ZYLORIC
Allopurinol

1. NAME OF THE MEDICINAL PRODUCT
Allopurinol 100 mg tablets
Allopurinol 300 mg tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Allopurinol 100 mg
Allopurinol 300 mg
For the full list of excipients, *see section 6.1 List of excipients*.

3. PHARMACEUTICAL FORM
Tablets.

4. CLINICAL INFORMATION
4.1 Therapeutic indications
Allopurinol is indicated for reducing urate/uric acid formation in conditions where urate/uric acid deposition has already occurred (e.g. gouty arthritis, skin tophi, nephrolithiasis) or is a predictable clinical risk (e.g. treatment of malignancy potentially leading to acute uric acid nephropathy).

The main clinical conditions where urate/uric acid deposition may occur are:
- idiopathic gout;
- uric acid lithiasis;
- acute uric acid nephropathy;
- neoplastic disease and myeloproliferative disease with high cell turnover rates, in which high urate levels occur either spontaneously, or after cytotoxic therapy;
- certain enzyme disorders which lead to overproduction of urate, for example;
  - hypoxanthine-guanine phosphoribosyltransferase, including Lesch-Nyhan syndrome;
  - glucose-6-phosphatase including glycogen storage disease;
  - phosphoribosylpyrophosphate synthetase;
  - phosphoribosylpyrophosphate amidotransferase;
  - adenine phosphoribosyltransferase.

Allopurinol is indicated for the management of 2,8-dihydroxyadenine (2,8-DHA) renal stones related to deficient activity of adenine phosphoribosyltranferase.

Allopurinol is indicated for the management of recurrent mixed calcium oxalate renal stones in the presence of hyperuricosuria, when fluid, dietary and similar measures have failed.

4.2 Posology and method of administration
General
The dosage should be adjusted by monitoring serum urate concentrations and urinary urate/uric acid levels at appropriate intervals.

Allopurinol may be taken orally once a day after a meal. It is well tolerated, especially after food. Should the daily dosage exceed 300 mg and gastrointestinal intolerance be manifested, a divided dose regimen may be appropriate.

Populations
- **Adults**

Allopurinol should be introduced at low dosage e.g. 100 mg/day to reduce the risk of adverse reactions and increased only if the serum urate response is unsatisfactory. Extra caution should be exercised if renal function is poor *(see section 4.2 Posology and method of administration - Renal impairment* and *section 4.4 Special warnings and precautions for use).*

The following dosage schedules are suggested:
- 100 to 200 mg daily in mild conditions,
- 300 to 600 mg daily in moderately severe conditions.

If dosage on a mg/kg bodyweight basis is required, 2 to 10 mg/kg bodyweight/day should be used.

- **Paediatric population (under 15 years)**

100-300 mg daily, the response should be seen after 48 hours of treatment and dosage is adjusted if necessary. Use in children is rarely indicated, except in malignant conditions (especially leukaemia) and certain enzyme disorders such as Lesch-Nyhan syndrome.

- **Elderly**

In the absence of specific data, the lowest dosage which produces satisfactory urate reduction should be used. Particular attention should be paid to advice in *section 4.2 Posology and method of administration - Renal impairment* and *section 4.4 Special warnings and precautions for use.*

- **Renal impairment**

Since allopurinol and its metabolites are excreted by the kidney, impaired renal function may lead to retention of the drug and/or its metabolites with consequent prolongation of plasma half-lives. In renal insufficiency, it is needed to take a serious consideration in starting treatment with 100 mg/day as maximum dose and increase it only if there is unsatisfaction on uric acid serum concentration. In severe renal insufficiency, it may be advisable to use less than 100 mg per day or to use single doses of 100 mg at longer intervals than one day.

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

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

- **Hepatic impairment**

Reduced doses should be used in patients with hepatic impairment.

Periodic liver function tests are recommended during the early stages of therapy.

