SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Allopurinol Viatris 100 mg tablets
Allopurinol Viatris 300 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 100 mg allopurinol.
Each tablet contains 300 mg allopurinol.

Excipients with known effects
Each tablet of Allopurinol Viatris 100 mg contains 48.2 mg of lactose.
Each tablet of Allopurinol Viatris 300 mg contains 145.9 mg of lactose and 2.6 mg of sunset yellow FCF (E110).
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

Each 100 mg tablet is white to off-white coloured, approximately 7.5 mm, round, biconvex uncoated with 'AL' and '100' separated by a score line on one side and plain on the other side.
Each 300 mg tablet is peach coloured, approximately 11 mm, round, biconvex uncoated with 'AL' and '300' separated by a score line on one side and plain on the other side.

The score line is not intended for breaking the tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Allopurinol Viatris is indicted in adults in:
- all forms of hyperuricaemia not controllable by diet including secondary hyperuricaemia of differing origin and in clinical complications of hyperuricaemic states, particularly manifest gout, urate nephropathy and for the dissolution and prevention of uric acid stones.
- the management of recurrent mixed calcium oxalate stones in concurrent hyperuricaemia, when fluid, dietary and similar measures have failed.

Allopurinol Viatris is indicted in children and adolescents in:
- Secondary hyperuricaemia of differing origin
- Uric acid nephropathy during treatment of leaukaemia
- Hereditary enzyme deficiency disorders, Lesch-Nyhan syndrome (partial or total hypoxanthin-guanin phosphoribosyl transferase deficiency) and adenine phosphoribosyl transferase deficiency.

4.2 Posology and method of administration

Posology

Adults and adolescents aged 15-18 years old
Allopurinol Viatris should be introduced at low dosage e.g. 100 mg/day to reduce the risk of adverse reactions and increased only if the serum urate response is unsatisfactory. Extra caution should be exercised if renal function is poor (see Renal impairment).

100 to 200 mg daily in mild conditions, 300 to 600 mg daily in moderately severe conditions or 700 to 900 mg daily in severe conditions.

Up to 300 mg Allopurinol Viatris can be given in a single dose. Doses exceeding 300 mg should be divided over the day.

If dosage based on mg/kg body weight is required, 2 to 10 mg/kg body weight/day should be used.

Paediatric population
Allopurinol Viatris 100 mg tablets: *paediatric population ≥15 kg body weight*
Allopurinol Viatris 300 mg tablets: *contain sunset yellow FCF and should not be given to children*

Children and adolescents 6 to 15 years: 10 to 20 mg/kg body weight/day up to a maximum of 400 mg daily given in three divided doses.
The safety and efficacy of allopurinol in children aged below 6 years has not been established. No data are available.
Use in children is rarely indicated except in malignant condition, especially in leukaemia and certain enzyme disorders, for example Lesch-Nyhan syndrome.

Elderly
No specific dosage recommendation, the lowest dosage which produces satisfactory urate reduction should be used. Refer to dosage advice in ’Renal impairment’ and ‘Special warnings and precautions for use’ and section 4.4.

Acute gouty attacks
When treatment with allopurinol is started, mobilisation of urate precipitation can result in a worsening of acute gouty attacks. Treatment with Allopurinol Viatris must therefore not be started in conjunction with an acute gouty attack, but only after the attack has subsided. When treatment is to be started after an acute gouty attack, an initial low dose (100 mg) is recommended, with incremental increases in order to avoid worsening. An effective anti-inflammatory medicinal product can also be given for one month. If the patient being treated with Allopurinol Viatris suffers an acute gouty attack, the treatment should continue while maintaining the same posology at the same time as the attack is treated with a suitable anti-inflammatory medicinal product.

As allopurinol is used to replace uricosuric agents, worsening of gouty attacks can be avoided if the uricosuric preparation used is discontinued gradually over a period of approximately one month after treatment with Allopurinol Viatris at a normal dose has begun.

Renal impairment
Since allopurinol and its metabolites are excreted by the kidney, impaired renal function may therefore lead to retention of the allopurinol and/or its metabolites with consequent prolongation of plasma half-lives. The following schedule may serve as guidance for adults:

Creatinine clearance (normal value 60 to 120 ml/min)	Dosage at reduced renal function
>20 ml/min	normal dose
10 to 20 ml/min	100 to 200 mg per day
<10 ml/min	100 mg/day or longer dose intervals

If facilities are available to monitor plasma oxipurinol concentrations, the dose should be adjusted to maintain plasma oxipurinol levels below 100 micromol/litre (15.2 mg/litre).

