Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Azathioprine 50mg film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 50mg Azathioprine.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablets

Azathioprine 50mg Tablets are pale, yellow, circular, film-coated biconvex tablets engraved with "AZA", score-lined and "50" on one face. The other face is plain.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Azathioprine 50mg Tablets are used as an immunosuppressant antimetabolite either alone or, more commonly, in combination with other agents (usually corticosteroids) and procedures which influence the immune response.

Therapeutic effect may be evident only after weeks or months and can include a steroid-sparing effect, thereby reducing the toxicity associated with high dosage and prolonged usage of corticosteroids.

Azathioprine 50mg Tablets, in combination with corticosteroids and/or other immunosuppressive agents and procedures, is indicated to enhance the survival of organ transplants, such as renal transplants, cardiac transplants and hepatic transplants; and to reduce the corticosteroid requirements of renal transplant recipients.

Azathioprine 50mg Tablets, either alone or more usually in combination with corticosteroids and/or other drugs and procedures, has been used with clinical benefit (which may include reduction of dosage or discontinuation of corticosteroids) in a proportion of patients suffering from the following:

Severe rheumatoid arthritis
Systemic lupus erythematosus
Dermatomyositis and polymyositis
Auto-immune chronic active hepatitis
Pemphigus vulgaris
Polyarteritis nodosa
Auto-immune haemolytic anaemia
Chronic refractory idiopathic thrombocytopenic purpura

4.2 Posology and method of administration

Route of administration: Oral
Transplantation - adults and children
Depending on the immunosuppressive regimen employed, a dosage of up to 5 mg/kg body weight/day may be given on the first day of therapy, either orally or intravenously.

Maintenance dosage should range from 1 to 4 mg/kg body weight/day and must be adjusted according to clinical requirements and haematological tolerance.

Evidence indicates that Azathioprine 50mg Tablets therapy should be maintained indefinitely, even if only low doses are necessary, because of the risk of graft rejection.

Dosage in other conditions - adults and children
In general, starting dosage is from 1 to 3 mg/kg body weight/day, and should be adjusted, within these limits, depending on the clinical response (which may not be evident for weeks or months) and haematological tolerance.

When therapeutic response is evident, consideration should be given to reducing the maintenance dosage to the lowest level compatible with the maintenance of that response. If no improvement occurs in the patient's condition within 3 months, consideration should be given to withdrawing Azathioprine 50mg Tablets.

The maintenance dosage required may range from less than 1 mg/kg body weight/day to 3 mg/kg body weight/day, depending on the clinical condition being treated and the individual patient response, including haematological tolerance.
In patients with renal and/or hepatic insufficiency, dosages should be given at the lower end of the normal range (see Special Warnings and Precautions for Use for further details).

Use in the elderly (see Renal and/or hepatic insufficiency)
There is limited experience of the administration of Azathioprine 50mg Tablets to elderly patients. Although the available data do not provide evidence that the incidence of side effects among elderly patients is higher than that among other patients treated with Azathioprine 50mg Tablets, it is recommended that the dosages used should be at the lower end of the range.
Particular care should be taken to monitor haematological response and to reduce the maintenance dosage to the minimum required for clinical response.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. Hypersensitivity to 6-mercaptopurine (6-MP) should alert the prescriber to probable hypersensitivity to Azathioprine 50mg Tablets.

Azathioprine 50mg Tablets therapy should not be initiated in patients who may be pregnant or who are likely to become pregnant without careful assessment of risk versus benefit (see Special Warnings and Precautions for Use and Pregnancy and Lactation).

4.4 Special warnings and precautions for use

Monitoring
There are potential hazards in the use of Azathioprine 50mg Tablets. It should be prescribed only if the patient can be adequately monitored for toxic effects throughout the duration of therapy.

It is suggested that during the first 8 weeks of therapy, complete blood counts, including platelets, should be performed weekly or more frequently in high dosage is used or if severe renal and/or hepatic disorder is present. The blood count frequency may be reduced later in therapy, but it is suggested that complete blood counts are repeated monthly or at least at intervals of not longer than 3 months.

Patients receiving Azathioprine 50mg Tablets should be instructed to report immediately any evidence of infection, unexpected bruising or bleeding or other manifestations of bone marrow depression.

