AZATHIOPRINE (Systemic)

Introduction

VA CLASSIFICATION (Primary/Secondary)¾IM403/MS109; GA400

Commonly used brand name(s):Imuran.

Note: For a listing of dosage forms and brand names by country availability, see Dosage Forms section(s).

Category

Immunosuppressant; antirheumatic (disease-modifying); bowel disease (inflammatory) suppressant; lupus erythematosus suppressant.

Indications

Note: Bracketed information in the Indications section refers to uses that are not included in U.S. product labeling.

Accepted

Transplant rejection, organ (prophylaxis)¾Azathioprine is indicated as an adjunct for prevention of rejection in renal homotransplantation 1.

[It is also indicated in the prevention of rejection in cardiac, hepatic, and pancreatic transplantation 12 .]

Arthritis, rheumatoid (treatment)¾Azathioprine is indicated for the management of severe, active, and erosive rheumatoid arthritis unresponsive to rest or conventional medications 1.

[Bowel disease, inflammatory (treatment) 35, 36] *

[Cirrhosis, biliary (treatment)] *

[Dermatomyositis, systemic (treatment) 39, 40, 45] *

[Glomerulonephritis (treatment)] *

[Hepatitis, chronic active (treatment) 37] *

[Lupus erythematosus, systemic (treatment) 38, 50] *

[Myasthenia gravis (treatment) 41] *

[Myopathy, inflammatory (treatment)] *

[Nephrotic syndrome (treatment) 42] *

[Pemphigoid (treatment)] * or

[Pemphigus (treatment)] *¾Azathioprine also is indicated in the treatment of other immunologic diseases including regional and ulcerative colitis, biliary cirrhosis, systemic dermatomyositis (polymyositis), glomerulonephritis, chronic active hepatitis, systemic lupus erythematosus (SLE), inflammatory myopathy, myasthenia gravis, nephrotic syndrome, pemphigus, and pemphigoid.

* Not included in Canadian product labeling.

Pharmacology/Pharmacokinetics

Physicochemical characteristics:

Molecular weight¾277.27 24

Mechanism of action/Effect:

The exact mechanism of immunosuppressive action is unknown since the exact mechanism of the immune response itself is complex and not completely understood. The immunosuppressive effects of azathioprine involve a greater suppression of delayed hypersensitivity and cellular cytotoxicity tests than of antibody responses 1.

Azathioprine antagonizes purine metabolism and may inhibit synthesis of DNA, RNA, and proteins; it may also interfere with cellular metabolism and inhibit mitosis.

The mechanism of action of azathioprine in rheumatoid arthritis and other immunologic diseases is unknown but may be related to immunosuppression 1.

Azathioprine has a steroid-sparing effect, which allows a reduction in steroid dose when the two are combined in chronic inflammatory diseases 1.

Absorption:

Well absorbed from the gastrointestinal tract 1.

Protein binding:

Low (30%) 1.

Biotransformation:

Largely converted to 6-mercaptopurine 1 and 6-thioinosinic acid (active metabolites). Further metabolism¾Hepatic, largely by xanthine oxidase, and in erythrocytes 1.

Proportions of metabolites vary among individual patients 1.

Half-life:

Approximately 5 hours (unchanged drug and metabolites) 1.

Onset of action:

In rheumatoid arthritis¾6 to 8 weeks 1.

In other inflammatory disorders¾4 to 8 weeks 3.

Time to peak concentration:

Serum¾1 to 2 hours 1.

Duration of action:

Immunosuppressant¾Clinical effects may persist for long periods after the medication is eliminated.

Elimination:

Hepatic (biliary) 1.

Renal (1 to 2% unchanged).

In dialysis¾Partially removable by hemodialysis 1.

Precautions to Consider

Carcinogenicity

Azathioprine has been shown to be carcinogenic in animals and may be associated with an increased risk of development of carcinomas in humans, especially skin cancer and reticulum cell tumors or lymphomas in renal transplant patients and acute myelocytic leukemia and some solid tumors in rheumatoid arthritis patients 1, 6.

The risk of neoplastic toxicity appears to be lower in rheumatoid arthritis patients than in renal transplant patients; however, there is evidence that the risk is increased with prior use of alkylating agents 1.

Mutagenicity

Mutagenic effects have been reported in animals, and chromosomal abnormalities (reversible when azathioprine is discontinued) have been noted in humans 1.

