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

Zurampic 200 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 200 mg of lesinurad.

Excipient with known effect: Each tablet contains 52.92 mg of lactose (as monohydrate).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet (tablet).

Oval, 5.7 x 12.9 mm, blue tablets.

Tablets are engraved with “LES200” on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Zurampic, in combination with a xanthine oxidase inhibitor, is indicated in adults for the adjunctive treatment of hyperuricaemia in gout patients (with or without tophi) who have not achieved target serum uric acid levels with an adequate dose of a xanthine oxidase inhibitor alone.

4.2 Posology and method of administration

Posology

The recommended dose of Zurampic is 200 mg once daily in the morning. This is also the maximum dose (see section 4.4).

Zurampic tablets must be co-administered at the same time as the morning dose of a xanthine oxidase inhibitor, i.e. allopurinol or febuxostat. The recommended minimum dose of allopurinol is 300 mg, or 200 mg for patients with moderate renal impairment (creatinine clearance [CrCL] of 30-59 mL/min). If treatment with the xanthine oxidase inhibitor is interrupted, Zurampic dosing must also be interrupted.

Patients should be informed that failure to follow these instructions may increase the risk of renal events (see section 4.4).

Patients should be instructed to stay well hydrated (e.g. 2 litres of liquid per day).

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 may be performed as early as 4 weeks after initiating Zurampic treatment.

Gout flare prophylaxis with colchicine or a nonsteroidal anti-inflammatory drug (NSAID) is recommended for at least 5 months when starting therapy (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 (≥75 years) is limited (see section 4.4).

Renal impairment
Zurampic must not be initiated in patients with severe renal impairment (CrCL less than 30 mL/min), with end-stage renal disease or in patients on dialysis (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). Zurampic should not be initiated in kidney transplant recipients.

No dose adjustment is necessary in patients with mild or moderate renal impairment (CrCL of 30-89 mL/min) (see sections 4.8, 5.1 and 5.2). Zurampic should be used with caution in patients with a CrCL of 30 to less than 45 mL/min (see section 4.4).

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). Zurampic has not been studied in patients with severe hepatic impairment; therefore, dose recommendations cannot be given.

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

Method of administration

Oral use.

Zurampic should be taken in the morning with food and water.

4.3 Contraindications

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

Patients with 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

Renal events
Treatment with lesinurad 200 mg in combination with a xanthine oxidase inhibitor 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 Zurampic (see section 4.8). A higher incidence of serum creatinine elevations and renal-related adverse reactions including serious adverse reactions was observed with Zurampic 400 mg when given alone or in combination with a xanthine oxidase inhibitor, with the highest incidence when Zurampic was given as monotherapy. Zurampic should not be used as monotherapy or at doses above the recommended dose.

Experience with Zurampic in patients with an estimated CrCL (eCrCL) less than 45 mL/min is limited; therefore, Zurampic should be used with caution in patients with a CrCL from 30 mL/min to less than 45 mL/min.

Renal function should be evaluated prior to initiation of Zurampic 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 medications. Patients with serum creatinine elevations to greater than 1.5 times the pre-treatment value should be closely monitored. Zurampic should be interrupted if serum creatinine is elevated to greater 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. Zurampic should not be restarted without another explanation for the serum creatinine abnormalities.

Pre-existing cardiovascular disease
Zurampic 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. 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).

Acute gouty attacks (gout flares)
Gout flares may occur after initiation of therapy with Zurampic. This is due to reduction in serum uric acid levels resulting in mobilisation of urate from tissue deposits. Gout flare prophylaxis with colchicine or an NSAID is recommended for at least 5 months when starting Zurampic therapy (see section 4.2).

Zurampic 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 Zurampic decreases the frequency of gout flares.

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

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 Zurampic. Additional monitoring of lipids and blood pressure is recommended in patients using sensitive CYP3A substrate lipid lowering medicines (such as lovastatin or simvastatin) or antihypertensive medicines (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 Zurampic is co-administered. Female patients of childbearing age should practice additional methods of contraception and not rely on hormonal contraception alone when taking Zurampic (see sections 4.5 and 4.6).

