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INFORMATION ON AZATHIOPRINE (IMURAN)

What is Azathioprine (Imuran)?

- Azathioprine is an immunosuppressant
- It is used for preventing organ rejection in patients with organ transplants and for treating autoimmune diseases like rheumatoid arthritis
- It may be used in autoimmune hair loss conditions, including alopecia areata
- Azathioprine is a 'prodrug' that is non-enzymatically converted to 6-mercaptopurine.
 - 6-MP is then either inactivated by thiopurine methyltransferase (TPMT) to 6-methylmercaptopurine or by xanthine oxidase to 6-thiouric acid, or it is activated via a multistep enzymatic pathway to the putative active metabolites, the 6 thioguanine nucleotides (6-TGN)
 - This pharmacology is important as it explains why **all patients must have TPMT levels measured before** starting and explains by xanthine oxidase inhibitors like allopurinol cannot be used by those taking azathioprine.

Who should not take azathioprine?

Dr. Donovan will not prescribe to patients with:

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| a) TPMT deficiency (see boxed comment below) | f) patients using other immunosuppressants |
| b) cancer in the past | g) patients using certain other medications (allopurinol, etc) |
| c) anemias, blood count issues | h) patients who have used cyclophosphamide, melphalan or chlorambucil in the past |
| d) liver or kidney disease | |
| e) chronic infections | |

Patients with intermediate TPMT activity or the heterozygote genotypes should initially have an empiric reduction of 50% in drug dose. Patients with absent TPMT activity or the homozygous low activity genotypes are generally not treated in our clinic with azathioprine.

Only in rare situations will Dr Donovan prescribe azathioprine in pregnancy.

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What tests are needed before starting?

- Blood tests for CBC, TSH, ferritin, AST, ALT creatinine, urinalysis, LDH, bilirubin, zinc may be considered before starting. Consideration is given to ESR, CRP, ANA.
- TPMP gene testing is necessary in all patients

What tests are needed after starting?

- Blood tests for CBC, AST, ALT, bilirubin creatinine are needed at periodic intervals after starting
- Generally, Dr Donovan orders monitoring as follows:
 - CBC, AST, ALT, bilirubin, creatinine weekly for 4 weeks and then every 2 weeks for two times. Then monthly x 3 months and then every 2 months x 3.
 - If stable after that, it can be ordered every 3-4 months.
- Medication is stopped or reduced if WBC <1.5 or ANC less than 750 or PLT <80 or HBG<100 or LFTs increasing

What is the typical dose of azathioprine?

- The dose is based on weight of the patient
- The medication is used once or twice per day.
- Typically, most patients will start 1 mg/kg as a single once per day dose or divided into two doses. After two months, the dose can be increased. For example, Dr Donovan may start 50 mg per day and increase to 50 mg twice daily after 2 months.
- The dose may be increased to a maximum of 2.5 mg per kg

What are the side effects of azathioprine?

Dr. Donovan will review a complete list of side effects. Some of the side effects include:

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| • Fever | • Abdominal pain |
| • Night sweats | • Skin rashes |
| • Nausea, vomiting, joint pains, diarrhea | • Changes in blood counts |
| • Muscle pains | • Drug reactions (allergy) |
| • Loss of appetite | • Infections |
| • Irritation of the liver | • Cancer (skin cancer. Lymphomas, leukemias and others) |

Bone marrow suppression, gastrointestinal disturbances, hepatotoxicity, pancreatitis, fever and rash are common reasons that patients may stop azathioprine

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What precautions are needed while using azathioprine (Imuran)?

- Patients should use sunscreen while on azathioprine (Imuran)
- Patients should receive necessary vaccinations before starting
- Side effects should be conveyed to the doctor including bruising, sore throat, cough, fatigue, bloody stools, abdominal pain, fever
- Patients on azathioprine (Imuran) should avoid being around others who are sick
- Patients on azathioprine should report their medication to all other health care practitioners during any appointment
- A full skin examination should be done yearly