Supporting the “come back”

Cancer patients often delay and even abandon treatment because of devastating side effects.

Adjunctive agents that help relieve the physical and emotional stresses of chemotherapy not only make regimens more palatable but also improve the patient’s quality of life.

Ativan® (lorazepam) Injection can be an important, supportive adjunct.

Clinical studies suggest that Ativan® Injection can play a significant role in enhancing chemotherapy compliance.¹⁻⁵
Because of Ativan® Injection’s anxiolytic, sedative and amnesic effects, patients are better able to endure the rigors of their chemotherapy courses.

**Ativan® Injection reduces recall of chemotherapy.**

The reduction of recall for the chemotherapy experience is considered by most patients to be not only acceptable but highly desirable.1-5

In fact, many patients actually request subsequent pretreatment with Ativan® Injection and strongly prefer regimens that include it, regardless of incidence or intensity of any emetic episodes.3

The pharmacologic effects of Ativan® Injection require that care be taken on the day of therapy to prevent patients from undertaking any activity requiring their full awareness or coordination.

Please see important information on the following page.

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ATIVAN® (LORAZEPAM) INJECTION I.V.

2 mg I.V. 30 to 60 minutes prior to chemotherapy

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DESCRIPTION
Ativan® (lorazepam) Injection, a benzodiazepine with anxiolytic and sedative effects, is intended for IM or IV use. It has the chemical formula C7H7NO6.5H2O (1:3-dihydrate 3-hydroxy-2H-1,4-benzodiazepine-2-one). Lorazepam is a nearly white powder almost insoluble in water. Each mL of intravenous injection contains 1 mg lorazepam with 0.008 mg sodium hydroxide as an electrolyte and 0.6 mg of alcohol as a preservative.

CLINICAL PHARMACOLOGY
IM or IV administration of recommended doses of 2 to 4 mg lorazepam injection to adult patients is followed by dose-related effects of sedation (sleepiness or drowsiness), relief of preoperative anxiety, and inhibition of postoperative recall. (See CLINICAL PHASE, sedation (sleepiness or drowsiness) thus noted is such that most patients are able to respond to simple commands but are not able to perform skilled tasks. Patients with conditions marked by lack of recall of doses greater than absolute, as determined under conditions of careful patient questioning and testing, using tests designed specifically for the measurement of postoperative recall and biasing questions, have reported no perioperative events, or recognizing props from before surgery. Lack of recall and recognition was observed in about 80% of patients given 2 mg and 95% of patients given 4 mg lorazepam injection.

Intended effects of recommended adult dose of lorazepam injection usually last 6 to 8 hours. In rare instances and where patients received greater than recommended dose, excessive sleepiness and prolongation of recovery were observed. As with other benzodiazepines, untoward effects may result in CNS depressant effects of alcohol and other drugs were noted in isolated and rare cases for greater than absolute. Inpatient endoscopic procedures require adequate recovery room observations. (See WARNINGS.) Pharyngeal reflexes are not impaired when lorazepam injection is used for per-oral endoscopic procedures, therefore adequate topical or regional anaesthesia is recommended to minimize reflex activity associated with such procedures.

PHARMACODYNAMIC EFFECTS: Lorazepam Injection is reported to have CNS effects of other drugs, e.g., phenothiazines, narcotic analgesics, barbiturates, anticonvulsants, scopolamine, and MAO inhibitors when these drugs are used concurrently with lorazepam. (See CLINICAL PHASE, SERUM COLOID AND WARNINGS.) Use extreme care in giving lorazepam injection to elderly or very ill patients, or to infants and children, because of the potential for serious adverse reactions (e.g., hypotension, cardiac arrest, respiratory depression), and because of the potential for uterine relaxation due to the hypotensive and hypotensive properties of lorazepam. The effectiveness of the resuscitative equipment for ventilatory support should be readily available. (See WARNINGS.) Respiratory depression, particularly in infants and children, may occur when lorazepam is administered at higher than recommended doses (up to 10 mg). The use of lorazepam injection in patients with pre-existing CNS depressants, e.g., alcohol or other CNS depressants, is recommended.

