# BRAND NAME: IMURAN

AVAILABLE IN 50, 75 and 100 mg TABLETS

#### BACKGROUND

Diseases involving excessive activity of the immune system are called "immune-mediated" diseases and they are treated with suppression of the immune system. The cornerstone medication of immune suppression is prednisone; however, this medication may have undesirable side effects with long term use, thus it is helpful to look towards a second medication that can be used to reduce the prednisone amount used. Azathioprine is such a medication, though it is important to realize that while it is used to mitigate steroid side effects, it can certainly have adverse side effects of its own. In patients who do not have any problems with azathioprine (and most do not), prednisone can be reduced and possibly even discontinued.

Azathioprine

Azathioprine disrupts the synthesis of DNA and RNA. DNA synthesis is at the very heart of cell division because every time a cell replicates/divides, a new complete copy of its DNA must be accurately created. With DNA synthesis disrupted, new cells with intact working DNA cannot be created. Tissues that employ rapid cell division, such as the stimulated immune system, are especially vulnerable to such effects. In the immune system, lymphocytes become stimulated to proliferate and produce antibodies. They can do neither in the presence of azathioprine which means they cannot participate in immune-mediated disease.

Because Azathioprine can disrupt rapid cell division, its use also has application in treating cancers.

Because azathioprine is a DNA poison it has the potential to cause mutation. It should not be used in animals used for breeding nor should it be handled by pregnant women.

#### **HOW THIS MEDICATION IS USED**

Some typical immune mediated conditions that commonly require the use of azathioprine include:

- Immune mediated hemolytic anemia
- Immune mediated platelet destruction (thrombocytopenia)
- Pemphigus type skin diseases (especially pemphigus foliaceus)
- · Severe forms of inflammatory bowel disease
- Chronic Active Hepatitis (a progressive scarring disease of the liver)
- Myasthenia Gravis (immune mediated destruction of the nerve/muscle junctions)
- Systemic Lupus Erythematosus
- Rheumatoid/immune mediated arthritis

Azathioprine is typically started once a day and then tapered to every other day use and is almost always started in conjunction with other immune suppressive agents. Azathioprine can take up to six weeks to work.

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#### SIDE EFFECTS

One of the main issues with azathioprine is a problem with the bone marrow suppression. Cells of the bone marrow are rapidly dividing and thus at risk for suppression from azathioprine. For this reason, at least in early stages of use, Complete Blood Counts ("CBC's") are monitored frequently (typically every 2 weeks for the first couple of months).

Signs of a bone marrow problem that might be observable at home include abnormal bruising or inappropriate bleeding (bloody nose, bloody stool, blood in urine, excess bleeding from a minor wound etc.) If bone marrow suppression has not occurred in the first couple of months of therapy, it is unlikely that it will occur later on.

Some patients develop a liver toxicity with azathioprine. This should resolve with discontinuation of the medication but it is important to watch for any signs of nausea, diarrhea, or appetite loss. If these occur, especially in the first few weeks of starting azathioprine, discontinue the medication and notify your veterinarian of these effects.

Azathioprine can also promote pancreatitis (pancreatic inflammation). Again, signs of nausea/intestinal upset can result. If this occurs, discontinue azathioprine and notify your veterinarian.

## **INTERACTIONS WITH OTHER DRUGS**

Because it can take a good month or two before the effects of azathioprine are seen, it is a good idea to begin azathioprine in conjunction with an aggressive prednisone course. The prednisone will hopefully control the disease rapidly such that by the time the azathioprine has "kicked in," the prednisone can be tapered to a maintenance level.

Concurrent use of allopurinol can present a problem with azathioprine use. This normally would only come up in the event of a Dalmatian using allopurinol to control uric acid bladder stone issues. If azathioprine is to be used with allopurinol, the dose of azathioprine must be dramatically reduced.

## **CONCERNS AND CAUTIONS**

- Azathioprine tablets should be protected from light exposure. They should be kept in a colored plastic medication vial and stored in a drawer or cabinet if possible.
- Azathioprine should not be used in pregnant pets nor should it be handled by pregnant owners.
- Azathioprine should not be used in patients with pre-existing liver disease if possible. (It should be noted that most patients starting azathioprine have been on prednisone or other steroids and will have elevations in liver enzymes as a result of steroid exposure. This is not the same as having pre-existing liver disease and does not represent a problem.)
- Many experts feel that azathioprine should not be used in the cat at all.
- If azathioprine is to be discontinued after long term use, it is probably best to taper the dosage rather than discontinue abruptly as a rebound increase immune response can result.
- It is a good idea to wash your hands after handling azathioprine tablets.
- Several weeks are necessary for maximum effect of azathioprine to be evident. Other faster acting medications will be necessary during this time period.



Cats are sensitive to the bone marrow side effects of this drug. Best to pick a different medication.



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