Very elderly (≥75 years)
Therapeutic experience in patients 75 years and older is limited. Caution should be used when treating these patients with Zurampic.

Secondary hyperuricaemia
No studies have been conducted in patients with secondary hyperuricaemia (including organ transplant recipients).

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

4.5 Interaction with other medicinal products and other forms of interaction

Pharmacodynamic interactions

Salicylates
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 Zurampic. 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. There are no restrictions for doses of salicylates of 325 mg or less per day (i.e. for cardiovascular protection).

Thiazide diuretics
Consistent serum uric acid lowering was observed in patients who were receiving thiazide diuretics in the placebo-controlled clinical studies in combination with allopurinol or febuxostat.

Pharmacokinetic interactions

Effect of lesinurad on other medicinal products

CYP3A substrates
Mild to moderate induction of CYP3A by lesinurad may reduce plasma exposures of co-administered medicines that are sensitive substrates of CYP3A. In interaction studies conducted in healthy subjects with Zurampic 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 medicines that were CYP3A substrates required concomitant medicinal product change when treated with Zurampic 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).

Warfarin
In an interaction study conducted in healthy subjects with multiple doses of Zurampic 400 mg and single dose warfarin (25 mg), lesinurad led to a decrease in exposure of *R*-warfarin (the less active enantiomer) and had no effect on the exposure of *S*-warfarin (the more active enantiomer). Additionally, lesinurad led to a 6-8% decrease in International Normalised Ratio (INR) and Prothrombin Time (PT). The standard INR monitoring schedule should be applied, and no further actions are required.

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 Zurampic.

Based on interaction studies in healthy subjects or gout patients, Zurampic does not have clinically significant interactions with NSAIDs (naproxen and indomethacin), colchicine, repaglinide, tolbutamide, febuxostat or allopurinol. Zurampic slightly decreased exposure of oxypurinol (a URAT1 substrate), the major metabolite of allopurinol; however, the uric acid-lowering effect of the combination with allopurinol was significantly greater than for either substance alone.

Effect of other medicinal products on lesinurad

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 Zurampic 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 Zurampic is co-administered with a CYP2C9 inducer.

Rifampin
Rifampin, an inhibitor of OATPs and an inducer of CYP2C9, decreased lesinurad exposure and slightly reduced the amount of lesinurad excreted unchanged in urine with no clinically relevant effect. The lack of an observed interaction could be due to the combination of the induction of CYP2C9 and inhibition of OATP1B1 and 1B3.

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

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no data from the use of lesinurad in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

As a precautionary measure, it is preferable to avoid the use of Zurampic during pregnancy. Female patients of childbearing potential should not rely on hormonal contraception alone when taking Zurampic (see sections 4.4 and 4.5).

Breast-feeding
Available pharmacodynamic/toxicological data in rats have shown excretion of lesinurad in milk. A risk to the newborns/infants cannot be excluded. Zurampic should not be used during breast-feeding.

Fertility
The effect of lesinurad on fertility in humans has not been studied. In rats, there was no effect on mating or fertility with lesinurad (see section 5.3).

4.7 Effects on ability to drive and use machines

Lesinurad has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The safety of Zurampic 200 mg was evaluated in the Phase 3 combination therapy clinical trials (including extension studies). The most commonly reported adverse reactions during treatment with Zurampic 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 Zurampic therapy. The most common adverse reaction leading to discontinuation of Zurampic was blood creatinine increased (0.8%).

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 Zurampic 200 mg once daily in combination with a xanthine oxidase inhibitor, allopurinol or febuxostat.

Table 1 Adverse reactions by System Organ Class and frequency

System Organ Classification	Common	Uncommon	Rare
Infections and infestations	Influenza		
Immune system disorders			Hypersensitivity*
Metabolism and nutrition disorders		Dehydration	
Nervous system disorders	Headache		
Gastrointestinal disorders	Gastro-oesophageal reflux disease		
Renal and urinary disorders		Renal failure** Renal impairment Nephrolithiasis	
Investigations	Blood creatinine increased		

*Photodermatosis, photosensitivity reaction, dermatitis allergic, pruritus and urticaria.
**Includes the preferred terms: renal failure, renal failure chronic and renal failure acute.

