ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Duzallo 200 mg/200 mg film-coated tablets

Duzallo 300 mg/200 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Duzallo 200 mg/200 mg film-coated tablets

Each film-coated tablet contains 200 mg of allopurinol and 200 mg of lesinurad.

Excipient with known effect:

Each film-coated tablet contains 102.6 mg of lactose (as monohydrate).

Duzallo 300 mg/200 mg film-coated tablets

Each film-coated tablet contains 300 mg of allopurinol and 200 mg of lesinurad.

Excipient with known effect:

Each film-coated tablet contains 128.3 mg of lactose (as monohydrate).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

Duzallo 200 mg/200 mg film-coated tablets

Pale pink oblong film-coated tablets with 7 x 17 mm in size.
The film-coated tablets are engraved with “LES200” and “ALO200” on one side.

Duzallo 300 mg/200 mg film-coated tablets

Orange and slightly brownish oblong film-coated tablets with 8 x 19 mm in size.
The film-coated tablets are engraved with “LES200” and “ALO300” on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Duzallo is indicated in adults for the treatment of hyperuricaemia in gout patients who have not achieved target serum uric acid levels with an adequate dose of allopurinol alone.

4.2 Posology and method of administration

Posology

Dose titration with allopurinol to an adequate dose must be done before the patient is switched to Duzallo.

The choice of the dose strength of Duzallo depends on the allopurinol dose taken as individual tablet(s).
The recommended dose is one tablet of Duzallo (200 mg/200 mg or 300 mg/200 mg) once daily. This is also the maximum daily dose of Duzallo (see section 4.4).

Patients who are currently treated with allopurinol doses higher than 300 mg can be switched to Duzallo 200 mg/200 mg or Duzallo 300 mg/200 mg and should receive complementary doses of allopurinol to cover the total dose of allopurinol taken before switching to Duzallo.

Patients should be instructed to stay well hydrated.

Patients should be informed that failure to follow these instructions may increase the risk of renal events (see section 4.4).
The target serum uric acid level is less than 6 mg/dL (360 µmol/L). In patients with tophi or persistent symptoms, the target is less than 5 mg/dL (300 µmol/L). Testing for the target serum uric acid level can be performed after 4 weeks to consider treatment adjustment to target serum uric acid level.Gout flare prophylaxis needs to be considered (see section 4.4).

Special populations

Elderly (≥65 years)
No dose adjustment is necessary based on age (see section 5.2); however, elderly patients are more likely to have decreased renal function (see dosing recommendations for renal impairment). Experience in very elderly patients (≥75 years) is limited.

Renal impairment
Duzallo is contraindicated in patients with severe renal impairment (CrCL less than 30 ml/min), with end-stage renal disease, in patients on dialysis or in kidney transplant recipients (see sections 4.3 and 4.4). Based on its mechanism of action, lesinurad may not be effective in these patients (see section 5.1).
Duzallo should be used with caution in patients with a CrCL of 30 to less than 45 mL/min (experience with lesinurad in patients with an estimated CrCL (eCrCL) less than 45 mL/min is limited).

Hepatic impairment
No dose adjustment is necessary in patients with mild or moderate hepatic impairment (Child-Pugh classes A and B) (see section 5.2). Duzallo has not been studied in patients with severe hepatic impairment; therefore, no dose recommendations can be given for Duzallo.

Paediatric population
The safety and efficacy of Duzallo in children and adolescents under 18 years of age have not yet been established. No data are available.

Method of administration

Oral use.
Duzallo should be taken in the morning with food and water.

4.3 Contraindications

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

Tumour lysis syndrome or Lesch-Nyhan syndrome.

Severe renal impairment (CrCL less than 30 mL/min), end-stage renal disease, kidney transplant recipients or patients on dialysis (see section 4.2).

4.4 Special warnings and precautions for use

Pre-existing cardiovascular disease
Duzallo is not recommended in patients with unstable angina, New York Heart Association (NYHA) class III or IV heart failure, uncontrolled hypertension or with a recent event of myocardial infarction, stroke, or deep venous thrombosis within the last 12 months, due to insufficient data with lesinurad. For cardiovascular patients in a stable condition, the benefit/risk balance should be assessed for each individual patient on an ongoing basis, taking into account the benefits of lowering urate levels versus a potential increase in cardiac risk (see section 4.8).

Renal events

Treatment with lesinurad 200 mg in combination with allopurinol was associated with an increased incidence of serum creatinine elevations, which are related to increased renal uric acid excretion. Adverse reactions related to renal function can occur after initiating Duzallo (see section 4.8)

Renal function should be evaluated prior to initiation of Duzallo and monitored periodically thereafter (e. g. 4 times per year), based on clinical considerations, such as baseline renal function, volume depletion, concurrent illness or concomitant medicinal products. Patients with serum creatinine elevations to greater than 1.5 times the pre-treatment value should be closely monitored. Duzallo should be interrupted if serum creatinine is elevated to more than 2 times the pre-treatment value or in case of an absolute serum creatinine value greater than 4.0 mg/dL. Treatment should be interrupted in patients who report symptoms that may indicate acute uric acid nephropathy, including flank pain, nausea or vomiting, and measure serum creatinine promptly. Duzallo should not be restarted without another explanation for the serum creatinine abnormalities.

Effect of CYP2C9 genotype

Patients known to be CYP2C9 poor metabolisers should be treated with caution, as the potential risk of lesinurad renal-related adverse reactions may be increased (see sections 4.8 and 5.2).

Hypersensitivity syndrome, Stevens-Johnson-Syndrome (SJS) and toxic epidermal necrolysis (TEN)

Allopurinol hypersensitivity reactions can manifest in many different ways, including maculopapular exanthema, hypersensitivity syndrome (also known as DRESS) and SJS/TEN. Re-challenge should not be undertaken in patients with hypersensitivity syndrome and SJS/TEN. Corticosteroids may be beneficial in overcoming hypersensitivity skin reactions.

Duzallo and all additional doses of allopurinol should be discontinued immediately at the first appearance of allopurinol-induced skin rash or other signs which may indicate an allergic reaction and additional medical care should be provided as needed.

Hypersensitivity reactions to allopurinol may be increased in patients with decreased renal function receiving diuretics (in particular thiazides) and Duzallo concurrently (see sections 4.5 and 4.8).

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. If no HLA-B*5801 genotyping is available for patients with Han Chinese, Thai or Korean descent, the benefits should be thoroughly assessed and considered to 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 HLA-B*5801, especially in those who are of 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.

Acute gouty attacks (gout flares)

Gout flares may occur after initiation of therapy with Duzallo. This is due to reduction in serum uric acid levels resulting in mobilisation of urate from tissue deposits. Gout flare prophylaxis needs to be considered (see section 4.2).
Duzallo does not need to be discontinued because of a gout flare. The gout flare should be managed concurrently as appropriate for the individual patient. Continuous treatment with Duzallo decreases the frequency of gout flares.

Impaction of 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.

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.

Clinically relevant interactions with other medicinal products

CYP3A substrates
Lesinurad is a mild to moderate inducer of CYP3A (see section 4.5). An induction effect of lesinurad should be anticipated after 2 to 3 weeks of continuous co-administration of Duzallo. Additional monitoring of lipids and blood pressure is recommended in patients using sensitive CYP3A substrate lipid lowering medicinal products (such as lovastatin or simvastatin) or antihypertensive medicinal products (such as amlodipine, felodipine or nisoldipine), since their efficacy may be reduced (see section 4.5).

Hormonal contraceptives
Hormonal contraceptives, including oral, injectable, transdermal, and implantable forms, may not be reliable when Duzallo is co-administered. Female patients of childbearing age should practice additional methods of contraception and not rely on hormonal contraception alone when taking Duzallo (see sections 4.5 and 4.6).