- **Treatment of high urate turnover conditions e.g. neoplasia, Lesch-Nyhan syndrome**

It is advisable to correct existing hyperuricaemia and/or hyperuricosuria with allopurinol before starting cytotoxic therapy. Adequate hydration is important to maintain optimum diuresis and alkalinisation of the urine is advisable to increase solubility of urinary urate/uric acid. Dosage of allopurinol should be at the lower end of the recommended dosage schedule.

If urate nephropathy or other pathology has compromised renal function, the advice given in *section 4.2 Posology and method of administration - Renal impairment* should be followed. These steps may reduce the risk of xanthine and/or oxipurinol deposition complicating the clinical situation *(see section 4.5 Interactions with other medicinal products and other forms of interaction* and *section 4.8 Undesirable effects).*

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Hypersensitivity syndrome, SJS and TEN

Allopurinol hypersensitivity reactions can manifest in many different ways, including maculopapular exanthema, hypersensitivity syndrome (also known as DRESS) and SJS/TEN.

These reactions are clinical diagnoses, and their clinical presentations remain the basis for decision making. If such reactions occur at any time during treatment, allopurinol should be withdrawn immediately. Rechallenge should not be undertaken in patients with hypersensitivity syndrome and SJS/TEN. Corticosteroids may be beneficial in overcoming hypersensitivity skin reactions.

HLA-B*5801 allele

The HLA-B*5801 allele has been shown to be associated with the risk of developing allopurinol related hypersensitivity syndrome and SJS/TEN. The frequency of the HLA-B*5801 allele varies widely between ethnic populations: up to 20% in Han Chinese population, about 12% in the Korean population and 1 - 2% in individuals of Japanese or European origin. The use of genotyping as a screening tool to make decisions about treatment with allopurinol has not been established. If the patient is a known carrier of HLA-B*5801, the use of allopurinol may be considered if 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.

Hepatic and renal impairment
Reduced doses should be used in patients with hepatic or renal impairment. Patients under treatment for hypertension or cardiac insufficiency, for example with diuretics or ACE inhibitors, may have some concomitant impairment of renal function and allopurinol should be used with care in this group.

Chronic renal insufficiency and concomitant diuretic use, in particular thiazides, has been associated with an increased risk of allopurinol induced SJS/TEN, and other serious hypersensitivity reactions.

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

Acute gouty attacks
Allopurinol treatment should not be started until an acute attack of gout has completely subsided, as further attacks may be precipitated.

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

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

Xanthine deposition
In conditions where the rate of urate formation is greatly increased (e.g. malignant disease and its treatment, Lesch-Nyhan syndrome) the absolute concentration of xanthine in urine could, in rare cases, rise sufficiently to allow deposition in the urinary tract. This risk may be minimised by adequate hydration to achieve optimal urine dilution.

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 patient on long-term treatment with allopurinol (5.8%) in a long-term open label extension study.

If there is anorexia, reduced weight, and pruritic, it is considerable to evaluate the hepatic function.

Drowsiness and bone marrow depression are rarely happened.

Hypersensitivity reaction is increased in patient with renal insufficiency who used thiazide concurrent allopurinol. In this condition, the patient should be monitored.

4.5 Interactions with other medicinal products and other forms of interaction
6-mercaptopurine and azathioprine
Azathioprine is metabolised to 6-mercaptopurine which is inactivated by the action of xanthine oxidase. When 6-mercaptopurine or azathioprine is given concurrently with allopurinol, only one-quarter of the usual dose of 6-mercaptopurine or azathioprine should be given because inhibition of xanthine oxidase will prolong their activity.

Vidarabine (adenine arabinoside)
Evidence suggests that the plasma half-life of vidarabine is increased in the presence of allopurinol. When the two products are used concomitantly extra vigilance is necessary, to recognise enhanced toxic effects.

Salicylates and uricosuric agents inconsistent style
Oxipurinol, the major metabolite of allopurinol and itself therapeutically active, is excreted by the kidney in a similar way to urate. Hence, drugs with uricosuric activity such as probenecid or large doses of salicylate may accelerate the excretion of oxipurinol. This may decrease the therapeutic activity of allopurinol, but the significance needs to be assessed in each case.

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

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

Phenytoin
Allopurinol may inhibit hepatic oxidation of phenytoin but the clinical significance has not been demonstrated.