Description of selected adverse reactions

Renal events

Zurampic causes an increase in renal uric acid excretion, which may lead to transient increases in serum creatinine, renal-related adverse reactions and kidney stones. Although other doses have been studied, the recommended dose of Zurampic is 200 mg once daily in combination with a xanthine oxidase inhibitor.

In three 12-month placebo-controlled trials of Zurampic in combination with a xanthine oxidase inhibitor versus a xanthine oxidase inhibitor alone (placebo), serum creatinine elevations between 1.5-fold and 2-fold over baseline occurred in 3.9% of patients on Zurampic 200 mg, 10.0% of patients on Zurampic 400 mg and 2.3% on placebo; serum creatinine elevations 2-fold or greater over baseline

occurred in 1.8% of patients on Zurampic 200 mg, 6.7% of patients on Zurampic 400 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 Zurampic 200 mg (5.7%) and Zurampic 400 mg (11.8%) compared to placebo (4.5%), resulting in discontinuation of treatment in 1.2%, 3.3% and 1%, respectively (see section 4.4). The most frequent renal-related adverse reaction was blood creatinine increased (4.3% with Zurampic 200 mg and 7.8% with Zurampic 400 mg compared to 2.3% with placebo). In patients with moderate renal impairment, the incidence of renal-related adverse reactions was similar across all treatment groups: Zurampic 200 mg (12.7%), Zurampic 400 mg (16.3%) and placebo (13.3%). Serious renal-related adverse reactions, e.g. acute renal failure and renal impairment, were reported in patients treated with lesinurad 400 mg (1%) and placebo (0.4%) and in no patients on lesinurad 200 mg. Including the combination long-term extension studies, the incidences of serious renal-related adverse reactions (including acute renal failure) per 100 patient-years of exposure were 0.4 and 1.4 for Zurampic 200 mg and Zurampic 400 mg in combination with a xanthine oxidase inhibitor, respectively (see sections 4.2 and 4.4). Data from the long-term extension studies until 24 months revealed a renal safety profile consistent with that observed in the placebo-controlled studies.

In a 6-month double-blind, placebo-controlled monotherapy study of Zurampic, renal-related adverse reactions and serious renal-related adverse reactions (including acute renal failure) were reported in 17.8% and 4.7% of patients respectively, receiving Zurampic 400 mg alone and in no patients receiving placebo (see sections 4.2 and 4.4). Among serious renal-related adverse reactions: renal failure, renal failure acute and renal impairment were reported in 1.9%, 1.9% and 0.9% respectively, of patients receiving lesinurad 400 mg monotherapy and in no patients receiving placebo. Since the incidence of severe renal-related adverse events was increased with the monotherapy as compared to the combination therapy with a xanthine oxidase inhibitor, Zurampic should not be used as monotherapy (see sections 4.2 and 5.1).

Patients with a history of kidney stones were permitted entry into the 12-month studies of Zurampic in combination with a xanthine oxidase inhibitor. In these studies, kidney stone adverse reactions (nephrolithiasis being the most frequent) were reported in patients treated with Zurampic 200 mg (0.6%), Zurampic 400 mg (2.5%) and placebo (1.7%).

Cardiovascular safety
In the randomised, double-blind, placebo-controlled combination therapy clinical studies, the incidences of patients with adjudicated Major Adverse Cardiovascular Events (CV death, non-fatal myocardial infarction or non-fatal stroke) per 100 patient-years of exposure were: 0.71 (95% CI 0.23, 2.21) for placebo, 0.96 (95% CI 0.36, 2.57) for Zurampic 200 mg, and 1.94 (95% CI 0.97, 3.87) for Zurampic 400 mg, when used in combination with a xanthine oxidase inhibitor. A causal relationship with Zurampic has not been established. All patients with a Major Adverse Cardiovascular Event treated with Zurampic 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 Major Adverse Cardiovascular Events was 1/52 for placebo and 4/53 for Zurampic 200 mg, when used in combination with a xanthine oxidase inhibitor.