There are individuals with an inherited deficiency of the enzyme thiopurine methyltransferase (TPMT) who may be unusually sensitive to the myelosuppressive effect of azathioprine and prone to developing rapid bone marrow depression following the initiation of treatment with Azathioprine 50mg Tablets. This problem could be exacerbated by co-administration with drugs that inhibit TPMT, such as olsalazine, mesalazine or sulfasalazine. Also it has been reported that decreased TPMT activity increases the risk of secondary leukaemias and myelodysplasia in individuals receiving 6- mercaptopurine (the active metabolite of azathioprine) in combination with other cytotoxics (see section 4.8 Undesirable effects).

Patients with NUDT15 variant

Patients with inherited mutated NUDT15 gene are at increased risk for severe azathioprine toxicity, such as early leukopenia and alopecia, from conventional doses of thiopurine therapy. They generally require dose reduction, particularly those being NUDT15 variant homozygotes (see 4.2). The frequency of NUDT15 c.415C>T has an ethnic variability of approximately 10 % in East Asians, 4 % in Hispanics, 0.2 % in Europeans and 0 % in Africans. In any case, close monitoring of blood counts is necessary.

Renal and/or hepatic insufficiency

It had been suggested that the toxicity of Azathioprine 50mg Tablets may be enhanced in the presence of renal insufficiency, but controlled studies have not supported this suggestion. Nevertheless, it is recommended that the dosages used should be at the lower end of the normal range and that haematological response should be carefully monitored. Dosage should be further reduced if haematological toxicity occurs.

Caution is necessary during the administration of Azathioprine 50mg Tablets to patients with hepatic dysfunction and regular complete blood counts and liver function tests should be undertaken. In such patients, the metabolism of Azathioprine 50mg Tablets may be impaired and the dosage of Azathioprine 50mg Tablets should therefore be reduced if hepatic or haematological toxicity occurs.

Limited evidence suggests that Azathioprine 50mg Tablets is not beneficial to patients with hypoxanthine-guanine-phosphoribosyltransferase deficiency (Lesch-Nyhan syndrome). Therefore, given the abnormal metabolism in these patients, it is not prudent to recommend that these patients should receive Azathioprine 50mg Tablets.

Mutagenicity
Chromosomal abnormalities have been demonstrated in both male and female patients treated with Azathioprine 50mg Tablets. It is difficult to assess the role of Azathioprine 50mg Tablets in the development of these abnormalities.

Effects on fertility
Relief of chronic renal insufficiency by renal transplantation involving the administration of Azathioprine 50mg Tables had been accompanied by increased fertility in both male and female transplant recipients.

Carcinogenicity (See section 4.8 Undesirable Effects) Patients receiving immunosuppressive therapy, including azathioprine are at an increased risk of developing lymphoproliferative disorders and other malignancies, notably skin cancers (melanoma and non-melanoma), sarcomas (Kaposi's and non-Kaposi's) and uterine cervical cancer in situ. The increased risk appears to be related to the degree and duration of immunosuppression. It has been reported that discontinuation of immunosuppression may provide partial regression of the lymphoproliferative disorder.

A treatment regimen containing multiple immunosuppressants (including thiopurines) should therefore be used with caution as this could lead to lymphoproliferative disorders, some with reported fatalities. A combination of multiple immunosuppressants, given concomitantly increases the risk of Epstein-Barr virus (EBV)-associated lymphoproliferative disorders.

Patients receiving multiple immunosuppressive agents may be at risk of over-immunosuppression, therefore such therapy should be maintained at the lowest effective level.

Expose to sunlight and UV light should be limited and patients should wear protective clothing and use sunscreen with a high protection factor to minimize the risk of skin cancer and photosensitivity (see also section 4.8 Undesirable Effects).

Macrophage activation syndrome.
Macrophage activation syndrome (MAS) is a known, life-threatening disorder that may develop in patients with autoimmune conditions, in particular with inflammatory bowel disease (IBD), and there could potentially be an increased susceptibility for developing the condition with the use of azathioprine. If MAS occurs, or is suspected, evaluation and treatment should be started as early as possible, and treatment with azathioprine should be discontinued. Physicians should be attentive to symptoms of infection such as EBV and cytomegalovirus (CMV), as these are known triggers for MAS.