Renal dialysis
Allopurinol and its metabolites are removed by renal dialysis. If dialysis is required two to three times a week consideration should be given to an alternative dosage schedule of 300 to 400 mg Allopurinol Viatris immediately after each dialysis with none in the interim.

Hepatic impairment
Reduced doses should be used in patients with hepatic impairment.

Treatment of high urate turnover conditions, e.g. neoplasia, Lesch-Nyhan syndrome
It is advisable to correct existing hyperuricaemia and/or hyperuricosuria with Allopurinol Viatris before starting cytotoxic therapy. It is important to ensure adequate hydration to maintain optimum diuresis and to attempt alkalinisation of urine to increase solubility of urinary urate/uric acid. Dosage of allopurinol should be in the lower range.

If urate nephropathy or other pathology has compromised renal function, the advice given in 'Renal impairment' should be followed. These steps may reduce the risk of xanthine and/or oxipurinol deposition complicating the clinical situation (see sections 4.5 and 4.8).

Monitoring advice
The dosage should be adjusted by monitoring serum urate concentrations and urinary urate/uric acid levels at appropriate intervals.

Method of administration

For oral use.

Allopurinol Viatris should be taken orally after a meal to reduce possible gastrointestinal disorders.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Hypersensitivity syndrome, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)
Allopurinol should be withdrawn immediately when a skin rash or other evidence of sensitivity occurs due to the risk of severe hypersensitivity reactions (including SJS and TEN (also known as drug reaction with eosinophilia and systemic symptoms, DRESS) (see section 4.8 - Immune system disorders and Skin and subcutaneous tissue disorders).

If the skin reaction was mild, treatment with allopurinol may be resumed at a smaller dose and gradually increased. If the skin reaction returns, Allopurinol Viatris should be discontinued permanently.

Allopurinol hypersensitivity reactions can manifest in many different ways, including maculopapular exanthema, hypersensitivity syndrome (also known as DRESS) and SJS/TEN, amongst others. These reactions are clinical diagnoses and their clinical presentations remain the basis for decision making. If such reactions occur at any time during treatment, allopurinol should be withdrawn immediately. Re-administration should not be undertaken in patients with hypersensitivity syndrome and SJS/TEN. Corticosteroids may be beneficial in overcoming hypersensitivity skin reactions.

HLA-B*5801 allele
The HLA-B*5801 allele has been shown to be associated with the risk of developing allopurinol-related hypersensitivity syndrome and SJS/TEN. The frequency of the HLA-B*5801 allele varies widely between ethnic populations: up to 20% in Han Chinese population, 8-15% in the Thai, about 12% in the Korean population and 1-2% in individuals of Japanese or European origin.

Screening for HLA-B*5801 should be considered before starting treatment with allopurinol in patient subgroups where the prevalence of this allele is known to be high. Chronic kidney disease may increase the risk in these patients additionally. In case that no HLA-B*5801 genotyping is available for patients with Han Chinese, Thai or Korean descent the benefits should be thoroughly assessed and considered outweigh the possible higher risks before starting therapy. The use of genotyping has not been established in other patient populations.

If the patient is a known carrier of HLAB*5801 (especially in those who are from Han Chinese, Thai or Korean descent), allopurinol should not be started unless there are no other reasonable therapeutic options and the benefits are thought to exceed risks. Extra vigilance for signs of hypersensitivity syndrome or SJS/TEN is required and the patient should be informed of the need to stop treatment *immediately* at the first appearance of symptoms.

SJS/TEN can still occur in patients who are found to be negative for HLA-B*5801 irrespective of their ethnic origin.

Renal and hepatic impairment
Reduced doses must be used in patients with hepatic or renal impairment.
There is cumulative risk in patients with impaired renal function (see section 4.2). Patients under treatment for hypertension or cardiac insufficiency, for example with diuretics or ACE inhibitors, may have some concomitant impairment of renal function and allopurinol should be used with caution in this group.

Chronic renal impairment and concomitant use of diuretics, especially thiazides, have been associated with an increased risk of developing allopurinol-induced SJS/TEN and other serious hypersensitivity reactions.

Asymptomatic hyperuricaemia per se is generally not considered an indication for use of allopurinol. Fluid and dietary modification with management of the underlying cause may correct the condition.

