Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedure

JAYEMPI 10 MG/ML ORAL SUSPENSION
Azathioprine

PLGB 13581/0005

Nova Laboratories Limited

LAY SUMMARY

Jayempi 10 mg/ml oral suspension
Azathioprine

This is a summary of the Public Assessment Report (PAR) for Jayempi 10 mg/ml oral suspension. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

For practical information about using Jayempi 10 mg/ml oral suspension, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Jayempi 10 mg/ml oral suspension and what is it used for?
This product has been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 21 June 2021 (EMEA/H/C/005055/0000), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP). This is known as the EC Decision Reliance Procedure.

This application is for a hybrid medicine. This means that the medicine is similar to a reference medicine already authorised in the European Union (EU) called Imurek 50mg film-coated tablets, albeit with certain differences. In this case, Jayempi 10 mg/ml oral suspension has a different pharmaceutical form.

Jayempi 10 mg/ml oral suspension is used to:

- Prevent your body from rejecting an organ transplant. Jayempi is usually used together with other immunosuppressants for this purpose
- Treat some long-term diseases where the immune system is reacting against the body. Jayempi is usually used in combination with steroids or other anti-inflammatory medicines. These diseases include:
  - Severe rheumatoid arthritis or chronic polyarthritis (long term chronic inflammation of multiple joints) which cannot be controlled by other medicines
  - Chronic inflammatory bowel diseases (diseases of the gut such as Crohn's disease and ulcerative colitis)
  - Chronic hepatitis (autoimmune hepatitis), a liver disease
  - Systemic lupus erythematosus (a disease in which the immune system attacks different organs)
  - Dermatomyositis (worsening muscle inflammation together with skin rash)
  - Polyarteritis nodosa (inflammation of blood vessels)
  - Pemphigus vulgaris and bullous pemphigoid (diseases of blistering of the skin)
  - Behçet's disease (recurrent inflammation, especially of the eyes and the oral and genital mucous membranes).
  - Refractory autoimmune haemolytic anaemia (a blood disease in which the red blood cells are destroyed)
  - Chronic refractory idiopathic thrombocytopenic purpura (bleeding under the skin due to damage to the platelets and reduction of their numbers)
- Treat relapsing multiple sclerosis.
- Treat generalised myasthenia gravis (a disease that affects nerves and causes muscle weakness). In some cases Jayempi is given with a steroid at the start of treatment.

How does Jayempi 10 mg/ml oral suspension work?
This medicine contains the active ingredient azathioprine, which belongs to a group of medicines called immunosuppressants. Azathioprine works by reducing the activity of the immune system (the body's defences).

How is Jayempi 10 mg/ml oral suspension used?
The pharmaceutical form of this medicine is an oral suspension and the route of administration is oral (by mouth).

The dose of Jayempi depends on the patient's weight, the condition being treated, how well it is being controlled and their overall health. A doctor will work out the dose that is right for the patient and may adjust it during treatment. The doctor will tell the patient how long they should continue taking the medicine.

For preventing organ rejection after transplantation, the usual starting dose is 5 mg per kg weight each day and the dose is then reduced after a few weeks or months to between 1 and 4 mg per kg weight each day.

The dose for other conditions is usually between 1 and 3 mg per kg each day.

The patient's dose may be reduced if they have kidney or liver disease.

The dose for children and adolescents is the same as the adult dose.
The safety and efficacy of azathioprine in children have not yet been established for the treatment of chronic joint inflammation (juvenile idiopathic arthritis) and multiple sclerosis. Therefore, the use of Jayempi for these conditions in children is not recommended.

A reduced dose may be needed for elderly patients.

Jayempi should be taken at least 1 hour before or 2 hours after a meal or milk. The patient should drink some water after each dose of Jayempi. This helps to make sure that the full dose of the medicine enters the digestive system.

For further information on how Jayempi 10 mg/ml oral suspension is used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should always take the medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

What benefits of Jayempi 10 mg/ml oral suspension have been shown in studies?
Because Jayempi 10 mg/ml oral suspension is a hybrid medicine, studies in healthy volunteers consist of tests to determine that it is equivalent to the reference medicine.