Varicella Zoster Virus Infection (see also section 4.8 Undesirable Effects)

Infection with varicella zoster virus (VZV; chickenpox and herpes zoster) may become severe during the administration of immunosuppressants. Caution should be exercised especially with respect to the following:

Before starting the administration of immunosuppressants, the prescriber should check to see if the patient has a history of VZV. Serologic testing may be useful in determining previous exposure. Patients who have no history of exposure should avoid contact with individuals with chickenpox or herpes zoster. If the patient is exposed to VZV, special care must be taken to avoid patients developing chickenpox or herpes zoster, and passive immunisation with varicella- zoster immunoglobulin (VZIG) may be considered.
If the patient is infected with VZV, appropriate measures should be taken, which may include antiviral therapy and supportive care.

4.5 Interaction with other medicinal products and other forms of interactions

Allopurinol/ oxipurinol/ thiopurinol
Xanthine oxidase activity is inhibited by allopurinol, oxipurinol and thiopurinol which results in reduced conversion of biologically active 6- thioinosinic acid to biologically inactive 6-thiouric acid. When allopurinol, oxipurinol and/or thiopurinol are given concomitantly with 6-mercaptpurine or azathioprine, the dose of 6-mercaptopurine and azathioprine should be reduced to one-quarter of the original dose.

Neuromuscular blocking agents
Azathioprine 50mg Tablets can potentiate the neuromuscular blockade produced by depolarising agents such as succinylcholine and can reduce the blockade produced by non-depolarising agents such as tubocurarine. There is considerable variation in the potency of this interaction.

Warfarin
Inhibition of the anticoagulant effect of warfarin, when administered with azathioprine, has been reported.

Cytostatic/myelosuppressive agents
Where possible, concomitant administration of cytostatic drugs or drugs which may have a myelosuppressive effect such as penicillamine, should be avoided.

There are conflicting clinical reports of interactions, resulting in serious haematological abnormalities between Azathioprine 50mg Tablets and co-trimoxazole.

There has been a case report suggesting that haematological abnormalities may develop due to the concomitant administration of Azathioprine 50mg tablets and captopril.

It has been suggested that cimetidine and indomethacin may have myleosppressive effects, which may be enhanced by concomitant administration of Azathioprine 50mg tablets.

Other interactions
As there is in vitro evidence that aminosalicyclate derivatives (eg. Olsalazine, mesalazine or sulphasalazine) inhibit the TPMT enzyme, they should administered with caution to patients receiving concurrent Azathioprine therapy (see 4.4 special warnings and special precautions for use).

Furosemide has been shown to impair the metabolism of azathioprine by human hepatic tissue in vitro. The clinical significance is unknown.

Vaccines
The immunosuppressive activity of Azathioprine 50mg Tablets could result in an atypical and potentially deleterious response to live vaccines and so the administration of live vaccines to patients receiving Azathioprine 50mg Tablets therapy is contra-indicated on theoretical grounds.

A diminished response to killed vaccines is likely and such a response to hepatitis B vaccine has been observed among patients treated with a combination of azathioprine and corticosteroids.

A small clinical study has indicated that standard therapeutic doses of Azathioprine 50mg Tablets do not deleteriously affect the response to polyvalent pneumococcal vaccine, as assessed on the basis of mean anticapsular specific antibody concentration.

4.6 Fertility, pregnancy and lactation

Teratogenicity
Studies in pregnant rats, mice and rabbits using azathioprine in dosages from 5 to 15 mg/kg body weight/day over the period of organogenisis have shown varying degrees of foetal abnormalities. Teratogenicity was evident in rabbits at 10mg/kg body weight/day.

Evidence of the teratogenicity of Azathioprine 50mg Tablets in man is equivocal. As with all cytotoxic chemotherapy, adequate contraceptive precautions should be advised when either partner is receiving Azathioprine 50mg Tablets.

Mutagenicity
Chromosomal abnormalities, which disappear with time, have been demonstrated in lymphocytes from the off-spring of patients treated with Azathiprine 50mg Tablets. Except in extremely rare cases, no overt physical evidence of abnormality has been observed in the offspring of patients treated Azothioprine 50mg Tablets. Azathioprine and long-wave ultraviolet light have been shown to have a synergistic clastogenic effect in patients treated with azathioprine for a range of disorders.