Theophylline
Inhibition of the metabolism of theophylline 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 starting or increasing allopurinol therapy.

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 drugs. The cause of the reported association has not been established. However, it is recommended that in patients receiving allopurinol an alternative to ampicillin or amoxicillin is used where available.

Cyclophosphamide, doxorubicin, bleomycin, procarbazine, mechloroethamine
Enhanced bone marrow suppression by cyclophosphamide and other cytotoxic agents has been reported among patients with neoplastic disease (other than leukaemia) in the presence of allopurinol. However, in a well-controlled study of patients treated with cyclophosphamide, doxorubicin, bleomycin, procarbazine and/or mechloroethamine (mustine hydrochloride) allopurinol did not appear to increase the toxic reaction of these cytotoxic agents.

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

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

Diuretics
An interaction between allopurinol and furosemide that results in increased serum urate and plasma oxypurinol concentrations has been reported.

An increased risk of hypersensitivity has been reported when allopurinol is given with diuretics, in particular thiazides, especially in renal impairment.

Angiotensin-converting-enzyme (ACE) inhibitors
An increased risk of hypersensitivity has been reported when allopurinol is given with ACE inhibitors especially in renal impairment.

4.6 Fertility, pregnancy and lactation
Fertility
No text.

Pregnancy
There is inadequate evidence of safety of allopurinol in human pregnancy, although it has been in wide use for many years without apparent ill consequence *(see section 5.3 Pre-clinical safety data).*

Use in pregnancy only when there is no safer alternative and when the disease itself carries risks for the mother or unborn child.

Breastfeeding
Reports indicate that allopurinol and oxipurinol are excreted in human breast milk. Concentrations of 1.4 mg/litre allopurinol and 53.7 mg/litre oxipurinol have been demonstrated in breast milk from a woman taking allopurinol 300 mg/day. However, there are no data concerning the effects of allopurinol or its metabolites on the breast-fed baby.

4.7 Effects on ability to drive and use machines
Since adverse reactions such as somnolence, vertigo and ataxia have been reported in patients receiving allopurinol, patients should exercise caution before driving, using machinery or participating in dangerous activities until they are reasonably certain that allopurinol does not adversely affect performance.

4.8 Undesirable effects
For this product there is no modern clinical documentation which can be used as support for determining the frequency of undesirable effects. Undesirable effects may vary in their incidence depending on the dose received and also when given in combination with other therapeutic agents.

The frequency categories assigned to the adverse drug reactions below are estimates: for most reactions, suitable data for calculating incidence are not available. Adverse drug reactions identified through post-marketing surveillance were considered to be rare or very rare.

The following convention has been used for the classification of frequency:
Very common ≥1/10
Common ≥1/100 to < 1/10
Uncommon ≥1/1,000 to <1/100
Rare ≥1/10,000 to <1/1,000
Very rare <1/10,000

Adverse reactions in association with allopurinol are rare in the overall treated population and mostly of a minor nature. The incidence is higher in the presence of renal and/or hepatic disorder.

Tabulated summary of adverse reactions

System Organ Class	Frequency	Adverse Reaction
Infections and infestations	Very rare	Furuncle
Blood and lymphatic system disorders	Very rare	Agranulocytosis[1] Aplastic anaemia[1] Thrombocytopenia[1]
Immune system disorders	Uncommon	Hypersensitivity[2]
	Very rare	Angioimmunoblastic T-cell lymphoma[3]
Metabolism and nutrition disorders	Very rare	Diabetes mellitus Hyperlipidaemia
Psychiatric disorders	Very rare	Depression
Nervous system disorders	Very rare	Coma Paralysis Ataxia Neuropathy peripheral Paraesthesia Somnolence Headache Dysgeusia
Eye disorders	Very rare	Cataract Visual impairment Maculopathy
Ear and labyrinth disorders	Very rare	Vertigo
Cardiac disorders	Very rare	Angina pectoris Bradycardia
Vascular disorders	Very rare	Hypertension