Lactose intolerance

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

4.5 Interaction with other medicinal products and other forms of interaction

Not recommended concomitant use with:

Salicylates and non-selective uricosuric active substances such as probenecid
Salicylates at doses higher than 325 mg per day may decrease the serum uric acid lowering activity of lesinurad and should not be co-administered with Duzallo. There are no restrictions for doses of salicylates of 325 mg or less per day (i.e. for cardiovascular protection).
Consistent serum uric acid lowering was observed in patients who were receiving low dose acetylsalicylic acid in the placebo-controlled clinical studies in combination with allopurinol or febuxostat.
Oxypurinol, the major metabolite of allopurinol and itself therapeutically active, is excreted by the kidney in a similar way to urate.
Hence, medicinal products with known non-selective uricosuric activity such as probenecid or large doses of salicylates may accelerate the excretion of oxypurinol. This may decrease the therapeutic activity of Duzallo which contains the active substance allopurinol, but the significance needs to be assessed in each case.

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

Didanosine
In healthy volunteers and HIV patients receiving didanosine, plasma didanosine maximum plasma concentration (C_{max}) and area under the curve (AUC) values were approximately doubled with concomitant allopurinol treatment (300 mg daily) without affecting terminal half-life. Co-administration of these 2 active substances is generally not recommended. If concomitant use is unavoidable, a dose reduction of didanosine may be required, and patients should be closely monitored.

Epoxide hydrolase inhibitors (e.g. valproic acid, valpromide)
Inhibitors of microsomal Epoxide Hydrolase (mEH) (e.g. valproic acid, valpromide) may interfere with the metabolism of lesinurad. Duzallo should not be administered with inhibitors of mEH.

Concomitant use which needs to be taken into consideration:

Diuretics
An increased risk of hypersensitivity has been reported when allopurinol is given with diuretics, in particular thiazides, especially in renal impairment (see section 4.4 and section 5.1).

Angiotensin-converting-enzyme (ACE) inhibitors
Concurrent use of allopurinol and ACE inhibitors may lead to an increased risk of hypersensitivity, especially if there is pre-existing renal impairment.

6-mercaptopurine and azathioprine
Serum concentrations of 6-mercaptopurine and azathioprine can reach toxic levels unless dose reduction is undertaken. Patients taking Duzallo which contains the active substance allopurinol and 6-mercaptopurine or azathioprine must reduce their dose to 25 % of the intended dose of 6-

mercaptopurine or azathioprine. Patients should be closely monitored for therapeutic response and the appearance of toxicity.

Cytostatics
With administration of allopurinol and cytostatics (e.g. cyclophosphamide, doxorubicin, bleomycin, procarbazine, alkylating agents), blood dyscrasias occur more frequently than when these active substances are administered alone.
Blood count monitoring should therefore be performed at regular intervals.

Vidarabine (Adenine Arabinoside)
Evidence suggests that the plasma half-life of adenine arabinoside is increased in the presence of allopurinol and hence when these two active substances are administered concomitantly, extra vigilance is required to recognize enhanced toxic effects.

CYP3A substrates
Mild to moderate induction of CYP3A by lesinurad may reduce plasma exposures of co-administered medicinal products that are sensitive substrates of CYP3A. In interaction studies conducted in healthy subjects with lesinurad and CYP3A substrates, lesinurad reduced the plasma concentrations of sildenafil and amlodipine. HMG-CoA reductase inhibitors that are sensitive CYP3A substrates may interact with lesinurad. In the pivotal clinical trials, a greater proportion of patients using lipid lowering or anti-hypertensive medicinal products that were CYP3A substrates required concomitant medicinal product change when treated with lesinurad 200 mg in combination with a xanthine oxidase inhibitor, compared with patients treated with placebo in combination with a xanthine oxidase inhibitor (35% versus 28%, respectively). The possibility of reduced efficacy of concomitant medicinal products that are CYP3A substrates should be considered and their efficacy (e.g. blood pressure and cholesterol levels) should be monitored (see section 4.4).

Ciclosporin
Allopurinol can increase the plasma concentration of ciclosporin when concomitantly administered. The possibility of an increased occurrence of ciclosporin-specific adverse reactions is to be considered. Mild to moderate induction of CYP3A by concomitantly administered lesinurad may reduce or eventually reverse this effect. However, no data are available.
In transplant patients frequent measurement of ciclosporin levels and, if necessary, ciclosporin dosage adjustment is required, particularly during the introduction or withdrawal of Duzallo.

Hormonal contraceptives
Lesinurad is a mild to moderate inducer of CYP3A and therefore may lower plasma concentrations of some hormonal contraceptives, thereby decreasing contraceptive effectiveness (see sections 4.4 and 4.6).

CYP2B6 substrates
Based on *in vitro* data, lesinurad may be a mild inducer of CYP2B6 but this interaction has not been studied clinically. Therefore, it is recommended that patients are monitored for reduced efficacy of CYP2B6 substrates (e.g. bupropion, efavirenz) when co-administered with lesinurad.
Based on interaction studies in healthy subjects or gout patients, lesinurad does not have clinically significant interactions with NSAIDs (naproxen and indomethacin) or colchicine.

Theophylline
Inhibition of the metabolism of theophylline by allopurinol has been reported. The mechanism of the interaction may be explained by xanthine oxidase being involved in the biotransformation of theophylline in man. Theophylline levels should be monitored in patients undergoing Duzallo therapy.

Chlorpropamide
If Duzallo which contains the active substance allopurinol is given concomitantly with chlorpropamide when renal function is poor, there may be an increased risk of prolonged hypoglycaemic activity.

CYP2C9 inhibitors and inducers

Lesinurad exposure is increased when it is co-administered with inhibitors of CYP2C9. Fluconazole, a moderate CYP2C9 inhibitor, increased lesinurad AUC (56%) and C_{max} (38%), as well as the amount of lesinurad excreted unchanged in urine. Other moderate CYP2C9 inhibitors, such as amiodarone, would also be expected to affect lesinurad pharmacokinetics to a similar degree. Therefore, it is recommended that Duzallo should be used with caution in patients taking moderate inhibitors of CYP2C9. Lesinurad exposure is expected to decrease when it is co-administered with inducers of CYP2C9 (e.g. carbamazepine, a moderate CYP2C9 inducer). Monitor for decreased efficacy when Duzallo is co-administered with a CYP2C9 inducer.

Coumarin anticoagulants
An interaction between allopurinol and coumarins has been seen under experimental conditions. The clinical relevance is not clear. A possible interaction should be taken into account when a patient on oral anticoagulants is given Duzallo. All patients receiving coumarin anticoagulants must be carefully monitored.

Aluminium hydroxide
If aluminium hydroxide is taken concomitantly, allopurinol-containing medicinal products may have an attenuated effect. There should be an interval of at least 3 hours between the concomitant use of those medicinal products.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data from the use of lesinurad and limited amount of data from the use of allopurinol in pregnant women.
Studies in animals with lesinurad do not indicate direct or indirect harmful effects.
Studies with allopurinol are insufficient with respect to reproductive toxicity (see section 5.3).
As a precautionary measure, it is preferable to avoid the use of Duzallo during pregnancy. Female patients of childbearing potential should not rely on hormonal contraception alone (including oral, injectable, transdermal, and implantable forms) when taking Duzallo (see sections 4.4 and 4.5).

Breast-feeding

Allopurinol and its metabolite oxypurinol are excreted in human breast milk. Duzallo is not recommended during breastfeeding.

Fertility

The effect of lesinurad and allopurinol on fertility in humans has not been studied.
In male and female rats, there was no effect on mating or fertility with lesinurad.
Reproductive studies with allopurinol have been performed in rats and rabbits at doses up to twenty times the usual human dose and it was concluded that there was no impaired fertility.

4.7 Effects on ability to drive and use machines

Lesinurad has no or negligible influence on the ability to drive and use machines.
However, since adverse reactions such as somnolence, vertigo and ataxia have been reported in patients receiving allopurinol (see section 4.8), patients should exercise caution before driving, using machinery or participating in dangerous activities until they are reasonably certain that Duzallo does not adversely affect their ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The safety of lesinurad 200 mg was evaluated in the Phase 3 combination therapy clinical trials (including extension studies). The most commonly reported adverse reactions during treatment with lesinurad 200 mg are influenza, gastro-oesophageal reflux disease, headache and blood creatinine increased. The serious adverse reactions renal failure, renal impairment and nephrolithiasis have occurred uncommonly (less than 1 case per 100 patients) (see Table 1). In clinical trials, most adverse reactions were mild or moderate in intensity and resolved while continuing lesinurad therapy. The most common adverse reaction leading to discontinuation of lesinurad was blood creatinine increased (frequency 0.8%).
For allopurinol, undesirable effects may vary in their incidence depending on the dose received and also when given in combination with other medicinal products.