Pregnancy: Lorazepam given to pregnant women may cause fetal damage. Increased risk of congenital anomalies and CNS abberations is a concern noted in association with the use of benzodiazepines, diazepam and related benzodiazepines, during first trimester of pregnancy was suggested in several studies. In humans, blood levels from 2 mg of lorazepam injection to 4 mg IM or IV are associated with the incidence of anencephaly and other CNS defects, and CNS and skeletal defects, in rats and two strains of mice at 2.0 mg/kg. Lack of human studies and animal studies do not indicate that this is present. Although all these anomalies were not present in concurrent control group, they have been reported to occur rarely in human patients treated with lorazepam. There is evidence of fetal neurotoxic effects. Long-term effects on pregnancy are not known. Lorazepam injection is not indicated for use in women who are pregnant or who may become pregnant. (See WARNINGS.)

Information for Patients: As appropriate, inform patients of pharmacological effects, e.g., sedation, relief of anxiety and lack of drowsiness, of duration of these effects (about 8 hours), so they may adequately perceive relapse and the usefulness as an adjuvant to other treatment. (See WARNINGS.) Patients receiving lorazepam injections intravenously should be instructed that driving automobiles or operating hazardous machinery, or engaging in hazardous tasks, is one more dangerous, or may be done safely with lower concentration of lorazepam andlorazepam injection may produce more prolonged and profound effect, taking the form of excessive sleepiness, drowsiness, ataxia and disorientation of events. (See WARNINGS.) Patients should be instructed that driving may be impaired for as long as 5 to 8 hours after lorazepam injection due to additive effects on CNS depression seen with benzodiazepines in general. Any one of these conditions may make them unsafe to operate machinery or drive a motor vehicle.

Laboratory Tests: Urinalysis, liver function tests and blood cell counts were normal in all studies. Urinalysis: No significant changes were noted in the following: triglyceride, lipoprotein (LDL and HDL), serum calcium, phosphorus and total bilirubin levels. Drug interactions: Lorazepam injection, like other injectable benzodiazepines, produces CNS depression which may interact with other CNS depressants, e.g., MAO inhibitors and other benzodiazepines. When scopolamine is concomitantly used with injectable lorazepam increased incidence of sedation, hallucinations and mental aberrations was observed. (See WARNINGS.)

No laboratory test abnormalities were identified when lorazepam was given alone or concomitantly with another drug, e.g., narcotic analgesics, inhalation anaesthetics, spinalopuncture, atropine and various tranquilizing agents. (See WARNINGS.)

REFERENCES
The 1984 Nobel Prize in medicine was awarded to three immunologists: Cesar Milstein, 57 years old, born in Argentina, of the British Medical Research Council’s laboratory in Cambridge; Georges J. F. Köhler, 38, of the Basel Institute of Immunology, Switzerland; and Niels K. Jerne, 72, of the Basel Institute.

Milstein and Köhler developed the technique for producing monoclonal antibodies (Nature (Lond.), 256: 495–497, 1975). Jerne was recognized for his basic contributions to immunology that were among the precursors of the Milstein-Köhler work (see Science 226: 1025–1028, 1984). Another precursor was the development and maintenance of permanent cultures of myeloma cells, by Michael Potter (Physiol. Rev., 52: 631–719, 1972).

The impact of the Milstein-Köhler discovery was felt immediately in biomedical research, including cancer research, and has led to commercial exploitations. Monoclonal antibodies represent a culmination of research that started with the transplantation of tumors and the ability to grow mammalian cells in vitro. Tissue culture techniques were initiated in 1911 (see Cancer Research cover for November 1966). The derivation of colonies from single cells, or clones, was accomplished in 1948 (see Cancer Research cover for December 1981). In 1962, hybrids between somatic cells were described and produced at will (see Cancer Research cover for March 1979). Monoclonal antibodies arrived in 1975.

Pictured are Cesar Milstein (left) and Georges Köhler (right). The figure, from the Nature article of 1975, is on the isolation of one anti-sheep red blood cell-secreting cell clone.

We are indebted to Drs. Milstein and Köhler for their portraits and the figure.

M. B. S.