Gastrointestinal disorders	Uncommon	Vomiting[4] Nausea[4]
	Very rare	Haematemesis Steatorrhoea Stomatitis Change of bowel habit
Hepatobiliary disorders	Uncommon	Liver function test abnormal[5]
	Rare	Hepatitis (including hepatic necrosis and granulomatous hepatitis)[5]
Skin and subcutaneous tissue disorders	Common	Rash
	Rare	Stevens-Johnson syndrome/toxic epidermal necrolysis[6]
	Very rare	Angioedema[7] Drug eruption Alopecia Hair colour change
Renal and urinary disorders	Very rare	Haematuria Azotaemia
Reproductive system and breast Disorders	Very rare	Infertility male Erectile dysfunction Gynaecomastia
General disorders and administration site conditions	Very rare	Oedema Malaise Asthenia Pyrexia[8]

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

[2]A delayed multiorgan hypersensitivity disorder (known as hypersensitivity syndrome or DRESS) with fever, rashes, vasculitis, lymphadenopathy, pseudo lymphoma, arthralgia, leukopenia, 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, allopurinol should be withdrawn IMMEDIATELY AND PERMANENTLY.

Rechallenge should not be undertaken in patients with hypersensitivity syndrome and SJS/TEN. Corticosteroids may be beneficial in overcoming hypersensitivity skin reactions. When generalised hypersensitivity reactions have occurred, renal and/or hepatic disorder has usually been present particularly when the outcome has been fatal.

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

[4]In early clinical studies, nausea and vomiting were reported. Further reports suggest that this reaction is not a significant problem and can be avoided by taking allopurinol after meals.

[5]Hepatic dysfunction has been reported without overt evidence of more generalised hypersensitivity.

[6]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 Stevens-Johnson syndrome and toxic epidermal necrolysis (SJS/TEN).

Allopurinol should be withdrawn IMMEDIATELY in any patient developing signs or symptoms of a SJS/TEN, or other serious hypersensitivity reactions. The highest risk for SJS and TEN, or other serious hypersensitivity reactions, is within the first weeks of treatment. The best results in managing such reactions come from early diagnosis and immediate discontinuation of any suspect drug.

If allopurinol treatment has been discontinued due to mild skin reactions (i.e. not signs or symptoms of SJS/TEN, or other serious hypersensitivity reaction), allopurinol may be re-introduced at a low dose (e.g. 50 mg/day) and then gradually increased. The HLA-B*5801 allele has been shown to be associated with the risk of developing allopurinol related hypersensitivity syndrome and SJS/TEN. The use of genotyping as a screening tool to make decisions about treatment with allopurinol has not been established. If the original symptoms recur allopurinol should be PERMANENTLY withdrawn as more severe hypersensitivity reactions may occur (*see section 4.8 Undesirable effects - Immune system disorders*). If

SJS/TEN, or other serious hypersensitivity reactions cannot be ruled out, DO NOT re-introduce allopurinol due to the potential for a severe or even fatal reaction. The clinical diagnosis of SJS/TEN, or other serious hypersensitivity reactions remain the basis for decision making.

[7]Angioedema has been reported to occur with and without signs and symptoms of a more generalised allopurinol hypersensitivity reaction.

[8]Fever has been reported to occur with and without signs and symptoms of a more generalised allopurinol hypersensitivity reaction *(see section 4.8 Undesirable effects - Immune system disorders)*.

4.9 Overdose
Symptoms and signs
Ingestion of up to 22.5 g allopurinol without adverse effect has been reported. Symptoms and signs including nausea, vomiting, diarrhoea and dizziness have been reported in a patient who ingested 20 g allopurinol. Recovery followed general supportive measures.

Treatment
Massive absorption of allopurinol may lead to considerable inhibition of xanthine oxidase activity, which should have no untoward effects unless affecting concomitant medication, especially with 6-mercaptopurine and/or azathioprine. Adequate hydration to maintain optimum diuresis facilitates excretion of allopurinol and its metabolites. If considered necessary haemodialysis may be used.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Preparations inhibiting uric acid production.

ATC Code: M04AA01.

