SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Doxy 200, 200 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains doxycycline monohydrate equivalent to 200 mg of doxycycline base.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Round tablet, olive-yellow coloured, scored, with “Doxy 200” embossed on one face.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Doxycycline is used for the treatment of infections caused by sensitive pathogenic germs. The high prevalence of resistance of certain pathogenic germs should be taken into consideration.

- Respiratory tract infections: *Mycoplasma pneumoniae* pneumonia.
- Genito- urinary tract infections:
    - Infections due to *Chlamydia trachomatis* including uncomplicated urethral, endocervical infections and epididymo-orchitis.
    - Alternative drug in treatment of syphilis (in case of known allergy to penicillin)
    - Lymphogranuloma venereum
    - Acute pelvis affection
- Epidemic typhus
- Gastro-intestinal tract infections: cholera treatment (adjuvant)
- Stage I Lyme disease (including dermal form or erythema migrans)
- Leptospirosis
- Acne vulgaris and acne conglobata
- Malaria treatment and prophylaxis

4.2 Posology and method of administration

Adults

- Respiratory tract infections: single loading dose of 200 mg or 100 mg twice daily with 12 hours interval on the first day of treatment followed by a maintenance dosage of 100 mg once daily at the same time each day thereafter (5 to 10 days).
- uncomplicated urethral and endocervical infections caused by *Chlamydia trachomatis* :100 mg twice daily during 7 days
- Epididymo-orchitis caused by *Chlamydia trachomatis*: 100 mg twice daily during 10 days
- Primary and secondary syphilis: 100 mg twice daily during 14 days
- Lymphogranuloma venereum: 100 mg twice daily during 21 days

- Acute pelvis affection: 100 mg twice daily during 10 days always in association with an active antibiotic against *N. gonorrhoeae,* anaerobic bacteria, facultative gram negative anaerobic bacteria and streptococci.
- Epidemic typhus: single dose of 100 mg or 200 mg
- Cholera treatment (adjuvant): single dose of 300 mg
- Stage I Lyme disease (including dermal form): 100 to 200 mg daily during 10 to 20 days
- Leptospirosis: 2 x 100 mg daily during 7 days
- Acne: 50 mg daily during up to 12 weeks
- Malaria treatment (chloroquine-resistant falciparum malaria): 200 mg daily (as a single dose) or 100 mg twice daily with 12 hours interval) during at least 7 days. A fast acting schizonticide should be associated.
- Malaria prevention (in chloroquine-resistant falciparum malaria or in case of intolerance or contraindication to mefloquine or atovaquone/proguanil): 100 mg daily. The prophylaxis (prevention) should start 1 to 2 days before departure, and should continue throughout the stay (less than 4 months) and for 4 weeks after the return.

Paediatric population
Children aged between 8 and 12 years (see section 4.4)
The use of doxycycline for the treatment of acute infection in children aged between 8 and 12 years should be carefully justified in situations where other medicines are not available, are not likely to be efficient or are contraindicated.

For children of 45 kg or less – Initial dose:
- Treatment of acute infections: 4.4 mg/kg (either in a single dose or divided in two doses) with a maintenance dose of 2.2 mg/kg (either in a single dose or divided in two doses). In the of more serious infections, a maximum dose of 4.4 mg/kg should be administered in all the treatment course.
- Malaria treatment: 4 mg/kg (as a single dose or divided into 2 equal doses with 12 hours interval) on the first day, followed by 2 mg/kg (as a single dose or divided into 2 equal doses) during at least 6 days. A fast acting schizonticide should be associated.
- Malaria prevention: 2 mg/kg daily as a single dose. The prophylaxis (prevention) should start 1 to 2 days before departure, and should continue throughout the stay (less than 4 months) and for 4 weeks after the return.

For children of 45 kg and more – The adult dose should be used for the treatment of acute infections and for the treatment and prophylaxis of malaria.

Children under 8 years old
Doxycycline should not be used in children under 8 years old because of the risk of teeth discolouration.

Posology in case of renal failure
No dose reduction is required in patient with impaired renal function.
Studies up to now show that the administration of doxycycline at usual recommended doses do not result in excessive accumulation of this antibiotic in patients with impaired renal function.

Use in dialysis patients
Haemodialysis and peritoneal dialysis do not impact the half-life of doxycycline.

Posology in case of liver failure

Doxycycline should be administered carefully in patients with liver failure (see section 4.4).

Method of administration
DOXY 200 should be taken with adequate amounts of fluid (at least 100 ml of water). This should be done in the sitting or standing position and the patient should be advised to remain upright for at least thirty minutes after taking a dose. The medicine should be taken well before bedtime to reduce the risk of oesophageal irritation and ulceration.

In case of gastric irritation, it is recommended to take the tablet during a meal or with milk. Studies indicate that the absorption of doxycycline is less influenced by simultaneous ingestion of food or milk than the absorption of tetracycline.
The absorption of doxycycline in not markedly influenced by simultaneous ingestion of food or milk.