Pregnancy/Reproduction

Fertility¾Azathioprine has been reported to cause temporary depression in spermatogenesis and reduction in sperm viability and sperm count in mice at doses 10 times the human therapeutic dose

1 ; a reduced percentage of fertile matings occurred when animals received 5 mg per kg of body weight (mg/kg) 1.

Pregnancy¾Adequate and well-controlled studies in humans have not been done 1.

Azathioprine crosses the placenta 1.

Risk-benefit must be considered, especially during the first trimester, since azathioprine affects cell kinetics and can theoretically cause mutagenicity or teratogenicity.

There have been reports of limited immunologic abnormalities (lymphopenia, diminished immunoglobulin G [IgG] and immunoglobulin M [IgM] levels, cytomegalovirus [CMV] infection, and decreased thymic shadow; pancytopenia and severe immune deficiency) and other abnormalities (preaxial polydactyly in an infant whose mother received azathioprine and prednisone; meningomyelocele, bilateral dislocated hips, and bilateral talipes equinovarus in an infant whose father received azathioprine) in infants of renal homograft recipients treated with azathioprine 1.

Azathioprine is not recommended for use in pregnant women with rheumatoid arthritis 1.

Teratogenic effects (including skeletal malformations and visceral abnormalities) have been reported in rabbits and mice given doses equivalent to the human dose (5 mg/kg a day) 1.

FDA Pregnancy Category D 1.

Breast-feeding

Azathioprine is distributed, at low concentrations, into breast milk 1, 29.

Use by nursing mothers is not recommended because of possible adverse effects (especially tumorigenicity) in the infant 1.

Pediatrics

Appropriate studies performed to date have not demonstrated pediatrics-specific problems that would limit the usefulness of azathioprine in children.

Geriatrics

Although appropriate studies on the relationship of age to the effects of azathioprine have not been performed in the geriatric population, geriatrics-specific problems are not expected to limit the usefulness of this medication in the elderly. However, elderly patients are more likely to have age-related renal function impairment, which may require reduced dosage in patients receiving azathioprine.

Dental

The bone marrow-depressant effects of azathioprine may result in an increased incidence of microbial infection, delayed healing, and gingival bleeding. Dental work, whenever possible, should

be completed prior to initiation of therapy or deferred until blood counts have returned to normal. Patients should be instructed in proper oral hygiene during treatment, including caution in use of regular toothbrushes, dental floss, and toothpicks.

In addition, azathioprine rarely causes sores in the mouth and on the lips.

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

>> Allopurinol

(allopurinol-induced inhibition of xanthine oxidase-mediated metabolism may result in greatly increased azathioprine activity and toxicity 1, 25, 26, 27 ; concurrent use should be avoided if possible, especially in renal transplant patients, because of the high risk of 6-mercaptopurine [azathioprine metabolite] accumulation and consequent azathioprine toxicity if the transplanted kidney is rejected 2 ; if concurrent use is essential, it is recommended that azathioprine dosage be reduced to one quarter to one third of the usual dosage 1 , the patient be carefully monitored, and subsequent dosage adjustments be based on patient response and evidence of toxicity)

Angiotensin-converting enzyme inhibitors

(increased risk of anemia and leukopenia 1)

Blood dyscrasia-causing medications (see Appendix II)

(leukopenic and/or thrombocytopenic effects of azathioprine may be increased with concurrent or recent therapy if these medications cause the same effects; dosage adjustment of azathioprine, if necessary, should be based on blood counts)

>> Bone marrow depressants, other (see Appendix II) 1 or

Radiation therapy

(concurrent use with azathioprine may increase the bone marrow depressant effects of these medications and radiation therapy; dosage reduction may be required; use prior to azathioprine therapy may be associated with an increased risk of development of neoplasms 1)

>> Immunosuppressants, other, such as:

Chlorambucil

Corticosteroids, glucocorticoid

Cyclophosphamide

Cyclosporine

Mercaptopurine

Muromonab-CD3

(concurrent use with azathioprine may increase the risk of infection and development of neoplasms 1)

Vaccines, killed virus

(because normal defense mechanisms may be suppressed by azathioprine therapy, the patient's antibody response to the vaccine may be decreased. The interval between discontinuation of medications that cause immunosuppression and restoration of the patient's ability to respond to the vaccine depends on the intensity and type of immunosuppression-causing medication used, the underlying disease, and other factors; estimates vary from 3 months to 1 year)