Mechanism of action
Allopurinol is a xanthine-oxidase inhibitor.

Allopurinol and its main metabolite, oxipurinol 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.

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

5.2 Pharmacokinetic properties
Absorption
Allopurinol is active when given orally and is rapidly absorbed from the upper gastrointestinal tract. Studies have detected allopurinol in the blood 30 to 60 min after dosing. Estimates of bioavailability vary from 67% to 90%.

Peak plasma levels of allopurinol generally occur approximately 1.5 h after oral administration of allopurinol but fall rapidly and are barely detectable after 6 h. Peak plasma levels of oxipurinol generally occur after 3 to 5 h after oral administration of allopurinol and are much more sustained.

Distribution
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 oxipurinol will be present in the highest concentrations in the liver and intestinal mucosa where xanthine oxidase activity is high.

Biotransformation
The main metabolite of allopurinol is oxipurinol. Other metabolites of allopurinol include allopurinol-riboside and oxipurinol-7-riboside.

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

Allopurinol has a plasma half-life of about 0.5 to 1.5 h.

Oxipurinol is a less potent inhibitor of xanthine oxidase than allopurinol, but the plasma half-life of oxipurinol is far more prolonged. Estimates range from 13 to 30 h in man. Therefore, effective inhibition of xanthine oxidase is maintained over a 24 h period with a single daily dose of allopurinol. Patients with normal renal function will gradually accumulate oxipurinol until a steady-state plasma oxipurinol concentration is reached. Such patients, taking 300 mg of allopurinol per day will generally have plasma oxipurinol concentrations of 5 to 10 mg/litre.

Oxipurinol 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 h to 29 h. The large discrepancies in these values may be accounted for by variations in study design and/or creatinine clearance in the patients.

Special patient populations

- **Renal impairment**

Allopurinol and oxipurinol 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 oxipurinol concentrations of approximately 30 mg/litre after prolonged treatment with 300 mg allopurinol per day. This is approximately the concentration which would be achieved by doses of 600 mg/day in those with normal renal function. A reduction in the dose of allopurinol is therefore required in patients with renal impairment.

- **Elderly**

The kinetics of the drug are not likely to be altered other than due to deterioration in renal function *(see section 5.2 Pharmacokinetic properties - Renal impairment).*

5.3 Pre-clinical safety data

Carcinogenesis, mutagenesis

Cytogenetic studies show that allopurinol does not induce chromosome aberrations in human blood cells *in vitro* at concentrations up to 100 microgram/mL and *in vivo* at doses up to 600 mg/day for a mean period of 40 months.

Allopurinol does not produce nitroso compounds *in vitro* or affect lymphocyte transformation *in vitro*. Evidence from biochemical and other cytological investigations strongly suggests that allopurinol has no deleterious effects on DNA at any stage of the cell cycle and is not mutagenic. No evidence of carcinogenicity has been found in mice and rats treated with allopurinol for up to 2 years.

Teratogenicity

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.

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

As registered locally.

6.2 Incompatibilities

No data.

6.3 Shelf life

The expiry date is indicated on the packaging.

6.4 Special precautions for storage

Store below 30°C and keep dry. Protect from light.
Keep medicines out of the reach of children.

6.5 Nature and contents of container

As registered locally.

6.6 Special precautions for disposal and other handling
No data.

Not all presentations are available in every country.

ZYLORIC tablet 100 mg	Box, 6 blister @ 10 tablets, No.Reg. DKL9932004210A1
	Box, 20 blister @ 10 tablets, No. Reg. DKL9932004210A1
ZYLORIC tablet 300 mg	Box, 3 blister @ 10 tablets, No.Reg. DKL9932004210B1
	Box, 10 blister @ 10 tablets, No. Reg. DKL9932004210B1

HARUS DENGAN RESEP DOKTER

Manufactured by
PT Sterling Products Indonesia
Jakarta, Indonesia

For
PT Glaxo Wellcome Indonesia
Jakarta, Indonesia

PI based on ver CCDS18 + SC update to 30 (Date of issue: 8 June 2016) + *Rinjani*.

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