Very rare cases of aplastic anaemia with fatal outcome have been reported from treatment with allopurinol. Impaired renal function can be a risk factor and the posology should be adapted for this (see section 4.2). If there are signs/symptoms of blood damage discontinuation of allopurinol must be considered.

Acute gouty attacks
When treatment with allopurinol is started, mobilisation of urate precipitation can result in a worsening of acute gouty attacks. Treatment with Allopurinol Viatris must therefore not be started in conjunction with an acute gouty attack, but only after the attack has subsided.

In the early stages of treatment with allopurinol, as with uricosuric agents, an acute attack of gouty arthritis may be expected. Therefore, it is advisable to give prophylaxis with a suitable anti-inflammatory agent or colchicine for several months. The literature should be consulted for details of appropriate dosage and precautions and warnings.

If acute attacks develop in patients receiving allopurinol, treatment should continue at the same dosage while the acute attack is treated with a suitable anti-inflammatory agent.

Xanthine precipitation
For conditions where the body’s total urate quantity is considerably increased (e.g. during treatment of malignant diseases; with Lesch-Nyhan syndrome), the reduced urate formation during allopurinol treatment is accompanied by a relative increase of xanthine and hypoxanthine fractions. Under such conditions, the absolute xanthine concentration can also, in rare cases, increase and create xanthine deposits in the urinary tract. This risk can be reduced through adequate fluid intake. Alkalisation of the urine is of utmost importance when treating urate stones but is of less importance with xanthine stones. Xanthine crystals have been found in muscle tissue in patients undergoing allopurinol treatment, but the clinical significance of this is thought to be minimal.

Thyroid disorders
Increased TSH values (>5.5 µIU/mL) were observed in patients on long-term treatment with allopurinol (5.8%) in a long term open label extension study. Caution is required when allopurinol is used in patients with alteration of thyroid function.

Uric acid renal stones
Adequate therapy with allopurinol will lead to dissolution of large uric acid renal pelvic stones, with the remote possibility of impaction in the ureter.

6-mercaptopurine and azathioprine
Concomitant use of allopurinol with 6-mercaptopurine or azathioprine should be avoided as there have been reports of fatal cases (see section 4.5).

Allopurinol Viatris contains lactose. Patients with rare hereditary problems of galactose intolerance, the total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

This medicine also contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

Allopurinol Viatris 300 mg tablet also contains sunset yellow FCF (azo colouring agent). This may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

Ampicillin/Amoxicillin
An increase in frequency of skin rash has been reported among patients receiving ampicillin or amoxicillin concurrently with allopurinol compared to patients who are not receiving both drugs. The cause of the reported association has not been established. However, it is recommended that in patients receiving allopurinol an alternative to ampicillin or amoxicillin is used where available.

6-mercaptopurine and azathioprine
Azathioprine is metabolised to 6-mercaptopurine, which is inactivated by the action of xanthine oxidase. When 6-mercaptopurine or azathioprine is given concurrently with allopurinol, a xanthine oxidase inhibitor, inhibition of xanthine oxidase will prolong their activity. Serum concentrations of 6-mercaptopurine or azathioprine may reach toxic levels with consequent life-threatening pancytopenia and myelosuppression when these medicinal products are given concurrently with allopurinol. Therefore, concomitant use of allopurinol with 6-mercaptopurine or azathioprine should be avoided. If it is determined that co-administration with 6-mercaptopurine or azathioprine is clinically needed, dosing should be reduced to one quarter (25%) of the usual dose of 6-mercaptopurine or azathioprine and frequent haematologic monitoring should be ensured (see section 4.4).

Patients should be advised to report any signs or symptoms of bone marrow suppression (unexplained bruising or bleeding, sore throat, fever).

Vidarabine (adenine arabinoside)
There are reports that suggest that concomitant use of allopurinol and vidarabine can increase the risk of toxic effects of vidarabine.

Chlorpropamide
If allopurinol is given concomitantly with chlorpropamide when renal function is impaired, there may be an increased risk of prolonged hypoglycaemic activity because allopurinol and chlorpropamide may compete for excretion in the renal tubule.

Ciclosporin
Reports suggest that the plasma concentration of ciclosporin may be increased during concomitant treatment with allopurinol. The possibility of enhanced ciclosporin toxicity should be considered if the drugs are co-administered.

Cytostatics
With administration of allopurinol and cytostatics (e.g. cyclophosphamide, doxorubicin, bleomycin, procarbazine, alkyl halogenides), blood dyscrasias occur more frequently than when these active substances are administered alone.

