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 50 mg of Azathioprine.

Excipient(s) with known effect

Each tablet contains 70 mg lactose monohydrate

For the full list of excipents, see section 6.1.

3 PHARMACEUTICAL FORM

Film coated tablets.
Round, pale yellow coloured, biconvex tablets embossed AZ50 on one face and plain on the reverse.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Azathioprine is indicated as an immunosuppressant antimetabolite. It can be used alone or in combination with other agents (eg 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 (combined with corticosteroids/other immunosuppressive agents and procedures) is indicated to help the survival of transplant organs, eg renal/cardiac/hepatic transplants, and also to reduce the corticosteroid dosage of renal transplant patients.

Azathioprine has been used for the following indications (either alone or in addition to corticosteroids/other drugs and procedures) 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, autoimmune chronic active hepatitis, pemphigus vulgaris, polyarteritis nodosa, autoimmune haemolytic anaemia, chronic refractory idiopathic thrombocytopenic purpura.

4.2 Posology and method of administration

Posology
Patients with NUDT15 variant
Patients with inherited mutated NUDT15 gene are at increased risk for severe 6-mercaptopurine toxicity (see section "Special warnings and precautions for use"). These patients generally require dose reduction; particularly those being NUDT15 variant homozygotes (see section "Special warnings and precautions for use"). Genotypic testing of NUDT15 variants may be considered before initiating 6-mercaptopurine therapy. In any case, close monitoring of blood counts is necessary.

Transplantation - Adults and children:

Dependant on the immunosuppressive regimen employed an initial dosage of up to 5mg/kg bodyweight/day may be given, either orally or intravenously.

Maintenance dosage given may range from 1-4mg/kg bodyweight/day. Adjustments may be made in accordance with haematological tolerance and clinical response required.

Due to the risk of graft rejection, evidence indicates that low dosage azathioprine therapy should be maintained indefinitely.

Dosage in other conditions – adults and children:

The starting dosage is 1-3mg/kg bodyweight/day, and should be adjusted within this range dependant on clinical response (which may not be evident for weeks or months) and haematological tolerance.

Once the therapeutic response is evident, consideration should be given to a reduction in maintenance dose to the lowest level compatible with the maintenance of that response. If no improvement occurs in the patients condition within 3 months then consideration should be given to withdrawing azathioprine treatment.

The maintenance dosage may range from 1-3mg/kg bodyweight/day, depending on the clinical condition being treated and the individual patient response, including haematological tolerance.

Dosages should be kept at the lower end of the normal range for patients with renal and/or hepatic insufficiency.

Elderly (see renal and/or hepatic insufficiency)

There is limited data available on the administration of azathioprine to elderly patients. Although the available data do not provide evidence that the incidence of side effects among the elderly are higher than that in other patient groups, it is recommended that the dosages given 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.

Method of administration: Oral.

4.3 Contraindications

Hypersensitivity to azathioprine 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. Azathioprine therapy should not be initiated in patients who may be pregnant, or who are likely to be pregnant in the near future 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
Due to the potential hazards in the use of azathioprine, it should only be administered if the patient can be adequately monitored for toxic effects throughout the duration of therapy.

During the first 8 weeks of therapy, it is suggested that complete blood counts, including platelets, should be performed weekly or more frequently if 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 (see section 4.2 Posology and method of administration).

Patients receiving azathioprine 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. 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).

Renal and/or hepatic insufficiency:

It has been suggested that the toxicity of azathioprine 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 in the presence of renal insufficiency and that haematological response should be carefully monitored. Dosage should be further reduced if haematological toxicity occurs.

Patients with hepatic dysfunction should administer azathioprine with caution and regular complete blood counts and liver function tests should be undertaken. In such patients the metabolism of azathioprine may be impaired, and the dosage of azathioprine should therefore be reduced if hepatic or haematological toxicity occurs.

There is limited evidence suggesting that azathioprine is not beneficial to patients with hypoxanthine-guanine-phosphoribosyltransferase deficiency (Lesch-Nyhan

syndrome). Giving consideration to the abnormal metabolism in these patients, it is not recommended that these patients receive azathioprine.