>> Vaccines, live virus

(because normal defense mechanisms may be suppressed by azathioprine therapy, concurrent use with a live virus vaccine may potentiate the replication of the vaccine virus, may increase the side/adverse effects of the vaccine virus, and/or may decrease the patient's antibody response to the vaccine; immunization of these patients should be undertaken only with extreme caution after careful review of the patient's hematologic status and only with the knowledge and consent of the physician managing the azathioprine therapy. The interval between discontinuation of medications that cause immunosuppression and restoration of the patient's ability to respond to the vaccine depends on the intensity and type of immunosuppression-causing medication used, the underlying disease, and other factors; estimates vary from 3 months to 1 year. Patients with leukemia in remission should not receive live virus vaccine until at least 3 months after their last chemotherapy. In addition, immunization with oral poliovirus vaccine should be postponed in persons in close contact with the patient, especially family members)

Warfarin

(activity of warfarin may be decreased; increased doses of warfarin may be needed 43, 44)

Laboratory value alterations

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):

With physiology/laboratory test values

Alanine aminotransferase (ALT [SGPT]) and

Alkaline phosphatase and

Amylase and

Aspartate aminotransferase (AST [SGOT]) and

Bilirubin

(serum values may be increased in association with toxic hepatitis and biliary stasis, primarily in allograft recipients; may also be increased as part of a gastrointestinal hypersensitivity reaction 1 ; uncommon in rheumatoid arthritis patients 1)

Albumin, plasma and

Hemoglobin and

Uric acid in blood and urine

(concentrations may be decreased)

Mean corpuscular volume (MCV)

(may be increased; occurs commonly, as a sign of macrocytosis)

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)¾ not necessarily inclusive (>> = major clinical significance).

Risk-benefit should be considered when the following medical problems exist

>> Chickenpox, existing or recent (including recent exposure) or

>> Herpes zoster

(risk of severe generalized disease)

>> Gout

(because of interaction with allopurinol)

>> Hepatic function impairment

>> Infection

Pancreatitis

>> Renal function impairment

(increased risk of hematologic toxicity 1 ; a lower dosage of azathioprine is recommended for patients with impaired renal function 1)

>> Sensitivity to azathioprine 1

>> Xanthine oxidase deficiency, severe

(reduced metabolism may result in increased azathioprine activity and toxicity 3)

>> Caution should be used also in patients who have had previous cytotoxic drug therapy and radiation therapy.

Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; >> = major clinical significance):

>> Complete blood counts

(recommended at least weekly during the first 2 months of therapy 4 ; frequency may be reduced to monthly once the patient is stabilized)

Side/Adverse Effects

Note: The risk of hematologic and neoplastic toxicity appears to be lower in rheumatoid arthritis patients 1 because of the lower doses used 14.

Bone marrow depression may be more severe in renal transplant patients whose hemografts are undergoing rejection 1.

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:

Those indicating need for medical attention

Incidence more frequent

Leukopenia or infection fever or chills); cough or hoarseness); lower back or side pain); painful or difficult urination 5)¾leukopenia is usually asymptomatic; megaloblastic anemia 30 unusual tiredness or weakness)

Note: Leukopenia may be severe or delayed 1 and is dose-related 1.

It is not correlated with therapeutic effect 1.

The incidence of infection in renal transplant patients is 30 to 60 times that in patients taking azathioprine for rheumatoid arthritis 1.

Infections may be fatal 1.

Incidence less frequent¾dose-relatedHepatitis or biliary stasis 1, 32, 33¾asymptomatic; thrombocytopenia unusual bleeding or bruising); black, tarry stools); blood in urine or stools); pinpoint red spots on skin 5)¾usually asymptomatic

Note: Hepatotoxicity usually occurs within 6 months of transplantation and usually is reversible on withdrawal of azathioprine 1.

It is uncommon (incidence less than 1%) in rheumatoid arthritis patients 1.

Hepatotoxicity occurs more frequently at dosages above 2.5 mg per kg of body weight (mg/kg) per day 3.

Thrombocytopenia may be severe or delayed 1 and is dose-related 1.