Use in pregnancy and Lactation
Azathioprine 50mg Tablets should not be given to patients who are pregnant or likely to become pregnant without careful assessment of risk versus benefit.

There have been reports of premature birth and low birth weight following maternal exposure to azathioprine, particularly in combination with corticosteroids. There have also been reports of spontaneous abortion following either maternal or paternal exposure.

Azathioprine and/or its metabolites have been found in low concentrations in foetal blood and amniotic fluid after maternal administration of azathioprine.

Leucopenia and/or thrombocytopenia have been reported in a proportion of neonates whose mothers took azathioprine throughout their pregnancies. Extra care in haematological monitoring is advised during pregnancy.

Lactation
6-Mercaptopurine has been identified in the colostrum and breast milk of women receiving azathioprine treatment.

4.7 Effects on ability to drive and use machines

Due to the possibility of adverse drug reactions such as dizziness and because of individually occurring different reactions, the ability to participate actively in traffic or operate machines may be influenced adversely by azathioprine treatment. This is to be considered especially in combination with alcohol.

4.8 Undesirable effects

For this product there is no modern clinical documentation that can be used as support for determined the frequency of undesirable effects. Undesirable effects may vary in their incidence depending on the indication. The following convention has been utilised for utilized for the classification of frequency: Very common, ≥ 1/10; Common, ≥ 1/100 and <1/10; Uncommon ≥ 1/1000 and <1/100; Rare, ≥ 1/10,000 and <1/1000; Very rare, < 1/10,000.

<u>Infections and infestations</u>
Transplant patients receiving Azathioprine 50mg Tablets in combination with other immunosuppressants.
Very common: viral, fungal and bacterial infections

Other indications.
Uncommon: viral, fungal and bacterial infections.
Patients receiving Azathioprine 50mg Tablets alone, or in combination with other immunosupressants particularly corticosteroids, have shown increased susceptibility to viral, fungal and bacterial infections including severe or atypical infection with varicella, herpes zoster and other infectious agents (see also section 4.4 Special Warnings and Precautions for Use).

<u>Neoplasms benign and malignant (including cysts and polyps)</u>

Rare: neoplasms includinglymphoproliferative disorders, skin cancers (melanoma and non-melonoma), sarcomas (Kaposi's and non-Kaposi's) and uterine cervical cancer in situ, acute myeloid leukaemia and myelodysplasia (see also section 4.4 Special Warnings and Special Precautions for Use).

The risk of developing non-Hodgkin's lymphomas and other malignancies, notably skin cancers (melanoma and non-melanoma), sarcomas, (Kaposi's and non Kaposi's) and uterine cervical cancer in situ, is increased in patients who receive immunosuppressive drugs, particularly in transplant recipients receiving aggressive treatment and such therapy should be maintained at the lowest effective levels. The increased risk of developing non-Hodgkin's lymphomas in immunosuppressed rheumatoid arthritis patients compared with the general population appears to be related at least in part to the disease itself.

There have been rare reports of acute myeloid leukaemia and myelodysplasia (some in association with chromosomal abnormalities).

Blood and lymphatic system disorders

Very Common: Depression of bone marrow function; leucopenia

Common: Thrombocytopenia

Uncommon: Anaemia

Rare: Agranulocytosis, pancytopenia, aplastic anaemia, megaloblastic anaemia, erythroid hypoplasia.

Azathioprine 50mg Tablets may be associated with a dose-related generally reversible, depression of bone marrow function, most frequently expressed as leucopenia, but also sometimes as anaemia and thrombocytopenia seen rarely as agranulocytosis, pancytopenia and aplastic anaemia. These occur particularly in patients predisposed to myelotoxicity such as those with TPMT deficiency and renal or hepatic insufficiency and in patients failing to reduce the dose of Azathioprine 50mg Tablets when receiving concurrent allopurinol therapy.

Reversible, dose-related increase in mean corpuscular volume and red cell haemoglobin content have occurred in association with Azathioprine 50mg tablets therapy. Megaloblastic bone marrow changes have also been observed but severe megaloblastic anaemia and erythroid hypoplasia are rare.

Respiratory, thoracic and mediastinal disorders

Very rare: Reversible pneumonitis.
Reversible pneumonitis has been described very rarely.