Tabulated list of adverse reactions

Adverse reactions are classified according to frequency and System Organ Class. Frequency categories are defined according to the following conventions: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1/10000 to <1/1000) and very rare (<1/10,000).

Table 1 lists adverse reactions identified in clinical studies with patients receiving lesinurad 200 mg once daily in combination with allopurinol and those adverse reaction that are established for allopurinol alone.

Table 1 Adverse reactions by System Organ Class and frequency

System Organ Classification	Common	Uncommon	Rare	Very Rare
Infections and infestations	Influenza			Furuncle
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				Angioimmunoblastic T-cell lymphoma
Blood and lymphatic system disorders				Agranulocytosis*, aplastic anaemia*, thrombocytopenia*
Immune system disorders		Hypersensitivity**		
Metabolism and nutrition disorders		Dehydration		Diabetes mellitus, hyperlipidaemia
Psychiatric disorders				Depression

System Organ Classification	Common	Uncommon	Rare	Very Rare
Nervous system disorders	Headache			Coma, paralysis, ataxia, neuropathy, paraesthesia, drowsiness/somnolence, dysgeusia
Eye disorders				Cataract, vision disorders (visual impairment and blurred vision), maculopathy
Ear and labyrinth disorders				Vertigo
Cardiac disorders				Angina pectoris, bradycardia
Vascular disorders				Hypertension
Gastrointestinal disorders	Gastro-oesophageal reflux disease	Nausea, vomiting and diarrhoea		Recurrent haematemesis, steatorrhoea, stomatitis, changed stool frequency
Hepatobiliary disorders		Impaired liver function tests	Hepatitis	
Skin and subcutaneous tissue disorders	Rash			Stevens-Johnson syndrome, toxic epidermal necrolysis, angioedema, medicinal product eruption, alopecia, hair colour changes
Musculoskeletal and connective tissue disorders				Myalgia
Renal and urinary disorders		Renal failure***, renal impairment, nephrolithiasis	Urolithiasis	Haematuria, azotemia
Reproductive system and breast disorders				Male infertility, erectile dysfunction, gynaecomastia
General disorders and administration site conditions				Oedema, general malaise, asthaenia

System Organ Classification	Common	Uncommon	Rare	Very Rare
Investigations	Blood thyroid stimulating hormone increased****, blood creatinine increased			

* Very rare reports have been received of thrombocytopenia, agranulocytosis and aplastic anaemia, particularly in individuals with impaired renal and/or hepatic function

** Photodermatosis, photosensitivity reaction, dermatitis allergic, pruritus and urticaria.

*** Includes the terms: renal failure, renal failure chronic and renal failure acute.

**** 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.

Description of selected adverse reactions

Renal events
Duzallo which contains lesinurad as active substance causes an increase in renal uric acid excretion, which may lead to transient increases in serum creatinine, renal-related adverse reactions and kidney stones (see section 5.1).

Cardiovascular safety
No increased incidences for adjudicated Major Adverse Cardiovascular Events (MACE) were observed in the randomised, double-blind, placebo-controlled combination therapy clinical studies (CLEAR1 and CLEAR2) (see section 5.1).

Hypersensitivity
Rare cases of hypersensitivity (photodermatosis, photosensitivity reaction, dermatitis allergic, pruritus and urticaria) have been reported with lesinurad during the clinical programme. None of these were serious or required hospitalisation.

Immune system disorders
Hypersensitivity reactions may present themselves as fever, skin reactions, chills and arthralgia.
A delayed multi-organ hypersensitivity disorder (known as hypersensitivity syndrome or DRESS) with fever, rashes, vasculitis, lymphadenopathy, pseudo lymphoma, arthralgia, leucopenia, eosinophilia, hepato-splenomegaly, 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, it may be at any time during treatment, Duzallo should be withdrawn immediately and permanently.
Re-challenge should not be undertaken in patients with hypersensitivity syndrome.
When generalised hypersensitivity reactions have occurred, renal and/or hepatic disorder has usually been present particularly when the outcome has been fatal.

Skin reactions
Skin reactions are the most common reactions and may occur at any time during treatment. They may be pruritic, maculopapular, sometimes scaly, sometimes purpuric and rarely exfoliative, such as SJS/TEN. The highest risk for SJS and TEN, or other serious hypersensitivity reactions, is within the first weeks of treatment. Re-challenge should not be undertaken in patients with SJS/TEN.

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 national reporting system listed in Appendix V.

4.9 Overdose

Lesinurad

There is no specific treatment in the event of an overdose, and symptoms of overdose are not established.

Allopurinol

Based on literature and following ingestion of one single dose of 20 g allopurinol symptoms such as nausea, vomiting, diarrhoea and dizziness occurred in one patient. In another patient the intake of 22.5 g allopurinol caused no adverse reactions. A specific antidote is unknown.

If an overdose is suspected, patients should be managed by symptomatic and supportive care including adequate hydration. Particularly in the case of a co-administration with azathioprine or 6-mercaptopurine, absorption-reducing or elimination-increasing measures such as haemodialysis are indicated (haemodialysis may be considered in patients with severe renal or hepatic impairment).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antigout preparations, preparations inhibiting uric acid production.
ATC code: M04AA51

Mechanism of action

Duzallo contains lesinurad and allopurinol, two anti-hyperuricemic active substances with complimentary mechanisms of actions.

Lesinurad is a selective uric acid reabsorption inhibitor that inhibits uric acid transporter URAT1. URAT1 is responsible for the majority of the reabsorption of filtered uric acid from the renal tubular lumen. By inhibiting URAT1, lesinurad increases uric acid excretion and thereby lowers serum uric acid (sUA). Lesinurad also inhibits OAT4, a uric acid transporter involved in diuretic-induced hyperuricaemia.

Lesinurad, when combined with a xanthine oxidase inhibitor, increases uric acid excretion and decreases uric acid production resulting in greater sUA lowering.

Allopurinol is a xanthine-oxidase inhibitor. Allopurinol and its main metabolite oxypurinol lower the level of uric acid in plasma and urine by inhibition of xanthine oxidase, the enzyme catalyzing the oxidation of hypoxanthine to xanthine and xanthine to uric acid. 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. Other metabolites of allopurinol include allopurinol-riboside and oxypurinol-7-riboside.

Clinical efficacy and safety

The efficacy of lesinurad 200 mg once daily was studied in 2 multicentre, randomised, double-blind, placebo-controlled clinical studies in 812 adult patients (11% of these patients were elderly, ≥65 years old) with hyperuricaemia and gout in combination with allopurinol (CLEAR1 and CLEAR2). All

studies were of 12 months duration and patients received prophylaxis for gout flares with colchicine or NSAIDs during the first 5 months of lesinurad treatment.

Duzallo in inadequate responders
CLEAR1 and CLEAR2 enrolled patients with gout who were on a stable dose of allopurinol of at least 300 mg (or 200 mg for moderate renal impairment), had serum uric acid levels greater than 6.5 mg/dL and reported at least 2 gout flares in the previous 12 months. Across both studies, 61% of patients had mild or moderate renal impairment and 19% had tophi at baseline. Patients continued their allopurinol dose and were randomised 1:1:1 to receive lesinurad 200 mg, lesinurad 400 mg, or placebo once daily.

The primary efficacy endpoint in both CLEAR1 and CLEAR2 was the proportion of patients achieving a serum uric acid target level of less than 6 mg/dL by Month 6. In both studies, significantly more patients treated with lesinurad 200 mg in combination with allopurinol ≥ 300 mg/day (≥ 200 mg/day in subjects with moderate renal impairment) achieved the target serum uric acid level of less than 6 mg/dL by Month 6 and by Month 12 compared with patients receiving placebo in combination with allopurinol (see Table 3).