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.

<u>Other special populations</u>

Patients with renal impairment
No overall differences in safety of Zurampic were observed in patients with mild or moderate renal impairment (eCrCL of 30-89 mL/min) compared to patients with normal renal function (see sections 4.2 and 5.2).

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

There is no specific treatment in the event of an overdose, and symptoms of overdose are not established. In case of overdose, patients should be managed by symptomatic and supportive care including adequate hydration.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antigout preparations, preparations increasing uric acid excretion
ATC code: M04AB05

Mechanism of action
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. Lesinurad should only be used in combination with a xanthine oxidase inhibitor because combination use reduces the amount of uric acid available for excretion and decreases the risk of renal-related events.

Pharmacodynamic effects
Effects on serum uric acid and urinary excretion of uric acid
In healthy subjects, lesinurad 200 mg lowered sUA levels and increased renal clearance and fractional excretion of uric acid. Mean sUA reductions following Zurampic 200 mg administration alone were approximately 46% and 26% at 6 hours and 24 hours post-dose, respectively. When Zurampic 200 mg was added to a xanthine oxidase inhibitor (i.e. febuxostat), additional 25% and 19% of sUA reductions were observed at 6 hours and 24 hours post-dose, respectively.

Effect on cardiac repolarisation
Lesinurad at doses up to 1,600 mg did not demonstrate an effect on ECG parameters (including QTc interval) in healthy subjects.

Clinical efficacy and safety
The efficacy of Zurampic 200 mg and 400 mg once daily was studied in 3 multicentre, randomised, double-blind, placebo-controlled clinical studies in 1,537 adult patients (13% of these patients were elderly, ≥65 years old) with hyperuricaemia and gout in combination with a xanthine oxidase inhibitor, allopurinol (CLEAR1 and CLEAR2) or febuxostat (CRYSTAL). 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.

Based on these studies, Zurampic is only recommended at a dose of 200 mg once daily in combination with a xanthine oxidase inhibitor (see sections 4.2 and 4.4).

Zurampic as add-on to allopurinol 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 Zurampic 200 mg, Zurampic 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 Zurampic 200 mg in combination with allopurinol 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 2).