Incidence rare

Gastrointestinal hypersensitivity reaction 1, 47, 49 severe nausea and vomiting with diarrhea); sudden fever); joint pain); sudden unusual feeling of discomfort or illness); hepatic veno-occlusive disease 1, 7, 8, 9, 31 stomach pain); swelling of feet or lower legs)¾potentially fatal; hypersensitivity 10 fast heartbeat); sudden fever); muscle or joint pain); redness or blisters on skin 10, 11); pancreatitis, hypersensitivity 1, 10, 34 severe stomach pain with nausea and vomiting); pneumonitis cough); shortness of breath); sores in mouth and on lips

Note: Symptoms of the gastrointestinal hypersensitivity reaction usually develop within the first several weeks of therapy and are reversible on withdrawal of azathioprine 1 , although they will recur within hours after the first dose on rechallenge 1, 47, 49.

Hypotension may occasionally occur 1.

Hepatic enzymes may also be elevated 1.

Hypersensitivity reactions usually occur after at least 1 week of therapy 10 and are reversible on withdrawal 10.

The reaction may be more severe on rechallenge and can be fatal 10.

Those indicating need for medical attention only if they continue or are bothersome

Incidence more frequent

Loss of appetite; nausea or vomiting 1

Incidence less frequent

Skin rash 1

Those indicating the need for medical attention if they occur after medication is discontinued

Bone marrow depression, delayed 46 black, tarry stools); blood in urine); cough or hoarseness); fever or chills); lower back or side pain); painful or difficult urination); pinpoint red spots on skin); unusual bleeding or bruising)

Overdose

Clinical effects of overdose

The following effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:

Acute and/or chronic

Bleeding 1 pinpoint red spots on skin); unusual bleeding or bruising); diarrhea 1; leukopenia or infection 1 fever or chills); cough or hoarseness); lower back or side pain); painful or difficult urination); hepatotoxicity 1¾usually asymptomatic; however, liver function test abnormalities may occur; nausea 1; vomiting 1

Treatment of overdose

There is no published literature establishing the superiority of any specific techniques to treat azathioprine overdose. Treatment of azathioprine overdose is supportive 51.

To decrease absorption¾Although there is no literature on the usefulness of techniques to decrease absorption of azathioprine, gastric emptying within 30 minutes to 1 hour of ingestion may decrease systemic absorption 51.

To enhance elimination¾Hemodialysis can be used to enhance elimination. In one study, 45% of ingested azathioprine was removed during 8 hours of hemodialysis 1.

Monitoring¾White blood cell count and liver function tests should be monitored until the values return to normal. In one case of acute ingestion of 7500 mg of azathioprine, the values returned to normal after 6 days 1.

Patients in whom intentional overdose is confirmed or suspected should be referred for psychiatric consultation.

Patient Consultation

As an aid to patient consultation, refer to Advice for the Patient, Azathioprine (Systemic).

In providing consultation, consider emphasizing the following selected information (>> = major clinical significance):

Before using this medication

>> Conditions affecting use, especially:

Sensitivity to azathioprine

Pregnancy¾Use not recommended because of mutagenic or teratogenic potential

Breast-feeding¾Not recommended because of risk of serious side effects

Other medications, especially allopurinol or other immunosuppressants

Other medical problems, especially chickenpox, gout, hepatic function impairment, herpes zoster, infection, pancreatitis, renal function impairment, or xanthine oxidase deficiency

Proper use of this medication

>> Importance of not taking more or less medication than the amount prescribed

Caution with combination therapy; taking each medication at the right time

>> Checking with physician before discontinuing medication

Possible nausea or vomiting; taking after meals or at bedtime 3 to reduce stomach upset

Checking with physician if vomiting occurs shortly after dose is taken

>> Proper dosing

Missed dose¾ If dosing schedule is once a day¾Not taking missed dose and not doubling next one
If dosing schedule is several times a day¾Taking as soon as possible or doubling next dose; checking with physician if more than one dose is missed

>> Proper storage

Precautions while using this medication

>> Importance of close monitoring by physician

>> Avoiding immunizations unless approved by physician; other persons in patient's household should avoid immunizations with oral poliovirus vaccine; avoiding other persons who have taken oral poliovirus vaccine or wearing a protective mask that covers nose and mouth