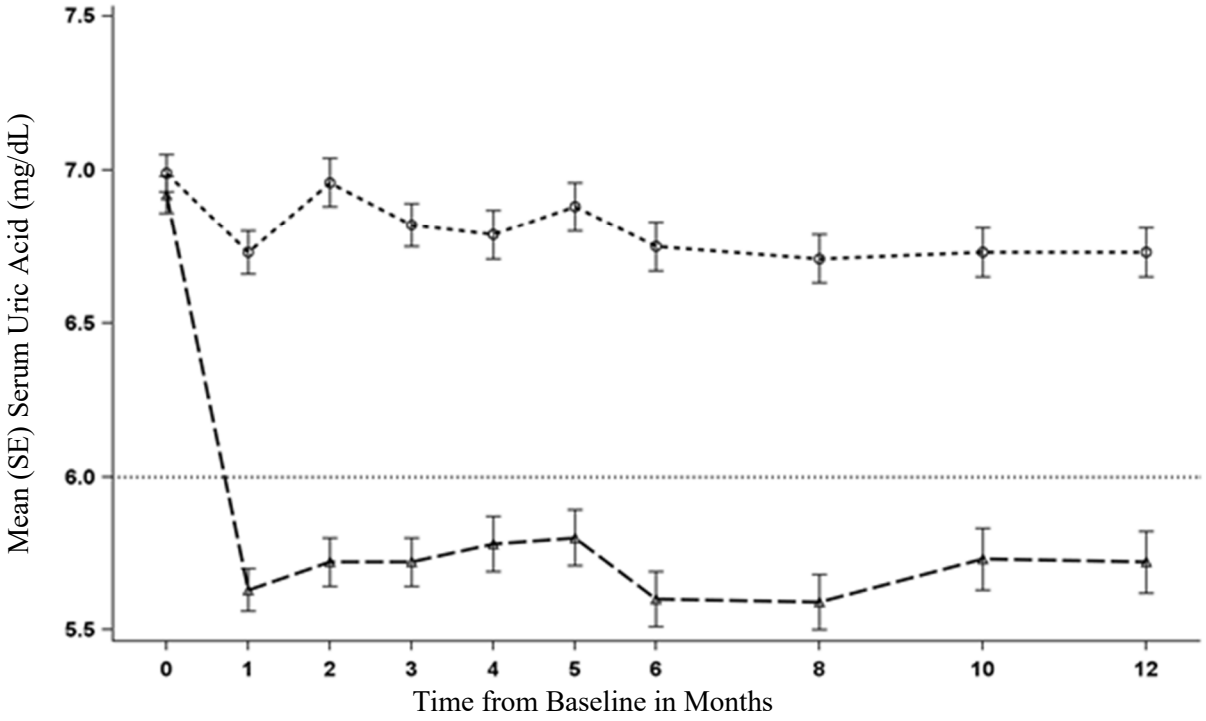
The stability of the sustained response was demonstrated with a greater proportion of patients treated with lesinurad 200 mg in combination with allopurinol achieving the target serum uric acid level at each visit for 3 consecutive months (Months 4, 5 and 6) compared to patients treated with placebo in combination with allopurinol (see Table 3).

Table 3 Proportion of patients who achieved target serum uric acid levels (<6 mg/dL) with lesinurad in combination with allopurinol - Pooled data from CLEAR1 and CLEAR2 studies

	Proportion of patients who met serum uric acid target (<6.0 mg/dL) N (%)		Difference in proportion (95% C.I.)
Timepoint	Placebo + allopurinol N=407	Lesinurad 200 mg + allopurinol N=405	Lesinurad 200 mg vs. placebo
Months 4, 5, 6	48 (12%)	155 (38%)	0.26 (0.21, 0.32)
Month 6	104 (26%)	222 (55%)	0.29 (0.23, 0.36)
Month 12	105 (26%)	203 (50%)	0.24 (0.18, 0.31)

Lesinurad when added to allopurinol caused a reduction of the mean serum uric acid levels, as compared to placebo, which was sustained in the long term in those patients who continued treatment (see Figure 1).

Figure 1 Mean serum uric acid levels in pooled clinical studies with lesinurad in combination with allopurinol in patients with inadequate response (sUA ≥6 mg/dL) to allopurinol alone



Treatment Group: --o-- Placebo + Allopurinol, —Δ— Lesinurad 200 mg + Allopurinol

In each of the studies, a greater proportion of patients treated with lesinurad 200 mg in combination with allopurinol compared with placebo in combination with allopurinol achieved a serum uric acid level of less than 5 mg/dL by Month 6 (CLEAR1: 29% versus 10%; CLEAR2: 35% versus 5%).

Primary end-point in patients with renal impairment
Consistent with the overall population, the proportion of patients with mild to moderate renal impairment (eCrCL 30-89 mL/min) who achieved target serum uric acid levels at Month 6 was 56% for lesinurad 200 mg versus 29% for placebo when added to allopurinol at doses ranging from 200 mg to 900 mg.

Clinical outcomes - gout flares requiring treatment
The rates of gout flare requiring treatment were low and comparable to placebo in the last 6 months of the randomised trials (after gout flare prophylaxis was discontinued) with median scores of zero. In the long-term uncontrolled extension trials, the rates of gout flares requiring treatment further decreased in the 60% of subjects who entered the extension studies and continued treatment with lesinurad 200 mg in combination with allopurinol or febuxostat for up to an additional year of treatment.

Clinical outcomes - concomitant use of thiazides
Consistent serum uric acid lowering was observed in patients who were receiving thiazide diuretics in the placebo-controlled clinical studies in combination with allopurinol.

Clinical outcomes - renal events
In two 12-month placebo-controlled trials of lesinurad in combination with allopurinol versus allopurinol alone (placebo), serum creatinine elevations between 1.5-fold and 2-fold over baseline occurred in 4.4% of patients on lesinurad 200 mg and 2.2% on placebo; serum creatinine elevations 2-fold or greater over baseline occurred in 1.5% of patients on lesinurad 200 mg and 0% on placebo. These serum creatinine elevations generally resolved, most without treatment interruption. Renal-related adverse reactions were reported in patients treated with lesinurad 200 mg (4.9%) compared to

placebo (4.2%), resulting in discontinuation of treatment in 1.0% for both treatment setups (see section 4.4).
The most frequent renal-related adverse reaction was blood creatinine increased (3.7% with lesinurad 200 mg compared to 2.2% with placebo). In patients with moderate renal impairment, the incidence of renal-related adverse reactions was similar across all treatment groups: Lesinurad 200 mg (13.4%) and placebo (12.5%). Serious renal-related adverse reactions, e.g. acute renal failure and renal impairment, were reported in patients treated with placebo (0.2%) and in no patients on lesinurad 200 mg.

Data from long-term extension studies until 52 months revealed a renal safety profile consistent with that observed in the placebo-controlled studies.

Patients with a history of kidney stones were permitted entry into the 12-month studies of lesinurad in combination with allopurinol. In these studies, kidney stone adverse reactions (nephrolithiasis being the most frequent) were reported in patients treated with lesinurad 200 mg (0.5%) and placebo (1.2%).

Clinical outcomes - cardiovascular safety
In the randomised, double-blind, placebo-controlled combination therapy clinical studies, the incidences of patients with adjudicated Major Adverse Cardiovascular Events (MACE; cardiovascular death, non-fatal myocardial infarction or non-fatal stroke) per 100 patient-years of exposure were 0.60 (95% confidence interval (C.I.) 0.15, 2.41) for placebo and 0.61 (95% C.I. 0.15, 2.43) for lesinurad 200 mg, when used in combination with allopurinol (CLEAR1 and CLEAR2). A causal relationship with lesinurad has not been established.
In the same trials, all patients with a MACE treated with lesinurad 200 mg had a history of heart failure, stroke or myocardial infarction. Post-hoc analyses in a subgroup of patients with high cardiovascular risk at baseline (as defined by transient ischemic attack, angina pectoris, heart failure, myocardial infarction, peripheral vascular disease and/or stroke), showed that the incidence of MACE was 0/39 for placebo and 2/43 for lesinurad 200 mg.

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with Duzallo in all subsets of the paediatric population for the treatment and prevention of hyperuricaemia (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

Lesinurad
The absolute bioavailability of lesinurad is approximately 100%. Lesinurad is rapidly absorbed after oral administration. Administration of Duzallo with a high-fat/high-calorie meal did not affect lesinurad AUC while C_{max} was reduced by 46% and Tmax increased from 2 to 4.5 h compared to administration under fasting conditions.
In clinical trials, lesinurad was administered with food, because the serum uric acid lowering was improved under fed conditions (see section 4.2).
Lesinurad is administered as a 50:50 mixture of lesinurad atropisomers. The ratio of atropisomer 1 to atropisomer 2 AUC(0-24) was 44:56 because atropisomer 1 undergoes more extensive metabolism than atropisomer 2, causing atropisomer 1 to have lower plasma exposure than atropisomer 2.