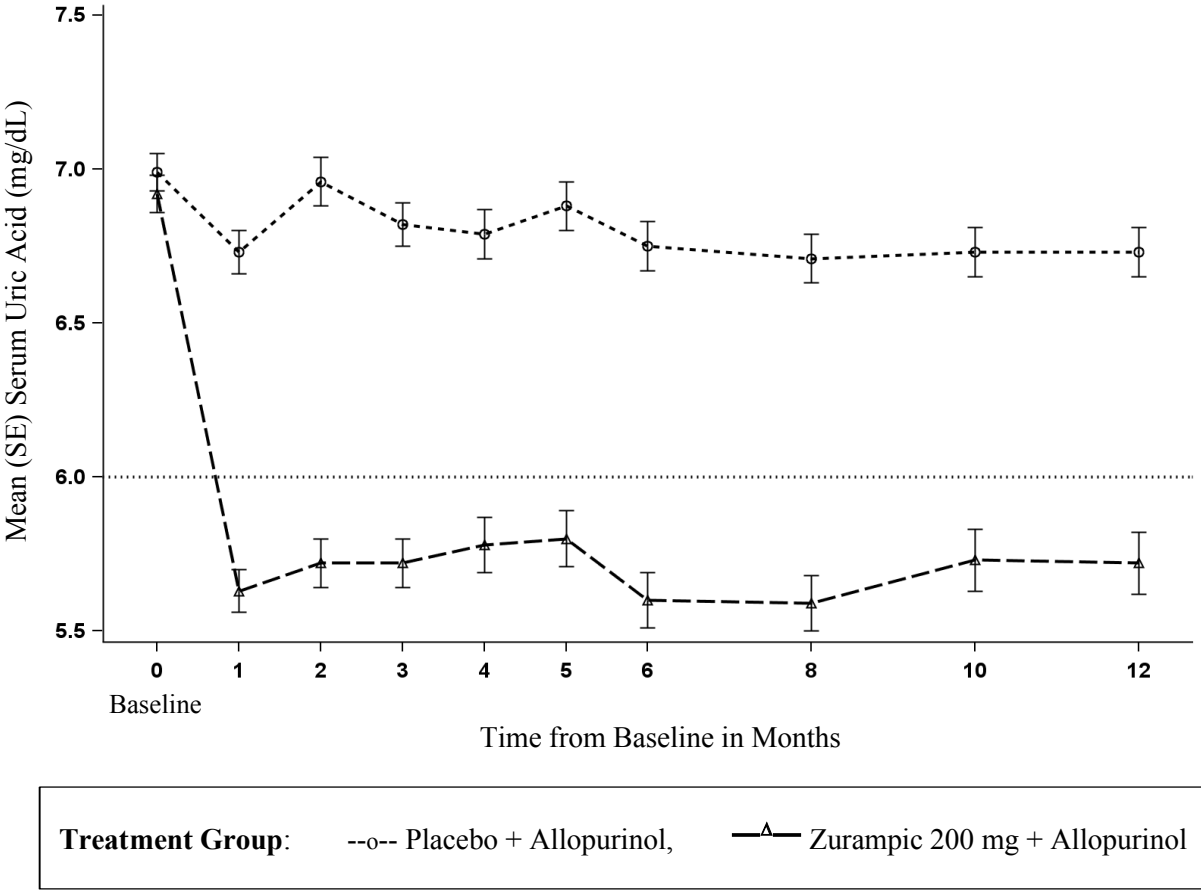
The stability of the sustained response was demonstrated with a greater proportion of patients treated with Zurampic 200 mg in combination with allopurinol achieving the target serum uric acid level at each visit for 3 consecutive months (Months 4, 5 and 6) compared to patients treated with placebo in combination with allopurinol (see Table 2).

Table 2 Proportion of patients who achieved target serum uric acid levels (<6 mg/dL) with Zurampic 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	Zurampic 200 mg + allopurinol N=405	Zurampic 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)

Zurampic when added to allopurinol caused an immediate 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 Zurampic in combination with allopurinol in patients with inadequate response (sUA ≥6 mg/dL) to allopurinol alone



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

Zurampic in combination with febuxostat in tophaceous gout
CRYSTAL enrolled gout patients with measurable tophi. Patients received febuxostat 80 mg once daily for 3 weeks and then were randomised 1:1:1 to once daily doses of Zurampic 200 mg, Zurampic 400 mg, or placebo in combination with febuxostat. Sixty-six percent of patients had mild or moderate renal impairment. Fifty percent of patients had a baseline sUA ≥5.0 mg/dL, which was after 3 weeks of treatment with febuxostat alone.

Zurampic when added to febuxostat caused an immediate 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.

In the subgroup of patients with a baseline sUA ≥5.0 mg/dL, after 3 weeks of febuxostat therapy, a significant difference was achieved at all study visits for Zurampic 200 mg in combination with febuxostat compared with placebo in combination with febuxostat (see Table 3).

Table 3 Proportion of patients with baseline sUA ≥5.0 mg/dLwho achieve target serum uric acid levels (<5 mg/dL) with Zurampic in combination with febuxostat

	Proportion of patients who met serum uric acid Target (<5.0 mg/dL) N(%)		Difference in proportion (95% C.I.)
Timepoint	Placebo + febuxostat 80 mg N=51	Zurampic 200 mg + febuxostat 80 mg N=59	Zurampic 200 mg vs. placebo
Months 4, 5, 6	6 (12%)	23 (39%)	0.27 (0.12, 0.42)
Month 6	12 (24%)	26 (44%)	0.21 (0.03, 0.38)
Month 12	12 (24%)	27 (46%)	0.22 (0.05, 0.39)

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 Zurampic 200 mg versus 29% for placebo when added to allopurinol, and 40% for Zurampic 200 mg versus 26% for placebo when added to febuxostat in patients with baseline sUA ≥5.0 mg/dL.