Gastrointestinal disorders

Uncommon: pancreatitis

Rare: Colitis, diverticulitis and bowel perforation reported in transplant population, severe diarrhoea in inflammatory bowel disease population.

A minority of patients experience nausea when first given Azathioprine 50mg Tablets. This appears to be relieved by administrating the tablets after meals.

Serious complications, including colitis, diverticulitis and bowel perforation, have been described in transplant recipients receiving immunosuppressive therapy. However, the aetiology is not clearly established and high dose corticosteroids may be implicated. Severe diarrhoea, recurring on re-challenge, has been reported in patients treated with azathioprine 50mg Tablets for inflammatory bowel disease. The possibility that exacerbation of symptoms might be drug-related should be borne in mind when treating such patients.

Pancreatitis has been reported in a small percentage of patients on azathioprine 50mg Tablets therapy, particularly in renal transplant patients and those diagnosed as having inflammatory bowel disease. There are difficulties in relating the pancreatitis to the administration of one particular drug, although re-challenge has confirmed an association with Azathioprine 50mg tablets on occasions.

Hepato-biliary disorders
Uncommon: Cholestasis and degeneration of liver function tests
Rare: Life threatening hepatic damage.

Cholestasis and deterioration of liver function have occasionally been reported in association with Azathioprine 50mg Tablets therapy and are usually reversible on withdrawal of therapy. This may be associated with symptoms of a hypersensitivity reaction (see Hypersensitivity reactions).

Rare, but life threatening hepatic damage associated with chronic administration of azathioprine has been described primarily in transplant patients. Histological findings include sinusoidal dilatation, peliosis -hepatis, veno-occlusive disease and nodular regenerative hyperplasia. In some cases withdrawal of azathioprine has resulted in either a temporary or permanent improvement in liver histology and symptoms.

Skin and subcutaneous tissue disorders

Rare: alopecia and photosensitivity

Hair loss has been described on a number of occasions in patients receiving azathioprine and other immunosuppressive agents. In many instances the condition resolved spontaneously despite continuing therapy. The relationship between alopecia and azathioprine treatment is uncertain.

Immune system disorders
Uncommon: hypersensitivity reactions.
Very rare: Stevens-Johnson syndrome and toxic epidermal necrosis.

Several different clinical syndromes, which appear to be idiosyncratic manifestations of hypersensitivity have been described occasionally following administration of Azathioprine 50mg Tablets. Clinical features include general malaise, dizziness, nausea, vomiting, diarrhoea, fever, rigors, exanthema, rash, vasculitis, myalgia, arthralgia hypotension, renal dysfunction, hepatic dysfunction and cholestasis (see Hepato-biliary disorders).

In many cases, re-challenge has confirmed an association with Azathioprine
50mg Tablets.

Immediate withdrawal of azathioprine and institution of circulatory support where appropriate have led to recovery in the majority of cases.

Other marked underlying pathology has contributed to the very rare deaths reported.

Following a hypersensitivity reaction to Azathioprine 50mg tablets, the necessity for continued administration of Azathioprine 50mg Tablets should be carefully considered on an individual basis.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2, Tel: +353 1 6764971; Fax: +353 1 6762517; Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Symptoms and signs

Unexplained infection, ulceration of the throat, bruising and bleeding are the main signs of over dosage with Imuran and result from bone marrow depression which may be maximal after 9 to 14 days. These signs are more likely to be manifest following chronic over dosage, rather than after a single acute overdose. There has been a report of a patient who ingested a single overdose of 7.5 g of azathioprine. The immediate toxic effects of this overdose were nausea, vomiting and diarrhoea, followed by mild leucopenia and mild abnormalities in liver function. Recovery was uneventful.

