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**STINCTIVE DESIGN 0.5, 1.0 and 2.0 mg**

**Brief Summary of Prescribing Information.**

**Indications and Usage:** Management of anxiety disorders or short-term relief of symptoms of anxiety or anxiety associated with depressive symptoms. Anxiety or tension associated with stress of everyday life usually does not require treatment with an anxiolytic. Effectiveness in long-term use, i.e., more than 4 months, has not been assessed by systematic clinical studies. Reassess periodically usefulness of the drug for the individual patient.

**Contraindications:** Known sensitivity to benzodiazepines or acute narrow-angle glaucoma.

**Warnings:** Not recommended in primary depressive disorders or psychoses. As with all CNS-acting drugs, warn patients not to operate machinery or motor vehicles, and of diminished tolerance for alcohol and other CNS depressants.

**Physical and Psychological Dependence:** Withdrawal symptoms like those noted with barbiturates have occurred following abrupt discontinuance of benzodiazepines (including convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Addiction-prone individuals, drug addicts and alcoholics, should be under careful surveillance when on benzodiazepines because of their predisposition to habituation and dependence. Withdrawal symptoms have also been reported following abrupt discontinuance of benzodiazepines taken continuously at therapeutic doses for several months.

**Precautions:** In depression accompanying anxiety, consider possibility for suicide. In elderly or debilitated patients, initial daily dosage should not exceed 2mg to avoid oversedation. Discontinue dosage gradually since abrupt withdrawal of any anti-anxiety agent may result in symptoms such as anxiety, agitation, irritability, tension, insomnia and occasional convulsions. In patients with usual precautions with impaired renal or hepatic function. Where gastrointestinal or vascular disorders coexist with anxiety, note that lorazepam has not been shown of significant effect in treating gastrointestinal or cardiovascular component. Esophageal dilation occurred in rats treated with lorazepam for more than 1 year at 6mg/kg/day. No effect dose was 1.25mg/kg/day (about 1/10th of maximum human therapeutic dose of 10mg/day). Effect was reversible only when treatment withdrawn within 2 months of first observation. Clinical significance is unknown; but use of pamidolone for prolonged periods and in geriatrics requires caution and frequent monitoring for signs of upper GI disease. Safety and effectiveness in children under 12 years have not been established.

**ADJUNCT LABORATORY TESTS:** Some patients have developed leukopenia; some have had increases in LDH. As with other benzodiazepines, periodic blood counts and liver function tests are recommended during long-term therapy.

**PHARMACOLOGICALLY SIGNIFICANT DRUG INTERACTIONS:** Benzodiazepines produce CNS depressant effects when administered with such medications as barbiturates or alcohol.

**MUTAGENESIS AND MUTAGENESIS:** No evidence of carcinogenic potential emerged in rats in an 18-month study. No studies regarding mutagenesis have been performed.

**TERATOGENICITY:** Reproductive studies were performed in mice, rats, and 2 strains of rabbits. Occasional anomalies (reduction of tarsals, tibia, metatarsals, malrotated limbs, gastroschisis, malformed and microphthalmia) were seen in drug-treated rabbits without relationship to dosage. Although these anomalies were not present in the concurrent control group, they have been reported to occur randomly in historical controls. At 40mg/kg and higher, there was evidence of fetal resorption and increased fetal loss in rabbits which was not seen at lower doses. Clinical significance of these findings is not known. However, increased risk of congenital malformations associated with use of tranquilizers (chloridiazepoxide, diazepam and meprobamate) during first trimester of pregnancy has been suggested in several studies. Because use of these drugs is rarely a matter of choice, use of lorazepam during this period should almost always be avoided. Possibility that a woman of child-bearing potential may be pregnant at institution of therapy should be considered. Advise patients if they become pregnant to communicate with their physician about desirability of continuing the drug. In humans, blood levels from umbilical cord blood indicate placental transfer of lorazepam and its glucuronide.

**LACTATION:** It is not known if oral lorazepam is excreted in human milk like other benzodiazepines. As a general rule, nursing should not be undertaken while on a drug since many drugs are excreted in milk.

**Adverse Reactions:** If they occur, are usually observed at beginning of therapy and generally disappear on continued medication or on decreasing dose. In a sample of about 3,500 anxious patients, most frequent adverse reaction is sedation (15.9%), followed by dizziness (6.9%), weakness and unsteadiness (3.4%). Less frequent are disorientation, depression, nausea, change in appetite, headache, sleep disturbance, agitation, dermatological symptoms, eye function disturbances, various gastrointestinal symptoms and autonomic manifestations. Incidence of sedation and dizziness increased with age. Small decreases in blood pressure have been noted but are not statistically significant, probably being related to relief of anxiety. Transient amnesia or memory impairment has been reported in association with the use of benzodiazepines.