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 Zurampic 200 mg in combination with allopurinol or febuxostat for up to an additional year of treatment.

Clinical outcomes - tophus resolution and reduction
In CRYSTAL, the proportion of subjects who experienced a complete resolution (defined as 100% resolution of at least one target tophus and no single tophus showing progression) of ≥1 target tophus was higher in the group treated with Zurampic 200 mg in combination with febuxostat compared with placebo in combination with febuxostat, although the difference was not statistically different (26% compared with 21%). After continued treatment of up to 24 months on Zurampic 200 mg in combination with febuxostat, the proportion of subjects who experienced complete resolution of at least one target tophus increased to 53% of subjects.

Paediatric population
The European Medicines Agency has waived the obligation to submit the results of studies with Zurampic 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
The absolute bioavailability of lesinurad is approximately 100%. Lesinurad is rapidly absorbed after oral administration. Following administration of a single oral dose of lesinurad in either the fed or fasted state, maximum plasma concentrations (C_{max}) were attained within 1 to 4 hours. C_{max} and AUC exposures of lesinurad increased proportionally with single doses of lesinurad from 5 to 1,200 mg. In the fed state, after a single dose of lesinurad 200 mg, geometric mean lesinurad C_{max} and AUC were 6 μg/mL and 29 μg/hr/mL, respectively. There was no apparent influence of the fat content in the meal on the pharmacokinetics of lesinurad. In clinical trials, Zurampic was administered with food, because the serum uric acid lowering was improved under fed conditions.

Zurampic 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.

Distribution
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 radioactivity was largely contained in the plasma space and did not penetrate or partition extensively into red blood cells.

Biotransformation
Lesinurad undergoes oxidative metabolism mainly via cytochrome P450 (CYP) 2C9 to intermediate metabolite M3c (not detected *in vivo*) and is subsequently metabolised by 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. It is unclear if metabolite plasma exposures are minimal. Metabolites are not known to contribute to the uric acid lowering effects of lesinurad.

Elimination
Renal clearance is 25.6 mL/min (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 ($t_{½}$) of lesinurad was approximately 5 hours following a single dose. Lesinurad does not accumulate following multiple doses.

Linearity/non-linearity
Following multiple once daily dosing of Zurampic, 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 CAR/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 and MATE2-K.

Special populations

Renal impairment
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).

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 Zurampic 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.

5.3 Preclinical safety data

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core
hypromellose
microcrystalline cellulose
lactose monohydrate
crospovidone type A
magnesium stearate

Tablet coat
hypromellose
titanium dioxide
triacetin
Indigo Carmine
Brilliant Blue FCF

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

Clear (PVC/PVDC/Aluminium) blister of 10 or 14 (calendar blister) tablets.
Pack sizes of 10, 28, 30, 98 in non-perforated blisters.
Pack size of 100 x 1 film-coated tablet in perforated unit dose blisters.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1080/001 10 film-coated tablets
EU/1/15/1080/002 28 film-coated tablets
EU/1/15/1080/003 30 film-coated tablets
EU/1/15/1080/004 98 film-coated tablets
EU/1/15/1080/005 100x1 film-coated tablets (unit dose)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18 February 2016

10. DATE OF REVISION OF THE TEXT

DD month YYYY

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 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 RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Grünenthal GmbH
Zieglerstr. 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.