Allopurinol
Allopurinol is rapidly absorbed from the gastrointestinal tract and is reported to have a plasma half-life of about one hour.
Administration of Duzallo with a high-fat/high-calorie meal did not affect allopurinol AUC while C_{max} was reduced by 18% and T_{max} increased from 1.25 to 3 h compared to administration under fasting conditions. Oxypurinol AUC and C_{max} was not affected by food.

Distribution

Lesinurad
Lesinurad is extensively bound to proteins in plasma (greater than 98%), mainly to albumin. Plasma protein binding is not meaningfully altered in patients with renal or hepatic impairment. The mean steady state volume of distribution of lesinurad was approximately 20 L following intravenous dosing. Mean plasma-to-blood ratios of lesinurad AUC and C_{max} were approximately 1.8, indicating that it did not penetrate or partition extensively into red blood cells.

Allopurinol
Allopurinol is negligibly bound by plasma proteins and therefore variations in protein binding are not thought to significantly alter clearance. The apparent volume of distribution of allopurinol is approximately 1.6 litre/kg which, suggests relatively extensive uptake by tissues. Tissue concentrations of allopurinol have not been reported in humans, but it is likely that allopurinol and oxypurinol will be present in the highest concentrations in the liver and intestinal mucosa where xanthine oxidase activity is high.

Biotransformation

Lesinurad
Lesinurad undergoes oxidative metabolism mainly via cytochrome P450 (CYP) 2C9 to intermediate metabolite M3c (not detected *in vivo*) and is subsequently metabolised by microsomal epoxide hydrolase (mEH) to metabolite M4; there is minimal contribution from CYP1A1, CYP2C19, and CYP3A to the metabolism of lesinurad. Atropisomer 1 is extensively metabolised by CYP2C9 whereas atropisomer 2 is minimally metabolised by both CYP2C9 and CYP3A4. Metabolites are not known to contribute to the uric acid lowering effects of lesinurad.

Allopurinol
The main metabolite of allopurinol is oxypurinol. Other metabolites of allopurinol include allopurinol-riboside and oxypurinol-7-riboside.

Elimination

Lesinurad
Renal clearance is 25.6 mL/min (coefficient of variation CV=56%). Lesinurad is highly protein bound and renal clearance is high (as compared to typical human glomerular filtration rate), indicating that active secretion plays an important role in the renal excretion of lesinurad. Within 7 days following single dosing of radiolabelled lesinurad, 63% of administered radioactive dose was recovered in urine and 32% of administered radioactive dose was recovered in faeces. Most of the radioactivity recovered in urine (>60% of dose) occurred in the first 24 hours. Unchanged lesinurad in urine accounted for approximately 30% of the dose. The elimination half-life (t½) of lesinurad was approximately 5 hours following a single dose. Lesinurad does not accumulate following multiple doses.

Allopurinol
Approximately 20% of the ingested allopurinol is excreted in the faeces. Elimination of allopurinol is mainly by metabolic conversion to oxypurinol by xanthine oxidase and aldehyde oxidase, with less than 10% of the unchanged active substance excreted in the urine. Allopurinol has a plasma half-life of about 0.5 to 1.5 hours.
Oxypurinol is a less potent inhibitor of xanthine oxidase than allopurinol, but the plasma half-life of oxypurinol is far more prolonged. Estimates range from 13 to 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 will gradually accumulate oxypurinol until a steady-state plasma oxypurinol concentration is reached. Such patients, taking 300 mg of allopurinol per day will generally have plasma oxypurinol concentrations of 5-10 mg/litre.
Oxypurinol is eliminated unchanged in the urine but has a long elimination half-life because it undergoes tubular reabsorption. Reported values for the elimination half-life range from 13.6 hours to 29 hours. The large discrepancies in these values may be accounted for by variations in study design and/or creatinine clearance in the patients.

Linearity/non-linearity

Following multiple once daily dosing of lesinurad, there was no evidence of time dependent changes in pharmacokinetic properties and dose proportionality was preserved.

In vitro assessment of interactions

Lesinurad is mainly metabolised by CYP2C9 and mEH, and to a lesser extent by CYP1A1, CYP2C19 and CYP3A. *In vitro*, lesinurad is an inhibitor of CYP2C8, but not of CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A4 and mEH. In addition, lesinurad is an *in vitro* inducer of CYP2B6 and CYP3A via constitutive androstane receptor (CAR)/pregnane X receptor (PXR). *In vivo*, lesinurad is neither an inhibitor nor an inducer of CYP2C9 and 2C8, but a mild to moderate inducer of CYP3A. CYP2B6 has not been studied *in vivo*.

Lesinurad is a substrate of OATP1B1, OAT1, OAT3 and OCT1. *In vitro*, lesinurad is an inhibitor of OATP1B1, OAT1, OAT3, OAT4 and OCT1 at clinically relevant plasma concentrations. However, the *in vivo* activity of OATP1B1, OAT1, OAT3 and OCT1 was not affected by lesinurad. Lesinurad is not an *in vitro* inhibitor of P-glycoprotein, BCRP, OATP1B3, MRP2, MRP4, OCT2, MATE1, MATE2-K and BSEP.

Special populations

Renal impairment
Lesinurad
The population pharmacokinetic analysis of clinical data in gout patients treated for up to 12 months estimated increases in lesinurad exposure of approximately 12%, 31% and 65% in patients with mild, moderate, and severe renal impairment, respectively, compared with patients with normal renal function.

Following administration of a single dose of lesinurad to individuals with renal impairment compared to those with normal renal function lesinurad C_{max} and AUC, respectively, were 36% and 30% higher (200 mg) in patients with mild renal impairment (eCrCL 60 to 89 mL/min), 20% and 73% higher (200 mg) and 3% and 50% higher (400 mg) in patients with moderate renal impairment (eCrCL 30 to 59 mL/min), and 13% higher and 113% higher (400 mg) in patients with severe renal impairment (eCrCL <30 mL/min).

Allopurinol
Allopurinol and oxypurinol clearance is greatly reduced in patients with poor renal function resulting in higher plasma levels in chronic therapy. Patients with renal impairment, where creatinine clearance values were between 10 and 20 ml/min, showed plasma oxypurinol 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 (see section 4.2).

Hepatic impairment
Following administration of a single dose of lesinurad at 400 mg in patients with mild (Child-Pugh class A) or moderate (Child-Pugh class B) hepatic impairment, lesinurad C_{max} was comparable and lesinurad AUC was 7% and 33% higher, respectively, compared to individuals with normal hepatic function. There is no clinical experience in patients with severe (Child-Pugh class C) hepatic impairment.

CYP2C9 poor metabolisers
Approximately half of an oral dose of lesinurad is cleared via CYP2C9 metabolism. The effect of CYP2C9 genotype on the pharmacokinetics of lesinurad was studied in 8 healthy subjects and 59 patients with gout following daily dosing of lesinurad ranging from 200 mg to 600 mg in the absence

or presence of a xanthine oxidase inhibitor. At the 400 mg dose, when compared with extensive CYP2C9 metabolisers (CYP2C9 *1/*1 [N=41]), increased lesinurad exposures were observed in intermediate CYP2C9 metabolisers (CYP2C9 *1/*3 [N=4], approximately 22% increase in AUC) and in poor CYP2C9 metabolisers (CYP2C9 *3/*3 [N=1], approximately 111% increase in AUC) accompanied with higher lesinurad renal excretion. However, individual values were well within the range observed in the extensive metaboliser subjects.

Patients who are known or suspected to be CYP2C9 poor metabolisers based on previous history or experience with other CYP2C9 substrates should use Duzallo with caution (see section 4.4).

