

Roy West

Immunization in Canada: Current Controversies

SUMMARY

Immunization, once used solely to control a disease, is now sufficiently widespread that elimination or even eradication of certain diseases has become possible. However, with greater control of disease, adverse reaction to immunization has taken on new prominence. Reporting of adverse reactions varies widely across Canada, and may be due to administrative differences—some provinces rely mostly on the public sector for immunizations, others on the private sector. Several controversies over immunizing agents remain, for example, live versus killed poliovirus vaccine, but generally immunization in Canada is now relatively uniform and safe. (*Can Fam Physician* 1985; 31:77-81).

SOMMAIRE

La pratique de l'immunisation, jadis utilisée seule pour contrôler une maladie, est maintenant répandue au point qu'il est devenu possible d'éliminer et même d'enrayer certaines maladies. Cependant, malgré un contrôle accru de la maladie, les réactions adverses aux immunisations ont pris une nouvelle envergure. Les rapports de ces réactions adverses varient considérablement au Canada, et peuvent s'expliquer par des différences administratives—certaines provinces confient davantage les immunisations au secteur public, et d'autres au secteur privé. Il persiste différentes controverses au sujet des agents d'immunisations, par exemple le vaccin au virus de la polio vivant versus tué. Mais, généralement, les immunisations au Canada sont maintenant relativement uniformes et inoffensives.

Key words: Immunization, adverse reaction, prevention

Dr. West is Provincial Epidemiologist in the Community Health Services Branch, Saskatchewan Health. Reprint requests to: 3475 Albert Street, Regina, SK. S4S 6X6.

SINCE THE 1930s, immunization has undergone many changes, in the types of immunizing agents available and who should receive them—the total population (usually in childhood), or selected high risk groups. In addition immunization has been delivered through both the public and private health care sectors. At times, community groups have given support, (e.g., during the poliomyelitis vaccination campaigns in the 1950s.

In recent years, primary immunization of Canadian infants has been shared largely between family physicians, pediatricians and public health

nurses. Because provincial governments have the major responsibility for health, patterns of delivery vary between the public and private sectors from province to province. Saskatchewan and Alberta immunize most infants and children through the public sector, whereas an increasing proportion is delivered by the private sector in the other provinces.

The federal government is responsible for regulating products, providing a national disease surveillance program and giving advice. This is given through the National Advisory Committee on Immunization (NACI) and published in the 'Green Book'—'A Guide to Immunization for Canadians'.¹ The first edition of these guidelines was published in 1980 and the second, which includes an extra chapter on Immunization of Health Care Workers, will be published in

the very near future.¹ In recent years infant and childhood immunization schedules have become very similar across the country. The major difference is that three provinces, Ontario, Nova Scotia, and Newfoundland, prefer the use of Salk (killed) rather than Sabin (live) poliomyelitis vaccine. The schedule in Prince Edward Island includes four doses of Salk and two doses of Sabin poliomyelitis vaccine.

Purpose of Immunization

For many years, the purpose of immunization was to help control communicable diseases by reducing the number of people susceptible to infection, thereby interrupting the chain of disease transmission.

Since the vaccination program

which eradicated smallpox in the world, two new targets are now considered. These are elimination and eradication. Elimination is total control in a geographic area (e.g., the elimination of measles in North America). Elimination does not prevent the importation of new cases and contact with susceptible people from other areas. Vigilance must be maintained for such people. Eradication is the total, global extinction of a disease. The World Health Organization has established criteria for diseases which it is feasible to eradicate. These criteria include:

- that the disease is readily recognizable clinically and can be confirmed by laboratory tests.
- that the disease has a short incubation period.
- that an effective vaccine is available.
- that the disease has no reservoir other than man.

Measles meets these criteria. However, in most parts of the world control of measles is still the target.