Blood count monitoring should therefore be performed at regular intervals.

Theophylline
High daily doses of allopurinol (e.g. 600 mg) reduces theophylline clearance and therefore control of theophylline levels is advisable.

Salicylates and uricosuric agents
Substances that increase the secretion of uric acid, e.g. probenecid and high doses of salicylates, can cause increased secretion of allopurinol's active metabolite, oxipurinol, which in turn can lead to a reduced therapeutic effect of allopurinol. This must be evaluated from case to.

Phenytoin
Allopurinol may inhibit the hepatic metabolism of phenytoin.

Coumarin anticoagulants
There have been rare reports of increased effect of warfarin and other coumarin anticoagulants when co-administered with allopurinol. Patients receiving coumarin anticoagulants should therefore be carefully monitored.

Didanosine
In healthy volunteers and HIV patients receiving didanosine, plasma didanosine C_{max} and AUC values were approximately doubled with concomitant allopurinol treatment (300 mg daily) without affecting terminal half-life. Dose reduction of didanosine should be considered when co-administered with allopurinol.

Diuretics
An interaction between allopurinol and furosemide that results in increased serum urate and plasma oxipurinol concentrations has been reported. An increased risk of hypersensitivity has been reported when allopurinol is given with diuretics, in particular thiazides, especially in the event of reduced kidney function.

Angiotensin-converting-enzyme (ACE) inhibitors
An increased risk of hypersensitivity has been reported when allopurinol is given with ACE inhibitors, especially in the event of reduced kidney function.

Aluminium hydroxide
If aluminium hydroxide is taken concomitantly, allopurinol may have an attenuated effect. There should be an interval of at least 3 hours between taking both medicines.

4.6 Fertility, pregnancy and lactation

Fertility
There are no data from the use of allopurinol on fertilty.

Pregnancy
There are no or limited amount of data from the use of allopurinol in pregnant women. Animal studies are insufficient with respect to reproductive toxicity.

Allopurinol should be used in pregnancy only when there is no safer alternative or when benefit outweighs the risks.

Breast-feeding
Allopurinol and it metabolite oxipurinol is excreted in the human breast milk. There are no data concerning the effects of allopurinol or its metabolites on the breast-fed baby.

Allopurinol during breastfeeding is not recommended. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from allopurinol therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

4.7 Effects on ability to drive and use machines

Drowsiness, dizziness and ataxia can occur during treatment with allopurinol. This should be taken into consideration in situations where a high degree of alertness is required, e.g. when driving or using machines.

4.8 Undesirable effects

For this product there is no modern clinical documentation which can be used as support for determining the frequency of adverse reactions. The incidence of adverse reactions is largely dose dependent and the risk is higher in the presence of renal and/or hepatic disorder.

The frequency categories assigned to the adverse drug reactions below are estimates. Adverse drug reactions are classified according to System Organ Class and frequency. The following convention has been used for the classification of frequency: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000),
not known (cannot be estimated from the available data).

Table 1. Tabulated summary of adverse reactions

System Organ Class	Frequency	Adverse reaction
Infections and infestations	Very rare	Furuncle
Blood and lymphatic system disorders	Very rare	Agranulocytosis[1] Aplastic anaemia[1] Thrombocytopenia[1] Leucopenia Leucocytosis Eosinophilia
Immune system disorders	Uncommon	Hypersensitivity[2]
	Rare	General hypersensitivity syndrome[3]
	Very rare	Angioimmunoblastic T-cell lymphoma[4] Anaphylactic shock Anaphylactic reaction
Metabolism and nutrition disorders	Very rare	Diabetes mellitus Hyperlipidaemia
Psychiatric disorders	Very rare	Depression
Nervous system disorders	Very rare	Coma Paralysis Ataxia Neuropathy peripheral Paraesthesia Neuritis peripheral Somnolence Headache Dysgeusia Seizures
	Not known	Aseptic meningitis
Eye disorders	Very rare	Cataract Visual impairment Maculopathy
Ear and labyrinth disorders	Very rare	Vertigo
Cardiac disorders	Very rare	Angina pectoris Bradycardia