What are the possible side effects of Jayempi 10 mg/ml oral suspension?
For the full list of all side effects reported with this medicine, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes

with the medicine. Patients can also report suspected side effects themselves, or a report can be made on behalf of someone else they care for, directly via the Yellow Card scheme at www.mhra.gov.uk/yellowcard or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Because Jayempi 10 mg/ml oral suspension is a hybrid medicine and is equivalent to the reference medicine, its benefits and possible side effects are taken as being the same as the reference medicine.

Why was Jayempi 10 mg/ml oral suspension approved?
MHRA decided that the benefits are greater than the risks and recommended that this medicine can be approved for use.

What measures are being taken to ensure the safe and effective use of Jayempi 10 mg/ml oral suspension?
A Risk Management Plan (RMP) has been developed to ensure that Jayempi 10 mg/ml oral suspension is used as safely as possible. Based on this plan, safety information has been included in the SmPC and the PIL, including the appropriate precautions to be followed by healthcare professionals and patients.

Routine pharmacovigilance is considered sufficient for all risks, except for the safety concern of potential medication errors. The Marketing Authorisation Holder will monitor medication error reports and submit these annually, as a post authorisation measure.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored and reviewed continuously.

Other information about Jayempi 10 mg/ml oral suspension
A marketing authorisation was granted in Great Britain on 06 July 2021.

The full PAR for Jayempi 10 mg/ml oral suspension follows this summary.

This summary was last updated in July 2021.

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I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Jayempi 10 mg/ml oral suspension (PLGB 13581/0005) could be approved.

The product is approved for the following indications:

- in combination with other immunosuppressive agents for the prophylaxis of transplant rejection in patients receiving allogenic kidney, liver, heart, lung or pancreas transplants. Azathioprine is indicated in immunosuppressive regimens as an adjunct to immunosuppressive agents that form the mainstay of treatment (basis immunosuppression).
- as an immunosuppressant antimetabolite either alone or, more commonly, in combination with other agents (usually corticosteroids) and/ or procedures which influence the immune response.
    - in patients who are intolerant to glucocorticosteroids or if the therapeutic response is inadequate despite treatment with high doses of glucocorticosteroids, in the following diseases:
    - severe active rheumatoid arthritis (chronic polyarthritis) that cannot be kept under control by less toxic agents (disease-modifying anti-rheumatic -medicinal products – DMARDs)
    - auto-immune hepatitis
    - systemic lupus erythematosus
    - dermatomyositis
    - polyarteritis nodosa
    - pemphigus vulgaris and bullous pemphigoid
    - Behçet's disease
    - refractory auto-immune haemolytic anaemia, caused by warm IgG antibodies
    - chronic refractory idiopathic thrombocytopenic purpura
- for the treatment of moderately severe to severe forms of chronic inflammatory bowel disease (IBD) (Crohn's disease or ulcerative colitis) in patients in whom glucocorticosteroid therapy is necessary, but where glucocorticosteroids are not tolerated, or in whom the disease is untreatable with other common means of first choice.
- in adult patients in relapsing multiple sclerosis, if an immunomodulatory therapy is indicated but beta interferon therapy is not possible, or a stable course has been achieved with previous treatment with azathioprine.
- for the treatment of generalised myasthenia gravis. Depending on the severity of the disease, Jayempi should be given in combination with glucocorticosteroids because of slow onset of action at the beginning of treatment and the glucocorticosteroid dose should be gradually reduced after several months of treatment.

The name of the active substance is azathioprine, which is an inactive pro-drug of 6-mercaptopurine (6-MP), which acts as a purine antagonist but requires cellular uptake and intracellular anabolism to thioguanine nucleotides (TGNs) for immunosuppression. TGNs and other metabolites (e.g. 6-methylmercaptopurine ribonucleotides) inhibit *de novo* purine synthesis and purine nucleotide interconversions. The TGNs are also incorporated into nucleic acids and this contributes to the immunosuppressive effects of the medicinal product. Other potential mechanisms of azathioprine include the inhibition of many pathways in nucleic acid biosynthesis, hence preventing proliferation and activity of cells involved in the immune response (B and T lymphocytes).