Caution if bone marrow depression occurs

>> Avoiding exposure to persons with bacterial or viral infections, especially during periods of low blood counts; checking with physician immediately if fever or chills, cough or hoarseness, lower back or side pain, or painful or difficult urination occurs

>> Checking with physician immediately if unusual bleeding or bruising; black, tarry stools; blood in urine or stools; or pinpoint red spots on skin occur

Caution in use of regular toothbrush, dental floss, or toothpick; physician, dentist, or nurse may suggest alternatives; checking with physician before having dental work done

Not touching eyes or inside of nose unless hands washed immediately before

Using caution to avoid accidental cuts with use of sharp objects such as safety razor or fingernail or toenail cutters

Avoiding contact sports or other situations where bruising or injury could occur

Side/adverse effects

Importance of discussing possible effects, including cancer, with physician

Signs of potential side effects, especially leukopenia, infection, megaloblastic anemia, hepatitis, biliary stasis, thrombocytopenia, gastrointestinal hypersensitivity reaction, hepatic veno-occlusive disease, hypersensitivity, pancreatitis, pneumonitis, and sores in mouth and on lips

Asymptomatic side effects, including hepatotoxicity

General Dosing Information

Patients receiving azathioprine should be under supervision of a physician experienced in immunosuppressive therapy 1.

A variety of dosage schedules and regimens of azathioprine, alone or in combination with other immunosuppressive agents, are used. The prescriber may consult the medical literature as well as the manufacturer's literature in choosing a specific dosage.

Dosage must be adjusted to meet the individual requirements of each patient, on the basis of clinical response and appearance or severity of toxicity.

Cadaveric kidneys frequently develop a tubular necrosis with delayed onset of adequate function, necessitating a reduction in azathioprine dosage. If persistent negative nitrogen balance occurs, dosage should be reduced.

Because of the delayed action of azathioprine, dosage should be reduced or the medication withdrawn at the first sign of an abnormally large or persistent decrease in leukocyte count (to less than 3000 per cubic millimeter) or platelet count (to less than 100,000 per cubic millimeter) or other evidence of bone marrow depression 1.

Therapy may be reinstituted at a lower dosage when leukocyte and platelet counts return to acceptable levels, usually after 7 to 10 days.

Special precautions are recommended in patients who develop thrombocytopenia as a result of administration of azathioprine. These may include extreme care in performing invasive procedures; regular inspection of intravenous sites, skin (including perirectal area), and mucous membrane surfaces for signs of bleeding or bruising; limiting frequency of venipuncture and avoiding intramuscular injections; testing urine, emesis, stool, and secretions for occult blood; care in use of regular toothbrushes, dental floss, toothpicks, safety razors, and fingernail and toenail cutters; avoiding constipation; and using caution to prevent falls and other injuries. Such patients should avoid alcohol and aspirin intake because of the risk of gastrointestinal bleeding. Platelet transfusions may be required.

Patients who develop leukopenia should be observed carefully for signs of infection. Antibiotic support may be required. In patients with neutropenia who develop fever, broad-spectrum antibiotic coverage should be initiated empirically, pending bacterial cultures and appropriate diagnostic tests.

If an infection develops, it must be treated promptly; reduction of azathioprine dosage and/or use of other drugs may be necessary 1.

If symptoms of toxic hepatitis or biliary stasis appear, azathioprine therapy may have to be withdrawn. Patients with existing hepatic function impairment should be monitored carefully and treated with conservative doses (some clinicians recommend an initial dose of two thirds the usual dose). If hepatic veno-occlusive disease is clinically suspected, it is recommended that azathioprine be permanently withdrawn 1.

If signs of homograft rejection occur, a larger dose may be necessary. However, the dose should not be increased to toxic levels 1.

Other therapy should be considered if signs of homograft rejection persist.

For parenteral dosage forms

Azathioprine may be administered by intravenous push or infusion. Time for infusion is usually 30 to 60 minutes, but may range from 5 minutes to 8 hours 1.

Diet/Nutrition

Gastrointestinal upset may be reduced by giving oral azathioprine in divided doses or after meals 1.