System Organ Class	Frequency	Adverse reaction
Vascular disorders	Very rare	Hypertension Vasculitis
Gastrointestinal disorders	Uncommon	Vomiting Nausea Diarrhoea
	Very rare	Haematemesis Steatorrhoea Stomatitis Change of bowel habit
Hepatobiliary disorders	Uncommon	Liver function test abnormal[5]
	Rare	Hepatitis (including hepatic necrosis and granulomatous hepatitis)[5]
Skin and subcutaneous tissue disorders	Common	Rash
	Rare	Granulomatous or maculopapular changes, itching, redness, skin exfoliation, Stevens-Johnson syndrome/toxic Epidermal necrolysis Lyell's syndrome Erythema multiforme
	Very rare	Angioedema[6] Drug eruption Alopecia Hair colour changes
	Not Known	Lichenoid drug reaction
Musculoskeletal and connective tissue disorders	Very rare	Myalgia Arthralgia
Renal and urinary disorders	Very rare	Haematuria Azotaemia Interstitial nephritis Xanthine stones Renal failure
Reproductive system and breast disorders	Very rare	Infertility male Erectile dysfunction Gynaecomastia
General disorders and administration site conditions	Very rare	Oedema Malaise Asthenia Pyrexia[7]
Investigations	Common	Blood thyroid stimulating hormone increased[8]

1. Very rare reports have been received of agranulocytosis, aplastic anaemia and thrombocytopenia, particularly in individuals with impaired renal and/or hepatic function, reinforcing the need for particular care in this group of patients.

2. Serious hypersensitivity reactions, including skin reactions associated with fever, rash, vasculitis, lymphadenopathy, pseudolymphoma, arthralgia, leucopenia, and/or eosinophilia (DRESS), Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) occur in rare cases (see *Skin and subcutaneous tissue disorders*). Related vasculitis and tissue response can manifest in different ways, including hepatosplenomegaly, hepatitis, abnormal liver function tests and loss of bile ducts (vanishing bile duct syndrome) (enlargement and loss of intrahepatic bile ducts) and kidney failure, and, in very rare cases, seizures. Other organs can also be affected (e.g. liver, lungs, kidneys, pancreas, myocardium and

colon). Very rare cases of acute anaphylactic shock have been reported. If such reactions occur, which can happen at any time during treatment, then allopurinol treatment must be immediately and permanently discontinued. Reintroduction should not be undertaken in patients with hypersensitivity syndrome and SJS/TEN. Corticosteroids may be beneficial in overcoming hypersensitivity skin reactions. A delayed multi-organ hypersensitivity disorder (known as hypersensitivity syndrome or DRESS) with fever, rashes, vasculitis, lymphadenopathy, pseudo lymphoma, arthralgia, leucopenia, eosinophilia, hepatosplenomegaly, abnormal liver function tests and vanishing bile duct syndrome (destruction and disappearance of the intrahepatic bile ducts) occurring in various combinations; other organs may also be affected (e.g. liver, lungs, kidneys, pancreas, myocardium, and colon); if such reactions do occur at any time during treatment, allopurinol should be withdrawn immediately and permanently; when generalised hypersensitivity reactions have occurred, kidney and/or liver disorder have usually been present, particularly when the outcome has been fatal.

3. General hypersensitivity syndrome including fever, angioedema, lymphadenopathy, vasculitis, arthralgia, eosinophilia, skin changes such as SJS, TEN, and kidney and liver function impairment.

4. Angioimmunoblastic T-cell lymphoma has been described very rarely following biopsy of a generalised lymphadenopathy. It appears to be reversible on withdrawal of allopurinol.

5. Hepatic dysfunction has been reported without clear evidence of more generalised hypersensitivity.

6. Angioedema has been reported to occur with and without signs and symptoms of a more generalised hypersensitivity reaction.

7. Fever has been reported to occur with and without signs and symptoms of a more generalised allopurinol hypersensitivity reaction (see ‘Immune system disorders’).

8. The occurrence of increased thyroid stimulating hormone (TSH) in the relevant studies did not report any impact on free T4 levels or had TSH levels indicative of subclinical hypothyroidism.

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 [To be completed nationally].

4.9 Overdose

Toxicity
10 g in adults produced moderate intoxication, while 22.5 g in a 15-year old after early ventricle emptying did not cause any symptoms.

