



Corporate Headquarters:
GATE PHARMACEUTICALS
650 Cathill Road
Sellersville, PA 18960
(215) 256 8400

Mailing Address:
GATE PHARMACEUTICALS
151 Domorah Drive, PO BOX 1008
Montgomeryville, PA 18936-1008
Toll Free: (800) 292 4283
Fax: (215) 653 0839

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Dear Health Care Provider:

GATE Pharmaceuticals would like to inform you of recent labeling changes concerning ORAP® (pimozide) Tablets.

Sudden, unexpected deaths have been known to occur in patients taking HIGH doses (greater than 10 mg) of ORAP. One possible mechanism for such deaths is prolongation of the QT interval predisposing patients to ventricular arrhythmia. Therefore, concomitant drugs which might impede metabolism of pimozide, and increase its plasma concentration could be hazardous.

Recent evidence suggests that pimozide is metabolized in part by the enzyme system cytochrome P450 3A (CYP 3A). In addition, two sudden deaths have been reported when clarithromycin, an inhibitor of CYP 3A, was added to ongoing high dose pimozide therapy.

Accordingly, concomitant use of drugs that are inhibitors of CYP 3A is now contraindicated with ORAP. These drugs include:

Macrolide antibiotics (such as clarithromycin, erythromycin, dirithromycin, troleandomycin)
Azole antifungal agents (such as itraconazole and ketoconazole)
Protease inhibitors (ritonavir, saquinovir, indinavir, nelfinavir)
Nefazodone
Zileuton

As a precaution, patients should also avoid grapefruit juice, because it contains substances that may inhibit the metabolism of pimozide by CYP 3A.

Finally, because CYP 1A2 may also contribute to the metabolism of ORAP, prescribers should be aware of the theoretical potential for drug interactions with inhibitors of this enzymatic system

GATE Pharmaceuticals is dedicated to providing important new information about our products to health-care providers. Professionals should be familiar with the CONTRAINDICATIONS, Clinical Pharmacology, Drug Interactions, and Interaction with Food sections of the labeling. Please refer to the enclosed package labeling for full prescribing information.

Sincerely,

A handwritten signature in black ink, appearing to read 'Wayne Mulcahy'.

Wayne Mulcahy, Ph.D.

Senior Director

Innovative Research & Development