This product has been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 21 June 2021 (EMEA/H/C/005055/0000), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP).

For the scientific discussion of the quality, non-clinical and clinical assessment conducted by the European Medicines Agency (EMA), please refer to the European Public Assessment Report, available on the EMA website.

This application was approved under Regulation 52A of the Human Medicines Regulation 2012, as amended (previously Article 10.3 of Directive 2001/83/EC, as amended).

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

A Marketing Authorisation was granted on 06 July 2021.

II. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION SUMMARY OF PRODUCT CHARACTERITICS (SmPC)

The SmPC is in line with current guidelines and is satisfactory.

PATIENT INFORMATION LEAFLET

The PIL is in line with current guidelines and is satisfactory.

LABEL

The labelling is in line with current guidelines and is satisfactory.

III. QUALITY ASPECTS

MHRA considered that the quality data submitted for this application is satisfactory.

The grant of a marketing authorisation(s) is/are recommended.

IV. NON-CLINICAL ASPECTS

MHRA considered that the non-clinical data submitted for this application is satisfactory.

The grant of a marketing authorisation is recommended.

V. CLINICAL ASPECTS

MHRA considered that the clinical data submitted for this application is satisfactory.

The grant of a marketing authorisation is recommended.

VI. RISK MANAGEMENT PLAN (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. In addition to routine pharmacovigilance and risk minimisation measures, the following post authorisation measures have been proposed:
Medication error reports specifically due to "conversion of patients from tablet to liquid

formulation and two dosing syringes" will be monitored annually and submitted as post authorisation measure.

This is acceptable.

VII. USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) has been provided with the application, in accordance with legal requirements.

The PIL has been evaluated via a user consultation study in accordance with legal requirements. The results show that the PIL meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

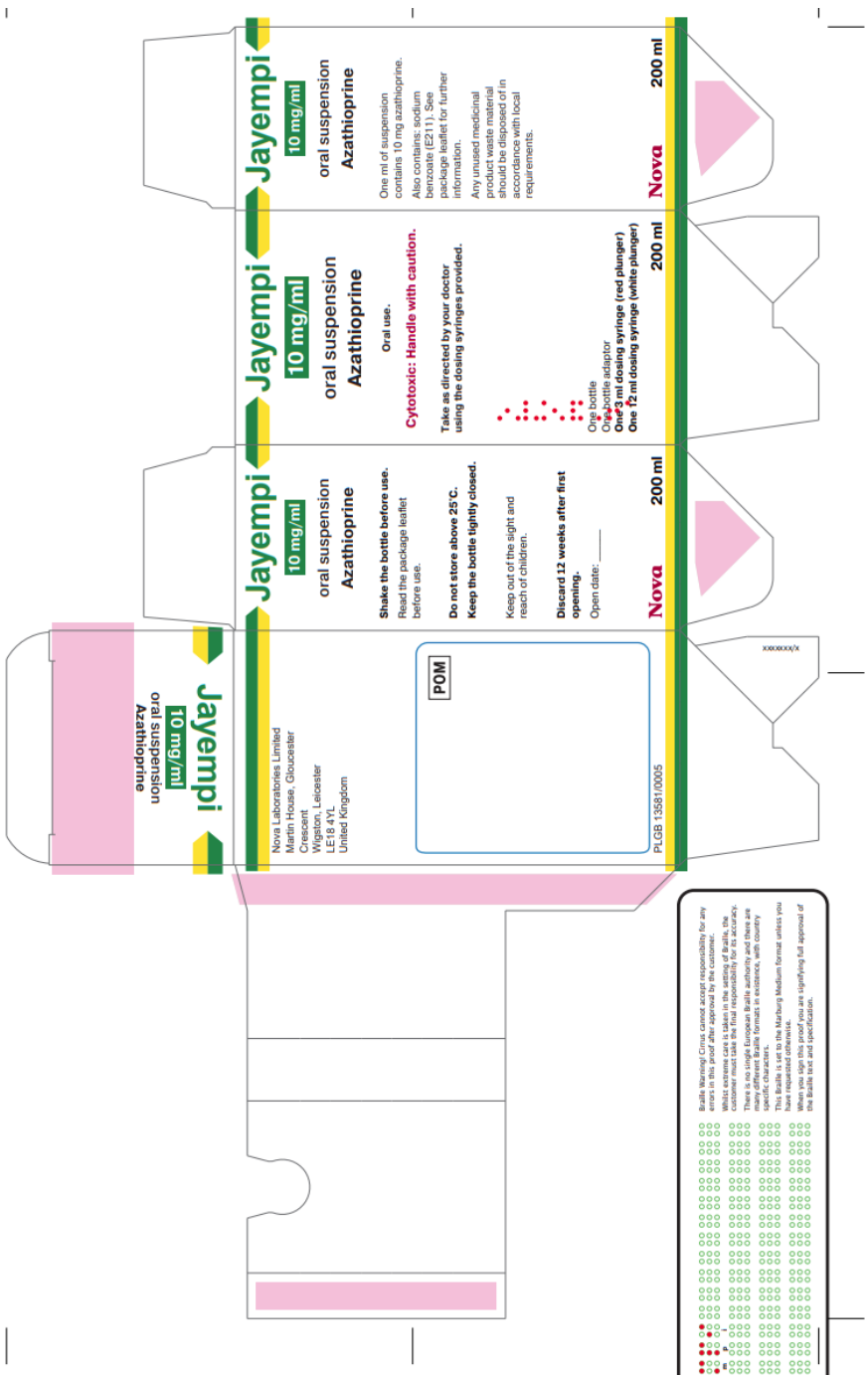
VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