Mutagenicity

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

Effects on fertility:

Relief of chronic renal insufficiency by renal transplantation involving the administration of azathioprine has been accompanied by increased fertility in both male and female transplant recipients.

Carcinogenicity (see also 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 reduction or 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.

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

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 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.

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.
Infections
Patients treated with 6-mercaptopurine alone or in combination with other immunosuppressive agents, including corticosteroids, have shown increased susceptibility to viral, fungal and bacterial infections, including severe or atypical infection, and viral reactivation. The infectious disease and complications may be more severe in these patients than in non-treated patients.
Prior exposure to or infection with varicella zoster virus should be taken into consideration prior to starting treatment. Local guidelines may be considered, including prophylactic therapy if necessary. Serologic testing prior to starting treatment should be considered with respect to hepatitis B. Local guidelines may be considered, including prophylactic therapy for cases which have been confirmed positive by serologic testing. Cases of neutropenic sepsis have been reported in patients receiving 6- mercaptopurine for ALL.

Patients with NUDT15 variant
Patients with inherited mutated NUDT15 gene are at increased risk for severe 6-mercaptopurine 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 section "Posology and method of administration"). 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.

Patient with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take this medicine.

Neuromuscular blocking agents
Special care is necessary when azathioprine is given concomitantly with neuromuscular blocking agents such as atracurium, rocuronium, cisatracurium or suxamethonium (also known as succinylcholine) (see section 4.5). Anesthesiologists should check whether their patients are administered azathioprine prior to surgery.

Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per 25mg tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Neuromuscular blocking agents
There is clinical evidence that azathioprine antagonises the effect of non-depolarising muscle relaxants. Experimental data confirm that azathioprine reverses the neuromuscular blockade produced by non-depolarising agents, and show that

azathioprine potentiates the neuromuscular blockade produced by depolarising agents (see section 4.4)

Allopurinol/oxipurinol/thiopurinol and other xanthine oxidase inhibitors:

Based on non-clinical data, other xanthine oxidase inhibitors, such as febuxostat, may prolong the activity of azathioprine possibly resulting in enhanced bone marrow suppression.
Concomitant administration is not recommended as data are insufficient to determine an adequate dose reduction of azathioprine.

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 and co-trimoxazole.

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

It has been suggested that cimetidine and indometacin may have myelosuppressive effects which may be enhanced by concomitant administration of azathioprine.

Other interactions:

As there is *in vitro* evidence that aminosalicylate derivatives (eg. olsalazine, mesalazine or sulfasalazine) inhibit the TMPT enzyme, they should be administered with caution to patients receiving concurrent azathioprine therapy (See Special warnings and 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 could result in an atypical and potentially deleterious response to live vaccines and so the administration of live vaccines to patients receiving azathioprine 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 do not deleteriously affect the response to polyvalent pneumococcal vaccine, as assessed on the basis of mean anti-capsular 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 bodyweight/day over the period of organogenesis have shown varying degrees of foetal abnormalities. Teratogenicity was evident in rabbits at 10 mg/kg bodyweight/day.

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

Mutagenicity

Chromosomal abnormalities, which disappear with time, have been demonstrated in lymphocytes from the off-spring of patients treated with azathioprine. Except in extremely rare cases, no overt physical evidence of abnormality has been observed in the offspring of patients treated with azathioprine. 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.

Pregnancy and Lactation
Azathioprine 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.

After maternal administration of azathioprine, the compound and its metabolites were found in low concentrations in foetal blood and amniotic fluid.

Thrombocytopenia and/or leucopenia were found in a proportion of neonates whose mothers took azathioprine throughout their pregnancies. Extra care in haematological monitoring is advised during pregnancy.

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

Fertility
Contraceptive measures must be taken by both male and female patients of reproductive age during, and for at least three months after the end of azathioprine therapy.

Azathioprine has been reported to interfere with the effectiveness of intrauterine contraceptive devices. Therefore it is recommended to use other or additional contraceptive measures.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

For this product there is no modern clinical documentation that can be used as support for determining the frequency of undesirable effects. Undesirable effects may vary in their incidence depending on the indication. The following convention has been utilised for the classification of frequency: Very common: ≥ 1/10; common ≥ 1/100 and < 1/10; uncommon ≥ 1/1000 and < 1/100; rare ≥ 1/10000 and < 1/1000; very rare < 1/10000.