**Overdosage:** In management of overdosage with any drug, bear in mind multiple agents may have been taken. Manifestations of overdosage include somnolence, confusion and coma. Induce emesis and/or undertake gastric lavage followed by general supportive care, monitoring vital signs and close observation. Hypotension, though unlikely, usually may be controlled with Levarterenol injection U.S.P. Usefulness of dialysis has not been determined.

**Ativan®**  
**for (lorazepam)**  
**Anxiety**

**Indications:** Individualize for maximum beneficial effects. Increase dose gradually as needed, giving higher evening dose before increasing daytime doses. Usual dosage, usually 2-3mg/day given b.i.d. or t.i.d.; dosage may vary from 1 to 4mg/day in divided doses. For elderly or debilitated, initially 1-2mg/day; insomnia due to anxiety or transient situational stress, 2-4mg h.s.

**Usual Dosage:** 0.5, 1.0 and 2.0mg tablets.

**Wyeth Laboratories**

**DRX**  
**VIEWPOINT**

**Venomous fish stings on the European seashore**

**Rogério A. F. Gonzaga, MD**

Fish stings in European waters are usually caused by weever fish, scorpion fish, and sometimes the Portuguese man-of-war. Generally these stings are not life threatening, but they can be extremely painful. Proper treatment can relieve the pain, minimize the venom's effects, and prevent infection.

**WEEVER FISH**—Greater and lesser weever fish (figure 1) have venomous spines on the main gill cover and front dorsal fin. Their sting is excruciatingly painful and causes spreading erythema and swelling.<sup>3,4</sup> Systemic manifestations are unusual. Death is extremely rare but has occurred as a result of respiratory failure.<sup>4</sup>

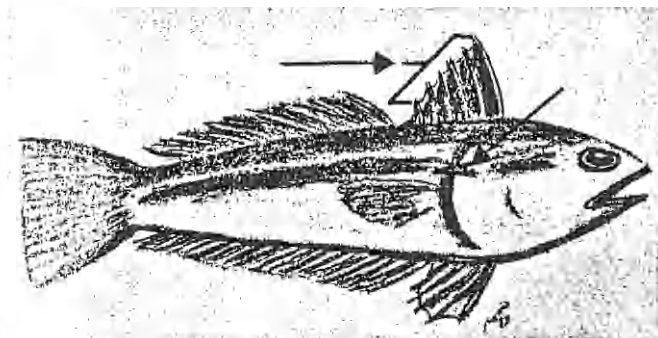
Pain is alleviated by administration of a systemic analgesic—meperidine (Demerol) or morphine—and injection of an anesthetic at the site of the injury.<sup>3,4</sup> Because the spines do not break off in tissue and the poison is rarely dangerous to life, the need for surgical debridement and wound closure remains controversial.<sup>4</sup> Tetanus prophylaxis and a short course of prophylactic antibiotics are indicated.<sup>4</sup>

An extremity is the most frequent site of a sting, and the affected member must be elevated to relieve edema. The rare sting that occurs elsewhere than on an extremity can be treated with local application of heat (as hot as the patient can stand) to help control pain and edema.<sup>5</sup> To be effective, the heat must be applied within half an hour of the sting.<sup>4</sup> Some investigators also recommend this treatment for stings on the extremities.

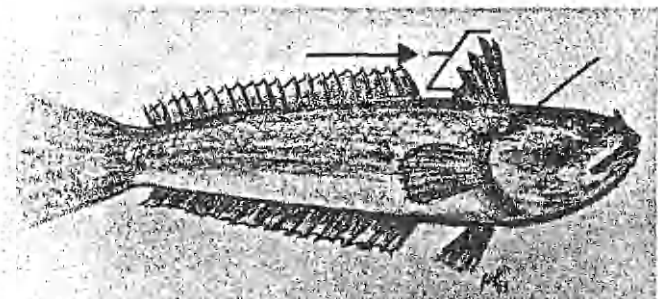
**SCORPION FISH**—Scorpion fish (figure 2) have poisonous spines on the gill covers and on the front lobe of the dorsal fin. The effects of their sting are similar to those of the weever fish, as is the treatment.

**PORTUGUESE MAN-OF-WAR**—This jellyfish (figure 3)—which is in fact a colony of free-floating individual organisms—has tentacles up to several meters long that contain nematocysts (stinging cells). These nematocysts inject venom into anyone who comes in contact with a tentacle, continuing their discharge for as long as contact is maintained<sup>3,6</sup> and causing intense pain and urticaria.

*continued*



a



b

Figure 1. Greater weever fish (*Trachinus draco* Linnaeus) (a) and lesser weever fish (*Echichthys vipera* Cuvier, formerly *Trachinus vipera*) (b).<sup>1,2</sup> Both types are yellow-gray (the lesser weever having deeper color) with whitish underside, a flat head with eyes located almost on top, and a large oblique mouth. Greater weever grows to 40 cm long, lesser weever to 16 cm. Arrows indicate areas that contain venom.

