AN IMPORTANT MESSAGE
TREATING CANCER

Clinical studies indicate that Ativan® (lorazepam) Injection can play a significant role in enhancing patient tolerance for and acceptance of chemotherapy. In studies comparing Ativan Injection to other adjunctive agents, patients expressed a strong preference for the regimen including Ativan Injection because of its anxiolytic, amnesic and sedative effects. The reduction of recall following administration of Ativan Injection was considered by most patients to be not only acceptable, but also desirable. Furthermore, due to its anxiolytic action, Ativan Injection was helpful in relieving the anxiety associated with the stresses of chemotherapy.

NEW ADJUNCTIVE AGENTS NEEDED
A study of 52 mastectomy patients on regimens of cyclophosphamide, methotrexate and 5-FU (CMF) revealed that over one fourth of patients failed to even complete a treatment course of 12 to 18 months, mostly because of the side effects associated with these agents. A recent survey of 56 oncology centers found up to 10% of patients refused further chemotherapy because of actual or feared side effects. Statistics such as these have spurred researchers to seek new adjunctive agents or combinations of existing agents that would increase the tolerability of chemotherapy.

ATIVAN® INJECTION:
A SUPPORTIVE ADJUNCT
In a study involving 18 patients receiving 36 courses of cis-platinum therapy, Ativan Injection was administered prior to therapy. Lack of recall for the chemotherapy infusion, and for the subsequent 8 hours, was reported in 33 of 36 courses of therapy studied. Furthermore, amnesia for the day of chemotherapy was reported in 29 courses. All 18 patients believed the lack of recall was highly desirable.

Dr. John Laszlo and colleagues from Duke Comprehensive Cancer Center, Durham, NC, and Memorial Sloan-Kettering Institute, New York, reported a pilot study involving 32 patients receiving cisplatin with or without other cytotoxic chemotherapy and adjunctive use of Ativan Injection. Thirty patients were evaluated over 45 courses of treatment (two were eliminated for protocol violations).

Dr. Laszlo observed that following lorazepam, recall of the day’s events was reduced for most patients. Post-treatment anxiety was also reduced. Almost all of the patients in the study requested lorazepam (Ativan Injection) pretreatment again for subsequent chemotherapy courses, regardless of incidence or intensity of emetic episodes. From this study, Dr. Laszlo concluded that lorazepam can be an effective agent for these patients.
A SIGNIFICANT ROLE IN ENHANCING COMPLIANCE IN CHEMOTHERAPY

Clearly, Ativan® (lorazepam) Injection represents an important supportive adjunct in chemotherapy. Patients' ability to tolerate the experience is usually enhanced. Their acceptance of a regimen incorporating Ativan Injection has been excellent. Thus, it is felt that many patients who might otherwise abandon treatment may now be more willing to proceed with Ativan Injection as an adjunct in their chemotherapy regimen.

If outpatients are treated with lorazepam injection, care must be taken on the day of treatment to prevent their undertaking any activity requiring full awareness or coordination.

REFERENCES:

Please see important information on the following page.
DESCRIPTION: Lorazepam (lorazepam) Injection, a benzodiazepine with anxiolytic and sedative effects, is intended for IM or IV use. It has the chemical formula C31H43ClN3O4 and is a white, odorless, practically tasteless, slightly bitter, amorphous powder. Lorazepam is a short-acting benzodiazepine and has a peak plasma concentration of 0.1 to 0.2 mg/L approximately 24 hours after administration.

INDICATIONS AND USAGE: Lorazepam is indicated for various medical conditions, including:

- Anxiety: Lorazepam is used to relieve anxiety symptoms such as restlessness, irritability, and tension.
- Seizures: Lorazepam is used to treat convulsive disorders, particularly in the management of status epilepticus.
- Sedation: Lorazepam is used to produce sedation for amnestic or anterograde amnesia, often in situations such as preoperative sedation, general anesthesia, and other surgical procedures.
- Agitation due to organic brain syndrome: Lorazepam can be used to manage agitation in patients with conditions such as delirium.
- Alcohol withdrawal: Lorazepam may be used to manage withdrawal symptoms in patients with alcohol dependence.

CONTRAINDICATIONS: Lorazepam is contraindicated in patients with a history of hypersensitivity to benzodiazepines or other members of the same chemical class, and in patients with a history of addiction to other drugs or substances.