Safety considerations for handling this medication

There is limited but increasing evidence and concern that personnel involved in preparation and administration of parenteral antineoplastics and immunosuppressants may be at some risk because of the potential mutagenicity, teratogenicity, and/or carcinogenicity of these agents, although the actual risk is unknown. USP advisory panels recommend cautious handling both in preparation and

disposal of antineoplastic and immunosuppressant agents. Precautions that have been suggested include:

· Use of a biological containment cabinet during reconstitution and dilution of parenteral medications and wearing of disposable surgical gloves and masks.

· Use of proper technique to prevent contamination of the medication, work area, and operator during transfer between containers (including proper training of personnel in this technique).

· Cautious and proper disposal of needles, syringes, vials, ampuls, and unused medication.A number of medical centers have developed detailed guidelines for handling of antineoplastic and immunosuppressant agents. 1

The manufacturer does not make any recommendations regarding the use of a biological containment cabinet or the wearing of disposable surgical gloves during reconstitution and dilution of azathioprine sodium for injection.

Oral Dosage Forms

Note: Bracketed uses in the Dosage Forms section refer to categories of use and/or indications that are not included in U.S. product labeling.

AZATHIOPRINE TABLETS USP

Usual adult and adolescent dose

Transplant rejection, organ (prophylaxis)¾Initial: Oral, 3 to 5 mg per kg of body weight 1 or 120 mg per square meter of body surface area a day, one to three days before or at the time of 1, 3 surgery, the dosage being adjusted to maintain the homograft without causing toxicity.

Maintenance: Oral, 1 to 3 mg per kg of body weight or 45 mg per square meter of body surface area a day.

Rheumatoid arthritis or
[Bowel disease, inflammatory] * or
[Cirrhosis, biliary] * or
[Dermatomyositis, systemic] * or
[Glomerulonephritis] * or
[Hepatitis, chronic active] * or
[Lupus erythematosus, systemic] * or
[Myopathy, inflammatory] * or
[Myasthenia gravis] * or
[Nephrotic syndrome] * or
[Pemphigoid] * or
[Pemphigus] *¾Initial: Oral, 1 mg per kg of body weight a day, the dosage being increased in increments of 500 mcg (0.5 mg) per kg of body weight a day after six to eight weeks, then every four weeks as necessary up to a maximum dose of 2.5 mg per kg of body weight a day.

Maintenance: Oral, the dosage being reduced to the minimum effective dose in decrements of 500 mcg (0.5 mg) per kg of body weight a day every four to eight 3 weeks.

Usual pediatric dose

See Usual adult and adolescent dose.

Strength(s) usually available

U.S.¾50 mg (Rx)[Imuran (scored) (lactose) 1] [Generic] (scored) 23

Canada¾50 mg (Rx)[Imuran (scored)]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 25 °C (59 and 77 °F), in a well-closed container 1.

Protect from light 1.

Parenteral Dosage Forms

Note: The dosing and strengths of the dosage form available are expressed in terms of azathioprine base.

AZATHIOPRINE SODIUM FOR INJECTION USP

Usual adult and adolescent dose

Transplant rejection, organ (prophylaxis)¾Initial: Intravenous 3 to 5 mg (base) per kg of body weight a day 1 prior to 3 , during, or soon after surgery, the dosage being adjusted to maintain the homograft without causing toxicity.

Maintenance: Intravenous, 1 to 3 mg (base) per kg of body weight a day.

Usual pediatric dose

See Usual adult and adolescent dose.

Size(s) usually available:

U.S.¾100 mg (base) (Rx)[Imuran (lyophilized) 1] [Generic]

Canada¾100 mg (base) (Rx)[Imuran (lyophilized)]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 25 °C (59 and 77 °F). Protect from light 1, 19.

Preparation of dosage form:

Azathioprine Sodium for Injection USP is reconstituted for intravenous use by adding 10 mL of sterile water for injection to the vial and swirling to dissolve 1.

Reconstituted solutions may be further diluted for administration by intravenous infusion with 0.9% sodium chloride injection or 5% dextrose and 0.9% sodium chloride injection 1.

Stability:

Reconstituted solutions of azathioprine are stable for 24 hours at room temperature 1.

Although solutions may be stable for longer periods, because there is no preservative, use within 24 hours is recommended for reasons of sterility 1.

Incompatibilities:

Mixing with alkaline solutions, especially on warming 1 , may result in conversion to 6-mercaptopurine 1.

Conversion to mercaptopurine also occurs in the presence of sulfhydryl compounds such as cysteine, glutathione, and hydrogen sulfide