Other special populations
Based on population pharmacokinetic analysis, age, gender, race and ethnicity do not have a clinically meaningful effect on the pharmacokinetics of lesinurad. Based on pharmacokinetic modelling simulations, patients with moderate renal impairment and reduced CYP2C9 activity (co-administration of a CYP2C9 inhibitor or a CYP2C9 poor metabolizer) are predicted to have an increase in AUC of approximately 200% in comparison to normal renal function and unimpaired CYP2C9 activity.

Pharmacokinetics in elderly patients
The kinetics of allopurinol are not likely to be altered other than due to deterioration in renal function (see section 5.2 renal impairment).

5.3 Preclinical safety data

Lesinurad

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

Allopurinol

In animal studies, long-term use of high allopurinol doses resulted in formation of xanthine precipitates, which led to changes in the urinary tract.

In vitro and *in vivo* studies conducted to date showed no evidence of mutagenic or carcinogenic potential.

One study in mice receiving intraperitoneal doses of 50 or 100 mg/kg on days 10 or 13 of gestation resulted in foetal abnormalities, however in a similar study in rats at 120 mg/kg on day 12 of gestation no abnormalities were observed.
Extensive studies of high oral doses of allopurinol in mice up to 100 mg/kg/day, rats up to 200 mg/kg/day and rabbits up to 150 mg/kg/day during days 8 to 16 of gestation produced no teratogenic effects

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Hydroxypropylcellulose
Microcrystalline cellulose
Lactose monohydrate
Crospovidone
Magnesium stearate

Tablet coat

Hypromellose
Titanium dioxide (E171)
Triacetin
Iron oxide yellow (E172)
Iron oxide red (E172)

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

Opaque (PVC/PVdC/Aluminium) blister.
Pack sizes of 10, 30 or 100 film-coated tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7. MARKETING AUTHORISATION HOLDER

Grünenthal GmbH
Zieglerstraße 6
52078 Aachen
Germany
Tel.: +49-241-569-0

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/18/1300/001
EU/1/18/1300/002
EU/1/18/1300/003
EU/1/18/1300/004
EU/1/18/1300/005
EU/1/18/1300/006

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

Grünenthal GmbH
Zieglerstraße 6
52078 Aachen
Germany

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports**

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder shall submit the first periodic safety update report for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk Management Plan (RMP)**

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON for 10, 30 and 100 film-coated tablets

1. NAME OF THE MEDICINAL PRODUCT

Duzallo 200 mg/200 mg film-coated tablets
allopurinol/lesinurad

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 200 mg allopurinol and 200 mg lesinurad

3. LIST OF EXCIPIENTS

Contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

10 film-coated tablets
30 film-coated tablets
100 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Grünenthal GmbH
Zieglerstraße 6
52078 Aachen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/18/1300/001	30 film-coated tablets
EU/1/18/1300/002	100 film-coated tablets
EU/1/18/1300/005	10 film-coated tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

duzallo 200 mg/200 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

Duzallo 200 mg/200 mg film-coated tablets
allopurinol/lesinurad

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Grünenthal GmbH

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON for 10, 30 and 100 film-coated tablets

1. NAME OF THE MEDICINAL PRODUCT

Duzallo 300 mg/200 mg film-coated tablets
allopurinol/lesinurad

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 300 mg allopurinol and 200 mg lesinurad

3. LIST OF EXCIPIENTS

Contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

10 film-coated tablets
30 film-coated tablets
100 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Grünenthal GmbH
Zieglerstraße 6
52078 Aachen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/18/1300/003	30 film-coated tablets
EU/1/18/1300/004	100 film-coated tablets
EU/1/18/1300/006	10 film-coated tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

duzallo 300 mg/200 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

Duzallo 300 mg/200 mg film-coated tablets
allopurinol/lesinurad

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Grünenthal GmbH

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Duzallo 200 mg / 200 mg film-coated tablets
allopurinol/lesinurad

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Duzallo is and what it is used for

Duzallo contains the active ingredients allopurinol and lesinurad. It is used to treat gout in adult patients in case allopurinol alone is not controlling your gout. Gout is a type of arthritis caused by the build-up of uric acid crystals around the joints. By lowering the amount of uric acid in the blood, Duzallo stops this build-up and may prevent further joint damage.

2. What you need to know before you take Duzallo

Do not take Duzallo if:
- you are allergic to allopurinol, lesinurad or any of the other ingredients of this medicine (listed in section 6)
- you have tumour lysis syndrome – a fast breakdown of cancer cells which can cause high uric acid levels
- you have Lesch-Nyhan syndrome – a rare inherited illness that starts in childhood where there is too much uric acid in the blood
- your kidneys work very poorly or you have end stage kidney disease (when the kidneys no longer work well enough to meet the body's need)
- you have received a kidney transplant
- you are on kidney dialysis.

Warnings and precautions
Talk to your doctor or pharmacist before taking Duzallo if:

- you have or have had heart failure or other heart problems
- your gout gets worse
  Some people may have more gout attacks (sudden or severe pain and swelling in a joint, also called a gout flare) when they start using Duzallo and during the first weeks or months of treatment. If this happens, keep taking Duzallo and talk to your doctor or pharmacist. The medicine is still working to lower uric acid. Over time, your gout attacks will occur less often if you keep taking Duzallo as advised by your doctor. Your doctor may give you other medicines to help prevent or treat the symptoms of gout attacks. and will tell you how long to take these other medicines.
- you have thyroid disorders

Rash and skin symptoms
Serious skin rashes (hypersensitivity syndrome, Stevens-Johnson syndrome, toxic epidermal necrolysis) have occured in patients taking allopurinol. The rash can involve ulcers of the mouth, throat, nose, genitals and conjunctivitis (red and swollen eyes). These serious skin rashes often come after flu-like symptoms such as fever, headache, body ache. The rash may cover large parts of the body with blistering and peeling of the skin. These serious skin reactions can be more common in:

- people of Han Chinese, Thai or Korean origin
- people who have problems with their kidneys and take this medicine and a diuretic (a medicine that increases urine) at the same time

If you develop a rash or any of these skin symptoms, **stop taking this medicine and contact your doctor immediately.**

Kidney problems
Duzallo may cause serious kidney problems (see section 4). Your doctor will check how well your kidneys are working before starting with Duzallo and during the Duzallo treatment. Your doctor may stop Duzallo if your blood tests show changes in how your kidneys are working or if you have symptoms of kidney problems. Your doctor may tell you to restart treatment with Duzallo when your kidneys improve.

Children and adolescents
Duzallo is not recommended for use in children and adolescents below 18 years of age.

Other medicines and Duzallo
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This is because Duzallo can affect the way some other medicines work. Also some other medicines can affect the way Duzallo works.

Tell your doctor or pharmacist if you are taking any of the following:

- acetylsalicylic acid – to relieve fever and pain at doses above 325 mg per day
- medicines to treat high blood pressure such as ACE inhibitors, water tablets (diuretics - medicines that increase the passing of urine) and calcium channel blockers e.g. amlodipine
- medicines to treat high cholesterol levels, e.g. simvastatin
- fluconazole – to treat fungal infections
- amiodarone – to treat heart rhythm problems
- valproic acid, valpromide, phenytoin or carbamazepine – to prevent fits (seizures), mood disorders and prevent migraines
- bupropion – for treating depression or to help stop smoking
- sildenafil – to treat erectile problems in men
- contraceptives – used to prevent pregnancy, including oral contraception (such as ‘the pill’), injections, patches and implants
- coumarin anticoagulants – to prevent and treat blood clots
- antibiotics like ampicillin or amoxicillin

- medicines to treat AIDS/HIV e.g. didanosine, efavirenz
- chlorpropamide, used for the treatment of diabetes
- theophylline, used for the treatment of breathing problems
- medicines used to reduce your immune response (immunosuppressants) e.g. ciclosporin, azathioprine
- vidarabine, used to treat herpes or chickenpox
- cytostatics (e.g. cyclophosphamide, doxorubicin, bleomycin, procarbazine, alkylating agents, mercaptopurine), used to treat cancer or rheumatic diseases
- aluminium hydroxide, used to treat heartburn and acid indigestion (you should leave an interval of at least 3 hours between taking the two medicines)

If any of the above apply to you (or you are not sure), talk to your doctor or pharmacist before taking Duzallo.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. It is preferable to avoid Duzallo when you are pregnant. Ask your doctor for advice.