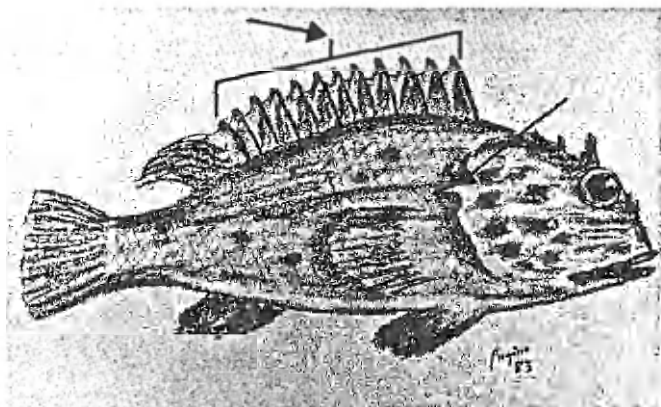


Figure 2. Scorpion fish (*Scorpaena* sp.).<sup>1,2</sup> Types vary from red to brown, with large spiny head, large mouth, and featherlike tentacles over eye. Some species grow to 20 cm long, others to 45 cm.



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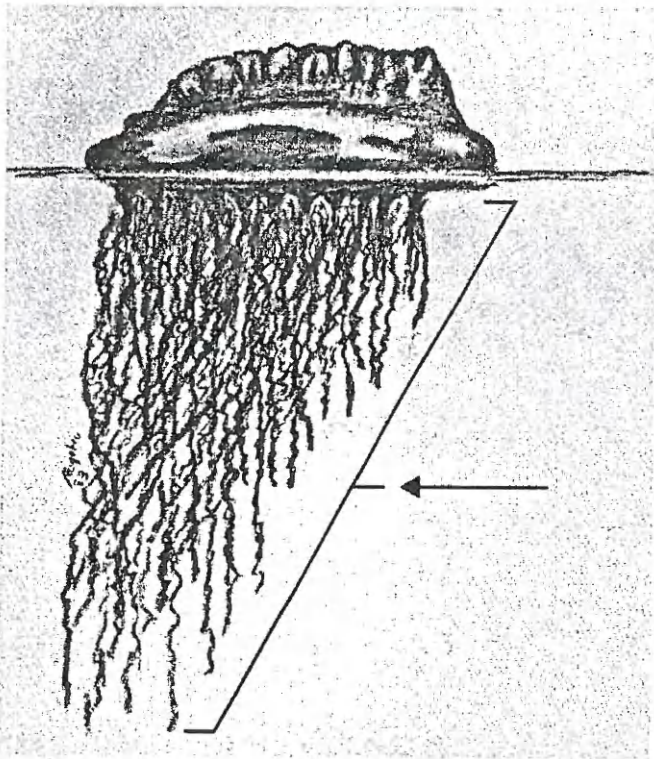
ONE TABLET A DAY  
**Tenoretic**<sup>®</sup>

Each tablet contains:

**TENORMIN**<sup>®</sup> (atenolol) 50 mg or 100 mg  
and chlorthalidone 25 mg

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**Figure 3.** Portuguese man-of-war (*Physalia physalis* Linnaeus).<sup>1,2</sup> Colony consists of free-floating organisms variously modified to provide a pneumatophore (float) up to 10x30 cm, stems, tentacles up to several meters long, feeding mouths, and reproductive structures. Pneumatophore is blue and red, tentacles blue and purple. Arrow indicates area that contains venom.

carial wheals locally. Systemic reactions may be absent or may consist of numbness and pain, arthralgia, headache, backache, nausea, vomiting, chills, fever, severe chest and abdominal pain, abdominal rigidity, dysphagia, hemolysis, and/or acute renal failure.<sup>3,6</sup> No deaths due solely to this sting have been reported.<sup>6</sup>

Most symptoms of this fish's sting can be controlled with meperidine and an antihistamine. Muscular cramps may be relieved with 10 ml of 10% calcium gluconate administered intravenously. Systemic compli-

cations are treated by the usual general measures, ie, analgesics for arthralgia, headache, or backache; antipyretics for fever; antispasmodics for abdominal pain.<sup>6,8</sup> For more severe reactions, intravenous fluids, vasopressors, or antiarrhythmic agents may be necessary.

Immediate inactivation of the nematocysts is mandatory. The affected area is cleansed with rubbing alcohol and dried with baking soda or talcum, after which the tentacles can be removed by shaving. Injected venom can then be neutralized with a compress moistened with an alkaline agent, such as baking soda.<sup>7</sup> Tetanus prophylaxis and a short course of prophylactic antibiotics should be prescribed.

In summary, fish stings usually result in a painful inflammatory reaction around the sting puncture. Treatment is aimed at relieving the pain, combating the effects of the venom, and preventing infection. These goals can be achieved with liberal use of major analgesics (such as meperidine or morphine), meticulous care of the wound, ancillary measures of general support, and a judicious course of prophylactic antibiotics. **FGM**

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