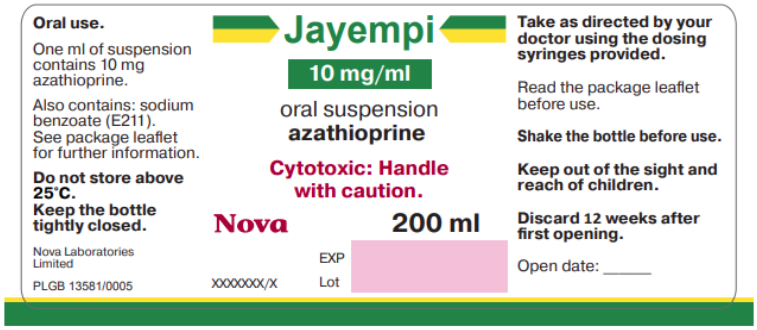
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The benefit/risk balance is, therefore, considered to be positive.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory.

In accordance with legal requirements, the current approved GB versions of the SmPC and PIL for this product are available on the MHRA website.

Representative copies of the labels at the time of licensing are provided below.


Jayempi
10 mg/ml
oral suspension
Azathioprine
Nova
200 ml
Shake the bottle before use.
Read the package leaflet before use.
Do not store above 25°C.
Keep the bottle tightly closed.
Keep out of the sight and reach of children.
Discard 12 weeks after first opening.
Open date: ____
Oral use.
Cytotoxic: Handle with caution.
Take as directed by your doctor using the dosing syringes provided.
One bottle
One bottle adaptor
One 5 ml dosing syringe (red plunger)
One 12 ml dosing syringe (white plunger)
One ml of suspension contains 10 mg azathioprine.
Also contains: sodium benzoate (E211). See package leaflet for further information.
Any unused medicinal product waste material should be disposed of in accordance with local requirements.
Nova Laboratories Limited
Martin House, Gloucester Crescent
Wigston, Leicester
LE18 4YL
United Kingdom
POM
PLGB 13581/0005
XXXXXXX/X
Braille reads: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Nova Laboratories Limited
PLGB 13581/0005
Jayempi
10 mg/ml
oral suspension
azathioprine
Cytotoxic: Handle with caution.
Nova
200 ml
XXXXXXX/X
EXP
Lot
Take as directed by your doctor using the dosing syringes provided.
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Shake the bottle before use.
Keep out of the sight and reach of children.
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Open date: _____

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Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations, where significant changes are made, are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPCs and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**