As control of communicable diseases increases and the impact of major epidemics lessens, the small but real adverse effects associated with immunization programs take on increasing importance.² Provision must be made for the few people harmed by population-wide immunization programs. This has become a major issue in the U.S. and until this question is satisfactorily answered costs of vaccines will continue to increase and routine programs will be in jeopardy.

Immunizing Agents

Considerable progress has been made towards producing pure, stable immunizing agents which have a high immunogenicity but a low rate of adverse reactions. Currently, several vaccine preparations are used for active immunization. Larke³ has described these in detail (see Table 1).

The future is probably in genetically-engineered, highly pure antigens for immunization. Until that time, the problems of adverse reactions, no matter how rare, must be faced.

Adverse Reaction

The true rate of adverse reactions to immunizing agents in Canada is un-

known. Current information is based on spontaneous adverse reaction reports sent by practicing health care professionals, either directly to the Adverse Reaction Program of the Federal Health Protection Branch, or indirectly through local and provincial health authorities. Table 2 illustrates the problems with this system. The volume of reports from the four western provinces is considerably higher than in eastern Canada. The table is for the time when the western provinces were switching from fluid diphtheria, pertussis and tetanus vaccines to the adsorbed product. This change in vaccines is clearly seen in the adverse reaction reports from the western provinces. Although not all eastern provinces made the switch, because DPT-polio was not available in the adsorbed form at that time, the rate of reporting reactions to the fluid vaccine is clearly different in eastern and western Canada. Does this reflect the fact that more immunizations are

given through the public sector in western Canada and therefore adverse reactions are more likely to be reported?

The utility of spontaneous adverse reaction reporting is questionable, particularly when under-reporting is evident. Some believe pertussis immunization may cause serious, acute neurological illness in children; this belief cannot be proved or disproved by a spontaneous adverse reaction reporting system. Although claims have been made from Britain of a significant association, no such association has been demonstrated in Canada. The position of NACI remains that the benefits of this vaccine far outweigh any associated risks.

Obviously, vaccination is not without a very low degree of risk. In the U.S., court action following non-negligent, vaccine associated disability has become relatively commonplace.^{13, 14} This has led many manufacturers to discontinue vaccine

TABLE 1
Vaccines Used for Active Immunization³

Vaccine	Examples
Whole microorganisms inactivated by heat or chemicals	Pertussis, typhoid, killed poliovirus
Fractions of extracted microorganisms	Pneumococcal and meningococcal polysaccharide vaccines
Toxoids made by formalin inactivation of purified bacterial toxins	Tetanus and diphtheria toxoids
Live, attenuated virus vaccines	Measles, rubella, mumps and Sabin poliovirus
Vaccines which afford 'cross protection'	Vaccinia virus gives protection against smallpox

TABLE 2
Reported Adverse Reactions to Adsorbed and Fluid DPT and DT, Canada, Jan 1980-Jun 1981¹³ (Source: Adverse Reaction Program, HPB, Ottawa)

Area	Jan-Jun 1981		Jan-Dec 1980	
	Adsorbed	Fluid	Adsorbed	Fluid
Newfoundland	0	0	0	0
Prince Edward Island	0	0	0	0
Nova Scotia	0	0	0	0
New Brunswick	0	0	0	2
Quebec	0	1	0	4
Ontario	0	0	0	2
Manitoba	8	0	3	3
Saskatchewan	20	5	2	15
Alberta	47	3	18	16
British Columbia	13	3	0	19
Canada (except Yukon and Northwest Territories)	88	12	23	61

production. To date, this has not been a problem in Canada.

However, Canadian governments should be discussing full, no-fault compensation for patients who suffer from one of the rare, but unpredictable, disabilities resulting from a recommended immunization program.

Immunization Schedules

Due to the efforts of the NACI, Canada is the closest it has ever been to having common, recommended vaccination schedules in all provinces.