Duzallo is not recommended during breastfeeding, as allopurinol passes into the breast milk.

Hormonal contraception (this includes oral, injectable, transdermal, and implantable forms) might not be reliable when taking Duzallo at the same time. Alternative methods of contraception should be considered. Ask your doctor for advice.

Driving and using machines
Duzallo may make you feel sleepy, dizzy or unsteady. Do not drive or operate machinery if you are affected.

Duzallo contains lactose
Duzallo tablets contain lactose (a type of sugar). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take Duzallo

Always take this medicine exactly as your doctor or pharmacist has told you. The choice of the dose strength of Duzallo depends on the allopurinol dose already taken as individual tablet(s) and will be decided by your doctor. Your doctor will tell you if additional doses of allopurinol are still necessary.

Duzallo is a tablet to be taken by mouth. The recommended dose is 1 tablet once a day in the morning.

Do not take more than 1 tablet per day.

Swallow the tablet whole with water and after breakfast in the morning. Drink plenty of water during the day to reduce the risk of kidney stones.

If you take more Duzallo than you should
If you take more of this medicine than you should, talk to a doctor or go to the nearest hospital immediately. You may feel sick or be sick, feel dizzy or have diarrhoea.

If you forget to take Duzallo
Do not take a double dose to make up for a forgotten dose. Wait and take your next dose of Duzallo the next morning.

If you stop taking Duzallo
Do not stop taking Duzallo without talking to your doctor first even if you feel better.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects

Kidney problems
If you notice any of the following side effects, ***stop taking Duzallo and see a doctor immediately*** as these may be signs of a problem with your kidneys – you may need urgent medical treatment.
The signs may include:
Uncommon – may affect up to 1 in 100 people
- pain in your side (below your ribs and above your hipbone),
- feeling sick (nausea),
- being sick (vomiting),
- changes in urination or difficulty urinating,
- feeling tired or unwell or loss of appetite.

Hypersensitivity
If you have a hypersensitivity (allergic) reaction, ***stop taking Duzallo and see a doctor immediately***.
The signs may include:
Uncommon - may affect less than 1 in 100 people
- flaking skin, boils or sore lips and mouth
- very rarely signs may include sudden wheeziness, fluttering or tightness in the chest and collapse.
- fever, skin rash, joint pain, and abnormalities in blood and liver function tests (these may be signs of a multi-organ sensitivity disorder)

Rare – may affect up to 1 in 1000 people
- potentially life-threatening skin rashes (Stevens-Johnson syndrome, toxic epidermal necrolysis) appearing initially as reddish target-like spots or circular patches often with central blisters on the trunk. Additional signs to look for include:
    - ulcers of the mouth, throat, nose, genitals, conjunctivitis (red and swollen eyes)
    - widespread blisters or peeling of the skin
    - flu-like symptoms

Very rare - may affect up to 1 in 10,000 people
- swelling of the lips, tongue, face, throat, difficulty swallowing or breathing or red-raised itchy skin/hives (angioedema)
- Duzallo may affect your blood, which can cause bruising more easily than usual, or you may get a sore throat or other signs of an infection. These effects usually occur in people with liver or kidney problems (agranulocytosis).

Other side effects

Common – may affect up to 1 in 10 people
- increased level of thyroid stimulating hormone in the blood,
- flu,
- headache,
- blood tests showing increased creatinine (which may be a sign of kidney problems),
- heartburn (acid reflux),
- skin rash.

Uncommon – may affect up to 1 in 100 people
- kidney stones,
- kidney stop working properly,
- skin reactions, including redness, itchy skin, lumpy rash (hives) and skin rash on exposure to sunshine,
- dehydration (loss of too much fluid from your body),
- feeling sick (nausea) or being sick (vomiting),
- diarrhoea,
- abnormal liver tests.

Rare – may affect up to 1 in 1000 people
- disorder of the liver (hepatitis).

Very rare – may affect up to 1 in 10,000 people
- chest pain, slow heartbeat, high blood pressure or a slow pulse,
- vomiting blood (recurrent hematemesis), presence of excess fat in the stool (steatorrhea),
- inflammation of the mucous membranes of the mouth (stomatitis), changed stool frequency (changed bowel motions),
- hair loss or discoloration,
- abnormal glucose metabolism (diabetes; your doctor may wish to measure the level of sugar in your blood to check if this is happening),
- high levels of cholesterol in your blood (hyperlipidaemia),
- depression,
- coma,
- weakness, numbness, unsteadiness on your feet, unable to move muscles (paralysis) or loss of consciousness,
- not able to control muscle movements (ataxia),
- sensation of tingling, tickling, pricking or burning of skin (paraesthesia),
- headache, dizziness, drowsiness or disturbance of your vision,
- cloudiness of the eye (cataract),
- a change in taste,
- blood in your urine (haematuria),
- male infertility or erectile dysfunction,
- enlargement of the breasts, in men as well as in women,
- build-up of fluid leading to swelling (oedema) particularly of your ankles,
- muscle aches,
- painful skin boil,
- damage to the nerves which can cause numbness, pain and weakness.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Duzallo

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton or blister foil after “EXP”. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Duzallo contains
The active substances are allopurinol and lesinurad.
Each Duzallo 200 mg / 200 mg film-coated tablet contains 200 mg of allopurinol and 200 mg of lesinurad.

The other ingredients are:
- tablet core: hydroxypropylcellulose, microcrystalline cellulose, lactose monohydrate, crospovidone, magnesium stearate
- film-coating: hypromellose, titanium dioxide (E171), triacetin, iron oxide yellow (E172), iron oxide red (E172)

What Duzallo looks like and contents of the pack
Duzallo 200 mg/200 mg film-coated tablets are pale pink oblong tablets and engraved with “LES200” and “ALO200” on one side.

Duzallo 200 mg / 200 mg tablets are available in blister packs of 10, 30 and 100 tablets.

Not all pack sizes may be marketed.

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Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

Package leaflet: Information for the patient

Duzallo 300 mg / 200 mg film-coated tablets
allopurinol/lesinurad

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Duzallo is and what it is used for

Duzallo contains the active ingredients allopurinol and lesinurad. It is used to treat gout in adult patients in case allopurinol alone is not controlling your gout. Gout is a type of arthritis caused by the build-up of uric acid crystals around the joints. By lowering the amount of uric acid in the blood, Duzallo stops this build-up and may prevent further joint damage.

2. What you need to know before you take Duzallo

Do not take Duzallo if:
- you are allergic to allopurinol, lesinurad or any of the other ingredients of this medicine (listed in section 6)
- you have tumour lysis syndrome – a fast breakdown of cancer cells which can cause high uric acid levels
- you have Lesch-Nyhan syndrome – a rare inherited illness that starts in childhood where there is too much uric acid in the blood
- your kidneys work very poorly or you have end stage kidney disease (when the kidneys no longer work well enough to meet the body's need)
- you have received a kidney transplant
- you are on kidney dialysis.

Warnings and precautions
Talk to your doctor or pharmacist before taking Duzallo if:

- you have or have had heart failure or other heart problems
- your gout gets worse
  Some people may have more gout attacks (sudden or severe pain and swelling in a joint, also called a gout flare) when they start using Duzallo and during the first weeks or months of treatment. If this happens, keep taking Duzallo and talk to your doctor or pharmacist. The medicine is still working to lower uric acid. Over time, your gout attacks will occur less often if you keep taking Duzallo as advised by your doctor. Your doctor may give you other medicines to help prevent or treat the symptoms of gout attacks. and will tell you how long to take these other medicines.
- you have thyroid disorders

Rash and skin symptoms
Serious skin rashes (hypersensitivity syndrome, Stevens-Johnson syndrome, toxic epidermal necrolysis) have occured in patients taking allopurinol. The rash can involve ulcers of the mouth, throat, nose, genitals and conjunctivitis (red and swollen eyes). These serious skin rashes often come after flu-like symptoms such as fever, headache, body ache. The rash may cover large parts of the body with blistering and peeling of the skin. These serious skin reactions can be more common in:

- people of Han Chinese, Thai or Korean origin
- people who have problems with their kidneys and take this medicine and a diuretic (a medicine that increases urine) at the same time

If you develop a rash or any of these skin symptoms, **stop taking this medicine and contact your doctor immediately.**

Kidney problems
Duzallo may cause serious kidney problems (see section 4). Your doctor will check how well your kidneys are working before starting with Duzallo and during the Duzallo treatment. Your doctor may stop Duzallo if your blood tests show changes in how your kidneys are working or if you have symptoms of kidney problems. Your doctor may tell you to restart treatment with Duzallo when your kidneys improve.