Infection and infestations

Transplant patients receiving azathioprine in combination with other immunosuppressants.

Very common: Viral, fungal and bacterial infections

Other indications
Uncommon: Viral, fungal and bacterial infections, infections associated with neutropenia

Patients receiving azathioprine alone, or in combination with other immunosuppressants, 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).

Neoplasms benign, malignant and unspecified (including cysts and polyps).

Rare: Neoplasms including lymphoproliferative disorders, skin cancers (melanomas and non-melanomas), sarcomas (Kaposi's and non-Kaposi's) and uterine cervical cancer in situ, acute myloid leukaemia and myelodysplasia (see also section 4.4 Special warnings and 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, erythriod hypoplasia

Azathioprine 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, and 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 when receiving concurrent allopurinol therapy.

Reversible, dose-related increases in mean corpuscular volume and red cell haemoglobin content have occurred in association with azathioprine therapy. Megaloblastic bone marrow changes have been observed but severe megaloblastic anaemia and erythroid hypoplasia is rare.

Respiratory, thoracic and mediastinal disorders

Very rare: Reversible pneumonitis

Reversible pneumonitis has been described very rarely.

Gastrointestinal reactions

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. This appears to be relieved by administering 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 rechallenge, has been reported in patients treated with azathioprine 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 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 rechallenge has confirmed an association with azathioprine on occasions.

Hepatobiliary disorders

Uncommon: Cholestasis, degeneration of liver function tests
Rare: Life-threatening hepatic damage

Cholestasis and deterioration of liver function have occasionally been reported in association with azathioprine 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 dilation, 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, photosensitivity
Not Known: Acute febrile neutrophilic dermatosis (Sweet's syndrome)

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, toxic epidermal necrolysis

Several different clinical syndromes, which appear to be idiosyncratic manifestations of hypersensitivity, have been described occasionally following administration of azathioprine. Clinical features include general malaise, dizziness, nausea, vomiting, diarrhoea, fever, rigors, exanthema, rash, vasculitis, myalgia, arthralgia, hypotension, renal dysfunction, hepatic dysfunction and cholestasis (see Hepatobiliary disorders). In many cases, re-challenge has confirmed an association with azathioprine.

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, the necessity for continued administration of azathioprine 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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms and signs

Unexplained infection, ulceration of the throat, bruising and bleeding are the main signs of overdosage with azathioprine 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 overdosage, 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 is not known, though azathioprine is partially dialysable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Immunosuppresive agent

ATC Code: L04A X01

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 which 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. Determinations of plasma concentrations of azathioprine or 6-MP have no prognostic value 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 may be evident only after several weeks or months of treatment.

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

Studies in mice with 35S-azathioprine showed no unusually large concentration in any particular tissue, but there was very little 35S found in the brain.

Plasma levels of azathioprine and 6-mercaptopurine do not correlate well with the therapeutic efficacy or toxicity of azathioprine.

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-mercaptopurine have been determined following intravenous administration of azathioprine have estimated the mean plasma T½ for azathioprine to be in the range of 6-28 minutes and the mean plasma T½ for 6-MP to be in the range 38-114 minutes after IV 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-mercaptopurine and 1-methyl-4-nitro-5-(S-glutathionyl)imidazole. A small proportion of the drug may be cleaved between the S 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

There are no additional data of clinical relevance to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Pregelatinised Starch,
Microcrystalline Cellulose,
Lactose Monohydrate,
Magnesium Stearate,
Povidone K30,
Polysorbate 80,
Sodium Starch Glycollate
Opadry YS-IR 7006 contains: Hypromellose 5 (E464), Macrogol/ PEG 400, macrogol/ PEG 6000.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Keep the container in the outer carton

6.5 Nature and contents of container

Clear transparent PVdC/PVC/Aluminium foil (Nitrocellulose coated) blister.
Pack size of 28, 30, 56, 60 or 100 or 1000 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Norton Healthcare Ltd
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8 MARKETING AUTHORISATION NUMBER(S)

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