- **Obligation to conduct post-authorisation measures**

The MAH shall complete, within the stated timeframe, the below measures:

Description	Due date
Non-interventional post-authorisation safety study (PASS): In order to investigate the cardiovascular risk in association with lesinurad exposure, mainly in patients with a history of cardiovascular disorders, the MAH shall conduct and submit the results of an observational prospective study according to an agreed protocol.	2Q 2019

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Zurampic 200 mg film-coated tablets
lesinurad

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 200 mg lesinurad

3. LIST OF EXCIPIENTS

Contains lactose. See package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

10 film-coated tablets
28 film-coated tablets
30 film-coated tablets
98 film-coated tablets
100 x 1 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
Zieglerstr. 6
52078 Aachen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1080/001 10 film-coated tablets
EU/1/15/1080/002 28 film-coated tablets
EU/1/15/1080/003 30 film-coated tablets
EU/1/15/1080/004 98 film-coated tablets
EU/1/15/1080/005 100x1 film-coated tablets (unit dose)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

zurampic 200 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

< PC: {number}
SN: {number}
NN: {number}>

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER NON-PERFORATED (10 TABLETS)
BLISTER PERFORATED UNIT DOSE
CALENDAR BLISTER (14 TABLETS)

1. NAME OF THE MEDICINAL PRODUCT

Zurampic 200 mg tablets
lesinurad

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Grünenthal GmbH

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Mon. Tue. Wed. Thu. Fri. Sat. Sun.

B. PACKAGE LEAFLET

Package leaflet: Information for the Patient

Zurampic 200 mg film-coated tablets
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 Zurampic is and what it is used for
2. What you need to know before you take Zurampic
3. How to take Zurampic
4. Possible side effects
5. How to store Zurampic
6. Contents of the pack and other information

1. What Zurampic is and what it is used for

Zurampic contains the active ingredient lesinurad and is used to treat gout in adult patients by lowering the levels of uric acid in the blood. Zurampic must be taken together with allopurinol or febuxostat, which are medicines called 'xanthine oxidase inhibitors' and are also used to treat gout by lowering the amount of uric acid in your blood.

Your doctor will prescribe Zurampic if your current medicine is not controlling your gout. You must use Zurampic together with either allopurinol or febuxostat.

How Zurampic works:
Gout is a type of arthritis caused by an accumulation of urate crystals around the joints. By lowering the amount of uric acid in the blood, Zurampic stops this accumulation and may prevent further joint damage.

2. What you need to know before you take Zurampic

Do not take Zurampic:
- if you are allergic to lesinurad or any of the other ingredients of this medicine (listed in section 6)
- if you have 'tumour lysis syndrome' – a fast breakdown of cancer cells which can cause high uric acid levels
- if you have 'Lesch-Nyhan syndrome' – a rare inherited illness that starts in childhood where there is too much uric acid in the blood
- if your kidneys work very poorly or you have 'End-Stage Kidney Disease'
- if you have received a kidney transplant
- if you are on kidney dialysis.

Do not take Zurampic if any of the above apply to you. If you are not sure, talk to your doctor or pharmacist before taking Zurampic.

Warnings and precautions
Talk to your doctor or pharmacist before taking Zurampic.

Look out for side effects
Zurampic may cause serious kidney problems (see section 4), which occur more frequently if Zurampic is taken alone (see section 3). Your doctor may ask you to have tests to check how your kidneys are working.

Tell your doctor before taking Zurampic if you have or have had heart failure or other heart problems.

If your gout gets worse
Some people may have more gout attacks (gout flares) when they start using Zurampic and during the first weeks or months of treatment. If this happens, keep taking Zurampic and talk to your doctor or pharmacist. The medicine is still working to lower uric acid. Over time, your gout attacks will happen less often if you keep taking Zurampic as advised by your doctor.

Your doctor may give you other medicines such as 'colchicine' and 'nonsteroidal anti-inflammatory drugs (NSAIDs)'. These are to help prevent or treat the symptoms of gout attacks (a sudden or severe pain and swelling in a joint). Your doctor will tell you how long to take these other medicines for.

Tests and checks
Your doctor will check how well your kidneys are working before starting and during treatment with Zurampic. Your doctor may consider stopping Zurampic if your blood tests indicate changes in how your kidneys are working (blood creatinine levels increase) or if you experience symptoms of kidney problems. Your doctor may tell you to restart treatment with Zurampic when your kidney function improves.