Treatment

There is no specific antidote. Gastric lavage has been used. Subsequent monitoring, including haematological monitoring, is necessary to allow prompt treatment of any adverse effects which may develop. The value of dialysis in patients who have taken an overdose of Azathioprine 50mg Tablets is not known, though azathioprine is partially dialysable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Therapeutic Group: Antineoplastic and Immunosuppressive agents,
ATC code: L04AX01

Azathioprine is an imidazole derivative of 6-mercaptopurine (6-MP). It is rapidly broken down *in vivo* into 6-MP and a methylnitroimidazole moiety. The 6-MP readily crosses cell membranes and is converted intracellularly into a number of purine thioanalogues, which include the main active nucleotide, thioinosinic acid. The rate of conversion varies from one person to another. Nucleotides do not traverse cell membranes and therefore do not circulate in body fluids. Irrespective of whether it is given directly or is derived *in vivo* from azathioprine, 6-MP is eliminated mainly as the inactive oxidised metabolite thiouric acid. This oxidation is brought about by xanthine oxidase, an enzyme that is inhibited by allopurinol. The activity of the methylnitroimidazole moiety has not been defined clearly. However, in several systems it appears to modify the activity of azathioprine as compared with that of 6-MP. Determination of plasma concentrations of azathioprine or 6-MP have no prognostic values as regards effectiveness or toxicity of these compounds.

While the precise modes of action remain to be elucidated, some suggested mechanisms include:

1. the release of 6-MP which acts as a purine antimetabolite.
2. the possible blockade of -SH groups by alkylation.
3. the inhibition of many pathways in nucleic acid biosynthesis, hence preventing proliferation of cells involved in determination and amplification of the immune response.
4. damage to deoxyribonucleic acid (DNA) through incorporation of purine thio-analogues.

Because of these mechanisms, the therapeutic effect of Azathioprine 50mg Tablets may be evident only after several weeks or months of treatment.

Azathioprine 50mg Tablets appears to be well absorbed from the upper gastro-intestinal tract.

Studies in mice with [^{35}S]-azathioprine showed no unusually large concentration in any particular tissue, and there was very little [^{35}S]-label found in brain.
Plasma levels of azathioprine and 6-MP do not correlate well with the therapeutic efficacy or toxicity of Azathioprine 50mg Tablets.

5.2 Pharmacokinetic properties

Azathioprine is well absorbed following oral administration. After oral administration of [^{35}S]-azathioprine, the maximum plasma radioactivity occurs at 1-2 hours and decays with a half-life of 4-6 hours. This is not an estimate of the half-life of azathioprine itself, but reflects the elimination from plasma of azathioprine and the [^{35}S]-containing metabolites of the drug. As a consequence of the rapid and extensive metabolism of azathioprine, only a fraction of the radioactivity measured in plasma is comprised of unmetabolised drug. Studies in which the plasma concentration of azathioprine and 6-MP have been determined following intravenous administration of azathioprine have estimated the mean plasma $T^1/_2$ for azathioprine to be in the range of 6-28 minutes and the mean plasma $T^1/_2$ for 6-MP to be in the range 38-114 minutes after i.v. administration of the drug.

Azathioprine is principally excreted as 6-thiouric uric acid in the urine. 1-methyl-4-nitro-5-thioimidazole has also been detected in urine as a minor excretory product. This would indicate that, rather than azathioprine being exclusive cleaved by nucleophilic attack at the 5-position of the nitroimidazole ring to generate 6-MP and 1-methyl-4-nitro-5-(S-glutathionyl) imidazole. A small proportion of the drug may be cleaved between the sulphur-atom and the purine ring. Only a small amount of the dose of azathioprine administered is excreted unmetabolised in the urine.

5.3 Preclinical safety data

No additional data of clinical relevance to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:
Microcrystalline cellulose,
Mannitol,
Maize starch,
Povidone K25,
Croscarmellose sodium,
Sodium stearyl fumarate,

Tablet coat:
Hypromellose,
Macrogol.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in the outer carton

6.5 Nature and contents of container

PVDC/PVC/Al Blister strips in a pack.
Pack sizes: 56 and 100 film-coated tablets.

6.6 Special precautions for disposal and other handling

The tablets are not intended to be broken.

Provided that the film-coating is intact, there is no risk in handling film-coated Azathioprine 50mg Tablets. Azathioprine 50mg Tablets should not be divided and, provided the coating is intact, no additional precautions are required when handling them.

Health professionals who handle Azathioprine 50mg Tablets should follow guidelines for the handling of cytotoxic drugs according to prevailing local recommendations and/or regulations.

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Relonchem Limited

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Widnes, WA8 0RP

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8 MARKETING AUTHORISATION NUMBER

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9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

June 2020