Symptoms and signs
Symptoms and signs including nausea, vomiting, diarrhoea and dizziness have been reported in a patient who ingested 20 g allopurinol. Recovery followed general supportive measures. For other conceivable symptoms, see section 4.8 Undesirable effects. Crystal precipitation in the urinary tract is possible

Treatment
Gastric lavage with carbon, if required. Ensure that there is good diuresis. Possible alkalinisation of the urine to pH 7. Symptomatic treatment.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Preparations inhibiting uric acid production, ATC code: M04AA01

Mechanism of action
The enzyme xanthine oxidase catalyses the conversion of hypoxanthine to xanthine and xanthine to uric acid. Allopurinol inhibits xanthine oxidase and lowers the urate level via reduced new formation. Allopurinol therefore lowers the uric acid level in serum, promotes the mobilisation of urate precipitation in the tissues, reduces the degree of urate secretion in urine and prevents the formation of urate stones and gravel in urine.

Pharmacodynamic effects
In addition to the inhibition of purine catabolism in some but not all hyperuricaemic patients, *de novo* purine biosynthesis is depressed via feedback inhibition of hypoxanthine-guanine phosphoribosyltransferase.

5.2 Pharmacokinetic properties

Absorption
Allopurinol is active when given orally and is rapidly absorbed. Estimates of bioavailability vary from 67% to 90%.

Peak plasma levels of allopurinol generally occur approximately 1.5 hours after oral administration of allopurinol. Peak levels of oxipurinol generally occur after 3 to 5 hours after oral administration of allopurinol.

Distribution
Allopurinol is negligibly bound by plasma proteins and therefore variations in protein binding are not expected to significantly alter clearance. The volume of distribution of allopurinol is approximately 1.6 litre/kg.

Biotransformation
The main metabolite of allopurinol is oxipurinol, which is also an inhibitor of xanthine oxidase. Other metabolites of allopurinol are allopurinol riboside and oxipurinol-7-riboside.

Elimination
Approximately 20% of the ingested allopurinol is excreted in faeces. Elimination of allopurinol is mainly by metabolic conversion to oxipurinol by xanthine oxidase and aldehyde oxidase, with approximately 10% excreted in the urine in unchanged form.

Allopurinol has a plasma half-life of about 1 to 2 hours
Oxipurinol is a less potent inhibitor of xanthine oxidase than allopurinol, but the plasma half-life of oxipurinol is much longer. The estimate is between 13 and 30 hours in man. Therefore effective inhibition of xanthine oxidase is maintained over a 24-hour period with a single daily dose of allopurinol. Patients with normal renal function taking 300 mg of allopurinol per day will generally have plasma oxipurinol concentrations of 5 to 10 mg/litre.

Special population

Renal impairment
Allopurinol and oxipurinol clearance is greatly reduced in patients with impaired renal function resulting in higher plasma levels in long-term treatment. Patients with renal impairment, creatinine clearance values between 10 and 20 ml/min had plasma oxipurinol concentrations of approximately 30 mg/litre after prolonged treatment with 300 mg allopurinol per day. This is approximately the concentration which would be achieved by doses of 600 mg/day in those with normal renal function. A reduction in the dose of allopurinol is therefore required in patients with renal impairment.

Elderly
The kinetics of the medicinal product are not expected to change except in cases with impaired renal function (see ‘Renal impairment’).

5.3 Preclinical safety data

Genotoxicity
Cytogenetic studies show that allopurinol does not induce chromosome abnormalities in human blood cells *in vitro* at concentrations up to 100 micrograms/ml and *in vivo* at doses up to 600 mg/day for an average period of 40 months.

Allopurinol does not form nitroso compounds *in vitro* and does not affect lymphocyte conversion *in vitro*.

Teratogenicity
A study in mice receiving intraperitoneal doses of 50 or 100 mg/kg on days 10 or 13 of gestation resulted in foetal abnormalities.

An *in vitro* study using foetal mouse salivary glands in culture to detect embryotoxicity indicated that allopurinol would not be expected to cause embryotoxicity without also causing maternal toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Allopurinol 100 mg Tablets
Lactose monohydrate
Maize starch
Povidone
Sodium starch glycolate
Stearic acid

Allopurinol 300 mg Tablets
Lactose monohydrate
Maize starch
Povidone
Sodium starch glycolate
Sunset yellow FCF aluminium lake (E110)
Stearic acid

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Allopurinol Viatris 100 mg Tablets are packed in PVDC/PVC-Aluminium foil blister packs in cardboard cartons of 20, 50, 60 and 100 tablets
Allopurinol Viatris 300 mg Tablets are packed in PVDC/PVC-Aluminium foil blister packs in cardboard cartons of 30, 60 and 100 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

[To be completed nationally]
24-01-2025