However, small differences still occur. I have already mentioned the choice of Salk virus or Sabin poliovirus vaccine. The exact timing of the routine immunization schedule for infants and children may vary slightly, but not greatly from that recommended by NACI (see Table 3). Also, if Sabin (oral) poliovirus vaccine is used, the need for six doses of poliovirus vaccine during childhood is debatable. NACI currently states that the doses of poliovirus vaccine at six months and 14-16 years may be omitted if live (oral) poliovirus vaccine is used. However, at this time, most Canadian jurisdictions continue to recommend that these doses be given.

The immunization of adults requires special attention. Guidelines for adult immunization are given in the 'Green Book'.¹ Such immunization may be primary series in those not immunized in childhood; other immunizations may be for those who have received an incomplete schedule, who received vaccines which are now considered inadequate (e.g., killed measles vaccine), were given incorrect procedures (e.g., concurrent

administration of immune globulin with live virus vaccine).

Specific Vaccines

Immunization is changing. Questions are raised about many immunization agents, the dose and route by which they are delivered, and the correct age or time for delivering the vaccine.

Poliovirus vaccine

The debate about live virus vs. killed poliovirus vaccines is longstanding. Melnick⁴ has comprehensively addressed the advantages and disadvantages of these two products. Both products have been successful in controlling paralytic poliomyelitis in Canada. Both are equally recommended by the NACI. However, the cost of producing the killed vaccine is higher, as a greater virus dosage is required to elicit a satisfactory immune response.

The other current issue concerns the number of doses of vaccine required during childhood to produce and maintain an adequate response. It is now felt that six doses of oral vaccine during childhood are not necessary and some authorities¹ suggest that this may be cut to four. It is still recommended that six doses of the killed product be given.

Diphtheria, pertussis and tetanus vaccine

No vaccine has created more controversy in recent times than the pertussis component of diphtheria, pertussis and tetanus vaccine. In April 1982, NBC television aired an hour-long show emphasizing the dangers of pertussis vaccine. The show was

based on the reported neurological problems associated with the vaccine in Britain.^{5,6} The vaccine was introduced in England in 1942. By 1974, it was estimated that 75% of British children were vaccinated against pertussis. Following allegations of adverse reactions after pertussis immunization, the estimated coverage of pre-school children dropped to 30% by 1978. British notifications of pertussis began to increase in 1977 and in 1978-1979 a major epidemic resulted in more than 100,000 cases of pertussis and 36 deaths.¹⁵ This British experience clearly shows that the continued, routine vaccination of infants is necessary to prevent a resurgence of pertussis. This policy is supported in Canada, which has continued to have low rates of whooping cough over the last ten years.

In 1980, diphtheria and tetanus toxoids became available in Canada in the adsorbed form, compared with the previously available fluid product. In the adsorbed preparation, the toxoid is combined with aluminum phosphate, which produces an agent which gives a higher immune response than that provided by the fluid product. These products are available alone, in combination with each other and combined with pertussis vaccine. This last product is the one most commonly used for primary immunization of children under seven.

Adsorbed vaccines must be given intramuscularly, compared with fluid preparations' subcutaneous route of injection. When the adsorbed products were introduced, higher rates of local adverse reactions, including sterile abscesses, were reported.⁷ A case has been made that this increased rate may be due partly to the amount of aluminum phosphate in the product. In addition, the intramuscular route of injection may have contributed to the problem.

Not all provinces switched to the DTP adsorbed product, as it was not initially available in a combined form with killed poliomyelitis vaccine. This combined quadruple antigen became available in Canada in 1984.

Historically, local or systemic reactions after DPT have been attributed to the pertussis component. The reaction rates from the combined vaccines are the same as from pertussis vaccine alone.