WARNINGS: Lorazepam should be used with caution in patients with a history of alcoholism, drug dependence, or addiction, as well as in patients with a history of depression or suicidal ideation.

ADVERSE REACTIONS: The most common adverse reactions associated with lorazepam use include:

- Somnolence
- Dizziness
- Sedation
- Fatigue
- Sleep disturbances
- Headache
- Urinary retention
- Constipation
- Nausea
- Vomiting
- Diarrhea
- Insomnia
- nightmares

Severe side effects include:

- Respiratory depression
- Hypotension
- Bradycardia
- Hypertension
- Cardiac arrhythmias

In cases of severe overdose or prolonged use, lorazepam can lead to dependence and withdrawal symptoms. Lorazepam is not recommended for use in children under the age of 6 due to its potential to cause respiratory depression.

PRECAUTIONS: Patients receiving lorazepam should be monitored for respiratory depression, especially if they have a history of respiratory impairment or if they are taking other medications that may cause respiratory depression.

DRUG INTERACTIONS: Lorazepam may interact with other drugs, including:

- Antihypertensives
- Anticoagulants
- Sedative-hypnotics
- Alcohol

These interactions can lead to increased levels of lorazepam, which may increase the risk of adverse effects.

POSSIBLE ADVERSE EFFECTS: Lorazepam may cause drowsiness or dizziness, which can impair the ability to perform tasks requiring concentration and attention. Patients should be warned about these effects and advised to avoid driving or operating heavy machinery until the effects of the medication are fully understood.

CLINICAL PHARMACOLOGY: Lorazepam is rapidly absorbed following IV or IM administration, with peak plasma concentrations achieved within 1 to 2 hours. It is extensively metabolized in the liver and the main metabolites are inactive. Lorazepam is primarily excreted unchanged in the urine.

Dr. Zorilin's Notes: Lorazepam is a useful medication for managing anxiety and sedating patients in various clinical settings. Its rapid onset and short duration make it particularly suitable for preoperative sedation and in patients requiring short-term benzodiazepine treatment. However, it should be used with caution in patients with a history of respiratory compromise or those taking medications that could potentiate its effects.

Pharmacokinetics: Lorazepam is rapidly absorbed after oral or IV administration. Its bioavailability is about 90%, and it is extensively metabolized in the liver. The main metabolites are inactive. Lorazepam is primarily excreted unchanged in the urine.
One of the unresolved mysteries in the history of cancer research concerns Johannes Fibiger (1867–1928), of Copenhagen, who, in 1913, reported (Z. Krebsforsch., 13: 219–280, 1913) that gastric cancer in rats was associated with a parasite of the nematode type. Gastric cancer was reproduced in rats inflicted with the nematode by being fed a special cockroach. Fibiger’s work was awarded a Nobel Prize in 1926, the first such recognition for cancer research. Attempts to repeat the observations in England, France, and the United States were unsuccessful, the histological diagnoses were questioned, and the role of vitamin A deficiency was proffered as an alternate hypothesis. A generally held opinion is that Fibiger’s was a “false discovery” and that the Nobel Prize was wrongly awarded [Wade, Science (Wash. DC), 202: 295–296, 1978].

Reassessment of Fibiger’s work has been published recently by Clemmesen (Acta Pathol. Microbiol. Scand. Sect. A Suppl., p. 270, 1978). The integrity of Fibiger was unquestioned, and his work was careful, meticulous, and extensive. Over a half century after Fibiger’s death, investigators still wonder about the possible explanation of his results (Prog. Exp. Tumor Res., 11: 1–20, 1969). One such explanation is contamination, by carcinogens, of the diet fed to Fibiger’s rats. Regina Schoental (Front. Gastrointest. Res., 4: 17–24, 1979) suggests such contamination by trichothecenes, toxic metabolites of Fusarium and certain other field fungi, which contaminate cereals and other foodstuffs. Fusarium mycotoxins have been shown to be carcinogenic in rats producing a variety of lesions and tumors, including benign and malignant tumors of the stomach (Cancer Res., 39: 2179–2189, 1979).

We are indebted to Drs. Johannes Clemmesen and Regina Schoental for this information. The photographs of stomach neoplasms and epithelial deposit in a lymph node are from Fibiger (Z. Krebsforsch., 13: 219–280, 1913).

M. B. S.