Children and adolescents
Duzallo is not recommended for use in children and adolescents below 18 years of age.

Other medicines and Duzallo
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This is because Duzallo can affect the way some other medicines work. Also some other medicines can affect the way Duzallo works.

Tell your doctor or pharmacist if you are taking any of the following:

- acetylsalicylic acid – to relieve fever and pain at doses above 325 mg per day
- medicines to treat high blood pressure such as ACE inhibitors, water tablets (diuretics - medicines that increase the passing of urine) and calcium channel blockers e.g. amlodipine
- medicines to treat high cholesterol levels, e.g. simvastatin
- fluconazole – to treat fungal infections
- amiodarone – to treat heart rhythm problems
- valproic acid, valpromide, phenytoin or carbamazepine – to prevent fits (seizures), mood disorders and prevent migraines
- bupropion – for treating depression or to help stop smoking
- sildenafil – to treat erectile problems in men
- contraceptives – used to prevent pregnancy, including oral contraception (such as ‘the pill’), injections, patches and implants
- coumarin anticoagulants – to prevent and treat blood clots
- antibiotics like ampicillin or amoxicillin

- medicines to treat AIDS/HIV e.g. didanosine, efavirenz
- chlorpropamide, used for the treatment of diabetes
- theophylline, used for the treatment of breathing problems
- medicines used to reduce your immune response (immunosuppressants) e.g. ciclosporin, azathioprine
- vidarabine, used to treat herpes or chickenpox
- cytostatics (e.g. cyclophosphamide, doxorubicin, bleomycin, procarbazine, alkylating agents, mercaptopurine), used to treat cancer or rheumatic diseases
- aluminium hydroxide, used to treat heartburn and acid indigestion (you should leave an interval of at least 3 hours between taking the two medicines)

If any of the above apply to you (or you are not sure), talk to your doctor or pharmacist before taking Duzallo.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. It is preferable to avoid Duzallo when you are pregnant. Ask your doctor for advice.

Duzallo is not recommended during breastfeeding, as allopurinol passes into the breast milk.

Hormonal contraception (this includes oral, injectable, transdermal, and implantable forms) might not be reliable when taking Duzallo at the same time. Alternative methods of contraception should be considered. Ask your doctor for advice.

Driving and using machines
Duzallo may make you feel sleepy, dizzy or unsteady. Do not drive or operate machinery if you are affected.

Duzallo contains lactose
Duzallo tablets contain lactose (a type of sugar). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take Duzallo

Always take this medicine exactly as your doctor or pharmacist has told you. The choice of the dose strength of Duzallo depends on the allopurinol dose already taken as individual tablet(s) and will be decided by your doctor. Your doctor will tell you if additional doses of allopurinol are still necessary.

Duzallo is a tablet to be taken by mouth. The recommended dose is 1 tablet once a day in the morning.

Do not take more than 1 tablet per day.

Swallow the tablet whole with water and after breakfast in the morning. Drink plenty of water during the day to reduce the risk of kidney stones.

If you take more Duzallo than you should
If you take more of this medicine than you should, talk to a doctor or go to the nearest hospital immediately. You may feel sick or be sick, feel dizzy or have diarrhoea.

If you forget to take Duzallo
Do not take a double dose to make up for a forgotten dose. Wait and take your next dose of Duzallo the next morning.

If you stop taking Duzallo
Do not stop taking Duzallo without talking to your doctor first even if you feel better.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects

Kidney problems
If you notice any of the following side effects, ***stop taking Duzallo and see a doctor immediately*** as these may be signs of a problem with your kidneys – you may need urgent medical treatment.
The signs may include:
Uncommon – may affect up to 1 in 100 people
- pain in your side (below your ribs and above your hipbone),
- feeling sick (nausea),
- being sick (vomiting),
- changes in urination or difficulty urinating,
- feeling tired or unwell or loss of appetite.

Hypersensitivity
If you have a hypersensitivity (allergic) reaction, ***stop taking Duzallo and see a doctor immediately***.
The signs may include:
Uncommon - may affect less than 1 in 100 people
- flaking skin, boils or sore lips and mouth
- very rarely signs may include sudden wheeziness, fluttering or tightness in the chest and collapse.
- fever, skin rash, joint pain, and abnormalities in blood and liver function tests (these may be signs of a multi-organ sensitivity disorder)

Rare – may affect up to 1 in 1000 people
- potentially life-threatening skin rashes (Stevens-Johnson syndrome, toxic epidermal necrolysis) appearing initially as reddish target-like spots or circular patches often with central blisters on the trunk. Additional signs to look for include:
    - ulcers of the mouth, throat, nose, genitals, conjunctivitis (red and swollen eyes)
    - widespread blisters or peeling of the skin
    - flu-like symptoms

Very rare - may affect up to 1 in 10,000 people
- swelling of the lips, tongue, face, throat, difficulty swallowing or breathing or red-raised itchy skin/hives (angioedema)
- Duzallo may affect your blood, which can cause bruising more easily than usual, or you may get a sore throat or other signs of an infection. These effects usually occur in people with liver or kidney problems (agranulocytosis).

Other side effects

Common – may affect up to 1 in 10 people
- increased level of thyroid stimulating hormone in the blood,
- flu,
- headache,
- blood tests showing increased creatinine (which may be a sign of kidney problems),
- heartburn (acid reflux),
- skin rash.

Uncommon – may affect up to 1 in 100 people
- kidney stones,
- kidney stop working properly,
- skin reactions, including redness, itchy skin, lumpy rash (hives) and skin rash on exposure to sunshine,
- dehydration (loss of too much fluid from your body),
- feeling sick (nausea) or being sick (vomiting),
- diarrhoea,
- abnormal liver tests.

Rare – may affect up to 1 in 1000 people
- disorder of the liver (hepatitis).

Very rare – may affect up to 1 in 10,000 people
- chest pain, slow heartbeat, high blood pressure or a slow pulse,
- vomiting blood (recurrent hematemesis), presence of excess fat in the stool (steatorrhea),
- inflammation of the mucous membranes of the mouth (stomatitis), changed stool frequency (changed bowel motions),
- hair loss or discoloration,
- abnormal glucose metabolism (diabetes; your doctor may wish to measure the level of sugar in your blood to check if this is happening),
- high levels of cholesterol in your blood (hyperlipidaemia),
- depression,
- coma,
- weakness, numbness, unsteadiness on your feet, unable to move muscles (paralysis) or loss of consciousness,
- not able to control muscle movements (ataxia),
- sensation of tingling, tickling, pricking or burning of skin (paraesthesia),
- headache, dizziness, drowsiness or disturbance of your vision,
- cloudiness of the eye (cataract),
- a change in taste,
- blood in your urine (haematuria),
- male infertility or erectile dysfunction,
- enlargement of the breasts, in men as well as in women,
- build-up of fluid leading to swelling (oedema) particularly of your ankles,
- muscle aches,
- painful skin boil,
- damage to the nerves which can cause numbness, pain and weakness.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Duzallo

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton or blister foil after “EXP”. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Duzallo contains
The active substances are allopurinol and lesinurad.
Each Duzallo 300 mg / 200 mg film-coated tablet contains 300 mg of allopurinol and 200 mg of lesinurad.

The other ingredients are:
- tablet core: hydroxypropylcellulose, microcrystalline cellulose, lactose monohydrate, crospovidone, magnesium stearate
- film-coating: hypromellose, titanium dioxide (E171), triacetin, iron oxide yellow (E172), iron oxide red (E172)

What Duzallo looks like and contents of the pack
Duzallo 300 mg/200 mg film-coated tablets are orange and slightly brownish oblong tablets and engraved with “LES200” and “ALO300” on one side.

Duzallo 300 mg / 200 mg tablets are available in blister packs of 10, 30 and 100 tablets.

Not all pack sizes may be marketed.

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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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