Because of an increased risk of adverse outcomes, pertussis vaccine is

TABLE 3
Routine Immunization Schedule for Infants and Children¹

Age	Immunization Against			
2 mos.	Diphtheria	Pertussis	Tetanus	Poliomyelitis
4 mos.	Diphtheria	Pertussis	Tetanus	Poliomyelitis
6 mos.	Diphtheria	Pertussis	Tetanus	Poliomyelitis*
12 mos.	Measles	Mumps	Rubella**	
18 mos.	Diphtheria	Pertussis	Tetanus	Poliomyelitis
4-6 yrs.	Diphtheria	Pertussis	Tetanus	Poliomyelitis
14-16 yrs.	Diphtheria***		Tetanus***	Poliomyelitis*

* This dose may be omitted if live (oral) poliovirus vaccine is used.

** Rubella vaccine is also indicated for all girls and women of childbearing age who lack proof of immunity.

*** Diphtheria and tetanus toxoid (Td), a combined adsorbed 'adult type' preparation for patients age seven and older, contains less diphtheria toxoid than preparations given to younger children, and is less likely to cause reactions.

not recommended in those aged seven or older. An adult preparation of diphtheria and tetanus toxoids is available, with a reduced dosage of diphtheria toxoid (Td, adult-type preparation). If the adsorbed adult preparation is used, a Schick test or sensitivity test is not considered necessary.

Measles, mumps and rubella vaccine (MMR)

These three live-virus vaccines are available as single antigens or combined. All provinces now recommend immunizing infants with the triple vaccine. Most provinces advise immunization at or just after one-year of age. However, Nova Scotia, New Brunswick, and Prince Edward Island promote its use after 15 months. Evidence to date indicates that such vaccination will result in long lasting immunity.⁸

Rubella vaccine should be offered to all women of child-bearing age who do not have either documented evidence of vaccination or laboratory evidence of previous infection.^{1,8} However, live measles, mumps or rubella vaccines should not be given to women who are already pregnant or suspected to be pregnant.

Influenza vaccines

Traditionally, influenza vaccines have been recommended for people of any age who have specific conditions which place them at high risk¹ and for older people, particularly those over age 65. Consideration may also be given to people who provide essential community service (e.g., hospital workers).

The efficacy of influenza vaccine in the face of an epidemic has never been truly demonstrated. In fact, the only attempt at mass influenza immunization was against the perceived threat of swine-flu in 1976. This resulted in a considerable threat to the credibility of influenza immunization specifically, and immunization programs generally.

During the 1960s and early 1970s some virologists believed that an understanding of the 'shifts' and 'drifts' of the antigens in the influenza A virus was being achieved.¹⁶ However,

events since 1976 have led to the proposed cyclical pattern, with similar strains of virus returning every 50-80 years and a major epidemic or pandemic every ten to 15 years, being drawn into question.

Only minor shifts in the two current strains of influenza A virus (H3 N2) and (H1N1) have occurred in the last seven to eight years, and so the usefulness of annually vaccinating the well elderly must be reexamined. The most recent recommendations for prevention and control of influenza, issued by the U.S. Immunization Practices Advisory Committee (ACIP), have decreased the emphasis on vaccinating healthy people over age 65.⁹

Rabies vaccine

The advent of rabies virus vaccine grown in human diploid cells (HDCV) was a major advance. The HDCV is now the vaccine of choice for both pre- and post-exposure immunization. The HDCV is a highly efficacious product which has reduced the chance of adverse reactions and at the same time improved the immune response and thereby reduced the number of doses required for post-exposure prophylaxis. A comprehensive set of recommendations for use is included in the 'Green Book' guide.¹

Currently, the advantages, disadvantages, and cost of small (0.1 ml) doses given intradermally compared with larger (1.0 ml) doses given by the deep subcutaneous or intramuscular route are under discussion.¹⁰ Considerable work is being done in this area, and the use of the intradermal route is slowly being introduced for pre-exposure vaccination in high risk groups. The intradermal route is not recommended at this time for the post-exposure treatment, although several trials are being undertaken in this area.^{11, 12}

Other vaccines

In recent years, hepatitis B vaccine, meningococcal polysaccharide vaccine and pneumococcal vaccines have been introduced. Each of these products is marketed for use in specific, high-risk individuals rather than for universal immunization programs. Specific de-

tails on the recommended use of these may be found elsewhere.^{1, 17}

Vaccination for travellers

The number of Canadians travelling outside North America has greatly increased. Thus, the risk of exposure to diseases not normally encountered in this country, but for which vaccines are available, is increased. These include polio, typhoid, cholera, and yellow fever. In certain parts of the world exposure to hepatitis (both A and B) should be considered.

