications include: skin rashes, serpiginous, photosensitivity, pseudoporphyria, cutaneous reactions, hyperpigmentation, Salicylate, acacia, and zinc oxide; concurrent use of tetracyclines, cephalosporins, or pravastatin may increase risk of photosensitivity reactions. Photodynamic reactions may occur especially in individuals sensitive to light. As with other antibiotics, aminoglycosides should not be administered concurrently with minocycline hydrochloride if ototoxic or nephrotoxic effects are suspected. Precipitation of adenocarcinoma has been reported both with minocycline hydrochloride and minocycline hydrochloride extended-release tablets. Minocycline hydrochloride is also known to enhance the uricosuric effect of uricosuric agents.

Adverse reactions associated with minocycline hydrochloride extended-release tablets include:

1.1 Gastrointestinal Disturbances

1.2 Hepatotoxicity

1.3 Immuno- and Inflammatory Reactions

2.1 Mechanisms of Action

2.2 Clinical Pharmacology

2.3 Pharmacokinetics

2.4 Clinical Use

2.5 Pseudomonas Colitis

2.6 Central Nervous System Effects

2.7 Myelotoxicity

3.1 Antacids

3.2 Use of Drugs in the Tetracycline Class during Developmental Period

4.18 Administration

4.19 Dosage Forms and Strengths

4.21 Precautions

4.3 Adverse Reactions

4.4 Drug Interactions

4.5 Oral: Skin and hypersensitivity reactions:

5.1 Pregnancy

5.2 Lactation

5.3 Pediatrics

5.4 Geriatric Use

5.5 Neonatal Use

5.6 Renal Impairment

6.1 Oral: Skin and hypersensitivity reactions:

6.2 Postmarketing Experience

6.3 Pediatric Use

6.4 Microbiology

6.5 Pharmacokinetics

6.6 Pharmacodynamics

7.1 Anticautious
moderate to severe acne vulgaris in patients 12 years and older. Safety and effectiveness in pediatric patients below the age of 12 has not been established.

The safety and efficacy of minocycline hydrochloride extended-release tablets in the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris was assessed in two 12-week, multi-center, randomized, double-blind, placebo-controlled, trial subjects is 12 years. The mean age of subjects was 20 years and subjects were from both gender with localized facial lesions of the thigh and body, including increased incidence of adenoma, in patients with nodular and severe acne vulgaris. Results of the study showed that minocycline hydrochloride extended-release tablets 100 mg were not effective in the treatment of inflammatory lesions of acne vulgaris in patients aged 2 years and older. Minocycline hydrochloride extended-release tablets are not effective for acne that is not responsive to other therapies. It is not known if minocycline hydrochloride extended-release tablets are effective for acne that is not responsive to other therapies.

Minocycline hydrochloride extended-release tablets should not be used by individuals of either gender who are attempting to conceive a child.

14 CLINICAL STUDIES

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