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

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

In particular, tell your doctor or pharmacist if you are taking any of the following medicines as they may interact with Zurampic and your doctor will need to know:

- acetylsalicylic acid – to relieve fever and pain - at doses above 325 mg per day
- medicines to treat high blood pressure, 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 or carbamazepine – to treat fits (seizures), mood disorders and prevent migraines
- sildenafil – to treat erectile dysfunction
- contraceptives – used to prevent pregnancy, including oral contraception (such as 'the pill'), injections, patches and implants
- rifampin – to treat tuberculosis
- warfarin – to prevent and treat blood clots forming in the legs, lungs, brain and heart.

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

Pregnancy and breast-feeding
You should avoid taking Zurampic during pregnancy or if you are 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.

Driving and using machines
Zurampic is not expected to affect you being able to drive a car or use any tools or machines.

Zurampic contains lactose
Zurampic 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 medicinal product.

3. How to take Zurampic

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Zurampic must always be taken together with your morning dose of either allopurinol or febuxostat. Failure to follow these instructions may increase the risk of kidney side effects (see section 4).

How much to take
The recommended dose is 1 tablet of 200 mg once a day in the morning. Do not take more than one (1) tablet of Zurampic per day.

Taking this medicine
- take in the morning with food and water
- take Zurampic at the same time as your morning dose of 'xanthine oxidase inhibitor' medicine – allopurinol or febuxostat. If you take Zurampic on its own you may be more likely to get kidney problems
- drink plenty of water during the day. Two litres is a good amount to drink.

If you stop taking your xanthine oxidase inhibitor medicine, you must also stop taking Zurampic. Zurampic must never be taken without a 'xanthine oxidase inhibitor' medicine. Failure to follow these instructions may increase the risk of kidney side effects.

If you take more Zurampic than you should
If you take more of this medicine than you should, talk to a doctor or go to the nearest hospital.

If you forget to take Zurampic
If you miss a dose of Zurampic, do not take a double dose to make up for a forgotten dose. Wait and take your next dose of Zurampic with your next morning dose of allopurinol or febuxostat. Ask your doctor or pharmacist if you are not sure about how to take your next dose.

If you stop taking Zurampic
Do not stop taking Zurampic without the advice of your doctor 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 – Uncommon – may affect up to 1 in 100 people
Stop taking Zurampic and see a doctor straight away if you notice any of the following side effects, as these may be signs of a problem with your kidneys – you may need urgent medical treatment:

- 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.

Other side effects include:
Common – may affect up to 1 in 10 people
- flu (influenza),
- headache,
- increase in the amount of creatinine in your blood - shown in tests,
- heartburn (acid reflux).

Uncommon – may affect up to 1 in 100 people
- kidney stones,
- dehydration (loss of too much fluid from your body).

Rare – may affect up to 1 in 1000 people
- skin reactions, including redness, itchy skin, lumpy rash (hives) and skin rash on exposure to sunshine.

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 Zurampic

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.

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 Zurampic contains
- the active substance is lesinurad.
- each Zurampic 200 mg film-coated tablet (tablet) contains 200 mg of lesinurad.
- the other ingredients are:
- tablet core: hypromellose, microcrystalline cellulose, lactose monohydrate (see section 2), crospovidone, magnesium stearate
- film-coating: hypromellose, titanium dioxide, triacetin, indigo carmine, brilliant blue FCF.

What Zurampic looks like and contents of the pack
Zurampic 200 mg: a blue, oval, dimensions 5.7 x 12.9 mm, film-coated tablet, engraved with "LES200" on one side.

Zurampic 200 mg tablets are available in clear blisters in pack sizes of 10, 28, 30 or 98 non-perforated blisters and 100 x 1 perforated unit dose blisters.

Not all pack sizes may be marketed.

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This leaflet was last revised in {MM/YYYY}.

Other sources of information

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