Vaccination requirements will vary depending on the individual's destination, length of stay and activities. In general, people going on vacation for a short time are over-vaccinated against typhoid and perhaps under-vaccinated against polio.

The World Health Organization produces regular updates for countries in which yellow fever and cholera vaccination is required. These are distributed through provincial health authorities.

Passive immunization

Standard immune serum globulin (or gamma globulin) is available for treatment of those exposed to measles, rubella and hepatitis A.

Specific immune globulins available are hepatitis B, rabies, pertussis, tetanus, and varicella-zoster as well as botulism, diphtheria and gas gangrene antitoxins.

The recommended use of all these products is described in the 'Green Book'.¹

Conclusion

Immunization schedules across Canada are more consistent than they have ever been. However, provincial differences do occur, particularly in the use of Salk and Sabin poliomyelitis vaccine. There are also differences in the provincial provision of vaccines, such as influenza and hepatitis B vaccine, and vaccines for travellers.

In general, Canadian immunization programs are safe and effective and have greatly reduced the occurrence of infectious diseases. For example, from 1953-1983 the disease rates per

100,000 population have been reduced from 28.3 to zero for paralytic poliomyelitis, from 0.9 to <0.1 for diphtheria, and from 380 to 3.8 for measles.^{18, 20}

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Xanax[®] tablets (alprazolam)

ACTION: XANAX (alprazolam) is a benzodiazepine with anxiolytic properties.

Orally administered alprazolam is readily absorbed in man with peak plasma concentrations occurring 1 to 2 hours following administration. The half-life range of alprazolam is 6 to 20 hours following single dose administration. With multiple doses, given 3 times daily, steady state is reached within 7 days. Alprazolam and its metabolites are excreted primarily in the urine. Degradation of alprazolam occurs mainly by oxidation yielding the primary metabolites α -hydroxy-alprazolam and a benzophenone derivative. The α -hydroxymetabolite is further transformed to demethylalprazolam. The α -hydroxy-alprazolam and demethylalprazolam are active and appear to have half-lives similar to alprazolam but are present at only low levels in the plasma. Alprazolam is 80% protein-bound.

In sleep laboratory studies in man, alprazolam decreased sleep latency, increased duration of sleep and decreased the number of nocturnal awakenings. Alprazolam produced small decreases in both stage 3 and 4 and REM sleep. Alprazolam increased REM latency in a dose-related manner.

Alprazolam 0.5 mg, administered 3 times a day for 14 days, did not affect prothrombin times or plasma warfarin levels in male volunteers administered sodium warfarin orally.

INDICATIONS: XANAX (alprazolam) is indicated for the short-term symptomatic relief of excessive anxiety in patients with anxiety neurosis.

CONTRAINDICATIONS: XANAX (alprazolam) is contraindicated in patients with known hypersensitivity to alprazolam or other benzodiazepines. XANAX is also contraindicated in pregnancy, in infants and in patients with myasthenia gravis and acute narrow angle glaucoma.

WARNINGS: XANAX (alprazolam) is not recommended for use in patients whose primary diagnosis is psychosis or depression.

Driving and Hazardous Activities: As with other CNS-active drugs, patients receiving XANAX should be cautioned not to undertake activities requiring mental alertness, judgement and physical coordination such as driving or operating machinery, particularly in the early phases of dose adjustment, and until it has been established that they do not become drowsy or dizzy while taking XANAX. Alcohol and benzodiazepines should never be mixed when driving because of the unpredictable CNS depressant effects of this combination.

Use in Pregnancy: The safety of the use of XANAX in pregnancy has not been established. Therefore, XANAX is not recommended for use during pregnancy. Several studies have suggested an increased risk of congenital malformations associated with the use of the benzodiazepines chloridazepoxide and diazepam, and meprobamate, during the first trimester of pregnancy. Since alprazolam is also a benzodiazepine derivative, its administration is rarely justified in women of childbearing potential. If the drug is prescribed to a woman of childbearing potential she should be warned to consult her physician regarding the discontinuation of the drug if she intends to become or suspects that she is pregnant.

Use in Nursing Mothers: Studies in rats have indicated that XANAX and its metabolites are secreted into the milk. Therefore, nursing should not be undertaken while a patient is receiving the drug.

Use in Children and Adolescents: The safety and efficacy of XANAX in patients under the age of 18 years has not been established.

PRECAUTIONS: *Use in the Elderly:* Elderly and debilitated patients, or those with organic brain syndrome, have been found to be prone to the CNS depressant activity of benzodiazepines even after low doses. Manifestations of this CNS depressant activity include ataxia, over-sedation and hypotension. Therefore, medication should be administered with caution to these patients, particularly if a drop in blood pressure might lead to cardiac complications. Initial doses should be low and increments should be made gradually, depending on the response of the patient, in order to avoid oversedation, neurological impairment and other possible adverse reactions.

Dependence Liability: XANAX (alprazolam) should not be administered to individuals prone to drug abuse. Caution should be observed in all patients who are considered to have potential for psychological dependence. Withdrawal symptoms have been observed after abrupt discontinuation of benzodiazepines. These include irritability, nervousness, insomnia, agitation, tremors, convulsions, diarrhea, abdominal cramps, vomiting and mental impairment. Since these symptoms may be similar to those for which the patient is being treated, it may appear that he has suffered a relapse upon discontinuation. It is suggested that XANAX should be withdrawn gradually if the individual is suspected of having become dependent, or the drug perhaps has been used in prolonged high doses.

Use in Mental and Emotional Disorders: It should be recognized that suicidal tendencies may be present in patients with emotional disorders, particularly when depressed and that protective measures and appropriate treatment may be necessary and should be instituted without delay.

Since excitement and other paradoxical reactions can result from the use of anxiolytic-sedatives in psychotic patients, XANAX should not be used in patients suspected of having psychotic tendencies. As with other benzodiazepines, XANAX should not be used in individuals with physiological anxiety or normal stress of daily living but only in the presence of disabling manifestations of an appropriate pathological anxiety disorder.

These drugs are not effective in patients with characterological and personality disorders or those with obsessive-compulsive disorders. XANAX is not recommended for the management of depressive or psychotic disorders.

Use in Patients with Impaired Renal or Hepatic Function: If treatment is necessary in patients with impaired hepatic or renal function, therapy should be initiated at a very low dose and the dosage increased only to the extent that it is compatible with the degree of residual function of these organs. Such patients should be followed closely and have periodic laboratory assessments.

Laboratory Tests: If XANAX is administered for repeated cycles of therapy, periodic blood counts and liver function tests are advisable.

Epileptic Patients: Since benzodiazepines may occasionally exacerbate grand mal seizures, caution is required when XANAX is used in epileptic patients and an adjustment may be necessary in their anticonvulsive medication. Abrupt withdrawal of XANAX should be avoided.

Drug Interactions: Benzodiazepines may potentiate or interact with effects of other CNS-acting drugs such as alcohol, narcotics, barbiturates, nonbarbiturate hypnotics, antihistamines, phenothiazines, butyrophenones, monoamine oxidase inhibitors, tricyclic antidepressants and anticonvulsants. Therefore, if XANAX is to be combined with other drugs acting on the CNS, careful consideration should be given to the pharmacology of the agent involved because of the possible additive or potentiating effects. Patients should also be advised against the simultaneous use of other CNS depressant drugs and should be cautioned not to take alcohol during the administration of XANAX.

ADVERSE REACTIONS: The most frequently reported adverse reactions with XANAX (alprazolam) were drowsiness, coordination difficulties and dizziness. Release of hostility and other paradoxical effects such as irritability, excitability and hallucinations are known to occur with the use of benzodiazepines.

Other side effects less frequently reported, listed by body systems, include the following:

Neurologic: Blurred vision, headache, seizures, slurred speech, difficulty in depth perception.

Psychiatric: Agitation, mental confusion, depression, irritability, nervousness, sleep disturbances, euphoria, lethargy, stupor.

Gastrointestinal: Dry mouth, nausea, non-specific gastrointestinal disturbances, vomiting.

Musculoskeletal: Muscle spasm, muscle weakness.

Cardiovascular: Hypotension, palpitations, tachycardia.

Dermatologic: Pruritus, rash.

Genitourinary: Incontinence, change in libido.

Hematologic: Decreased hemoglobin and hematocrit, increased and decreased WBC.

Hepatic: Elevations of alkaline phosphatase, bilirubin, SGOT, SGPT.

Miscellaneous: Increased and decreased blood sugar levels.

SYMPTOMS AND TREATMENT OF OVERDOSAGE: *Symptoms:* As in the management of overdose with any drug, it should be remembered that multiple agents may have been ingested. Overdose of XANAX (alprazolam) is manifested as an extension of its pharmacologic activity. Thus, varying degrees of CNS depressant effects such as somnolence and hypnosis can occur. Other manifestations of overdose may include muscle weakness, ataxia, dysarthria and particularly in children paradoxical excitement. In more severe cases diminished reflexes, confusion and coma may ensue.

Fatalities with benzodiazepines rarely occur except when other drugs, alcohol or aggravating factors are involved.

Treatment: Vomiting may be induced if the patient is fully awake. Vital signs should be monitored and general supportive measures should be employed as indicated. Gastric lavage should be instituted as soon as possible. Intravenous fluids may be administered and an adequate airway should be maintained.

Experiments in animals have indicated that cardiopulmonary collapse can occur with massive intravenous doses of alprazolam. This could be reversed with positive mechanical respiration and the intravenous infusion of levaterenol.

Animal experiments with alprazolam and related compounds have suggested that hemodialysis and forced diuresis are probably of little value.

DOSE AND ADMINISTRATION: The dosage of XANAX (alprazolam) must be individualized and carefully titrated in order to avoid excessive sedation or mental and motor impairment. As with other anxiolytic-sedatives, short courses of treatment should usually be the rule for the symptomatic relief of excessive anxiety and the initial course of treatment should not last longer than one week without reassessment of the need for a limited extension. If necessary, drug dosage can be adjusted after one week of treatment. Initially, not more than one week's supply of the drug should be provided and automatic prescription renewals should not be allowed. Subsequent prescriptions, when required, should be limited to short courses of therapy.

Usual Adult Dosage: The initial adult dosage of XANAX is 0.25 mg given 2 or 3 times daily. If required, increases may be made in 0.25 mg increments according to the severity of symptoms and patient response. It is recommended that the evening dose be increased before the daytime doses. Very severe manifestations of anxiety may require larger initial daily doses. The optimal dosage is one that permits symptomatic control of excessive anxiety without impairment of mental and motor function. Exceptionally, it may be necessary to increase dosage to a maximum of 3.0 mg daily, given in divided doses.

Elderly and Debilitated Patients: The initial dosage is 0.125 mg 2 or 3 times daily. If necessary, this dosage may be increased gradually depending on patient tolerance and response.

SUPPLIED: 0.25 mg (white) and 0.5 mg (peach) scored, ovoid-shaped tablets in bottles of 100 and 1000 tablets.

Product monograph available on request. CE 1756 2B

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