4.3 Contraindications

- Hypersensitivity to the active substance, to whatever tetracycline or to any of the excipients listed in section 6.1.
- Known obstructive oesophageal disorders, such as stricture or achalasia (Oesophagus irritation and ulceration)
- Doxy 200 should not be administered to children under the age of 8 years, in pregnant women or nursing mothers unless otherwise instructed by the doctor.

4.4 Special warnings and precautions for use

Cases of oesophageal injuries (oesophagitis and ulceration), sometimes serious, have been reported. Patients should be instructed to take DOXY 200 with a sufficient quantity of water (at least 100 ml), remain upright and wait at least 30 minutes before going to bed (see section 4.2). Discontinuation of doxycycline and investigation of oesophageal disorder should be considered if symptoms such as dyspepsia or retrosternal pain occur. Caution is required in the treatment of patients with known oesophageal reflux disorders

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including doxycycline, and has ranged in severity from mild to life-threatening. The potential symptoms are the following: massive aqueous diarrhoea (sometimes bloody), intense abdominal pains and cramps, nausea, dehydration, fever. Without treatment, these symptoms can turn into peritonitis, shock, toxic megacolon.

A colitis associated to the antibiotherapy might occur during the treatment with doxycycline in the 2 following months. The use of intestinal peristaltism inhibitors is contraindicated. A careful anamnesis should be carried out to establish the relation between the antibiotherapy and the occurrence of diarrhoea.

The use of antibiotics may occasionally result in over-growth of non-susceptible organisms, including *Candida*. The potential symptoms consist in frequent episodes of vaginitis, vaginal discharges or vaginal itching. If a resistant organism appears, the antibiotic should be discontinued and appropriate therapy instituted.

The anti-anabolic effects of tetracycline may induce an increase in blood ureic nitrogen levels. the clinical experience up to now shows that this phenomenon is not observed in patients on doxycycline that have an impaired renal function.

In case of prolonged treatment (long term therapy), periodic laboratory evaluation of organ systems, including haemopoietic, renal and hepatic studies, should be performed.

Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some patients taking tetracyclines, including doxycycline. The risk of phototoxicity is more significant in patients on a prolonged doxycycline treatment (malaria prophylaxis, treatment of acne), especially if the light intensity is high, as in tropical countries. The use of sun block should be considered. Patients likely to be exposed to sunlight or direct ultraviolet light should be advised that this reaction can occur with tetracycline drugs. The treatment should be discontinued at the first evidence of skin erythema.

The treatment of venereal diseases required appropriate diagnostic procedures. Patients on doxycycline for the treatment of a sexually transmitted disease still have a risk of developing other sexually transmitted infections. An appropriate management and a follow up of the patients are recommended.

Although doxycycline is not degraded into toxic epianhydro derivatives, the use of expired tablets should be avoided.

DOXY 200 should be administered with caution in patient undergoing anaesthesia with methoxyflurane (see section 4.5).

Tetracycline may exacerbate a disseminated lupus erythematosus.

Because of a risk of a weak neuromuscular blockade, it is recommended to be careful in case of administration of tetracyclines to patients with myasthenia gravis.

Antacids containing aluminium, calcium or magnesium, or other cations or others (as strontium ranelate), or bismuth salts, impair absorption and should not be given to patients taking doxycycline. In case of concomitant treatment with iron preparations, a sufficient time interval should be respected between the intake of these preparations and doxycycline.

Some patients with spirochete infections might experience Jarisch-Herxheimer reaction shortly after the initiation of a doxycycline treatment. It is advised to reassure the patients by informing that it is a consequence of an antimicrobial treatment of spirochete infection that usually spontaneously resolves.

Paediatric population
As other tetracycline, doxycycline forms a stable calcium complex in any generating bone tissue. A slower development of the fibula has been observed in premature children administered with 25 mg/kg every 6 hours oral tetracycline. This reaction was reversible at treatment stop.

The administration of a medicine of the tetracycline group during the period of teeth generation (from the second half of pregnancy, neonatal period and childhood up to 8 years old) might induce an irreversible change in teeth colour (yellowish, greyish, brownish). This undesirable effect is more frequent with the long term administration, but has been observed following repeated short term treatments. Enamel hypoplasia has also been reported.
Use doxycycline in children under 8 years old only if the potential benefits are greater than the risk in serious or deadly conditions (for instance Rocky Mountain spotted fever), only in the absence of appropriate therapeutic alternatives.

Although the risk of permanent teeth colouration is rare in children aged 8 to 12, the use of doxycycline should be carefully justified in situations where other medicines are not available, are not efficient or are contra-indicated.

4.5 Interaction with other medicinal products and other forms of interaction

There have been reports of prolonged prothrombin time in patients taking warfarin and doxycycline. Because the tetracyclines have been shown to depress plasma prothrombin activity, patients who are on coumarin anticoagulant therapy may require downward adjustment of their anticoagulant dosage.

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin (beta-lactamine), it is advisable to avoid giving doxycycline in conjunction with penicillin.

Antacids containing aluminium, calcium or magnesium, or other cations or others (as strontium ranelate), or bismuth salts, impair absorption and should not be given to patients taking doxycycline. In case of concomitant treatment with iron preparations, a sufficient time interval should be respected between the intake of these preparations and doxycycline.

As, in case of concomitant treatment with preparations containing iron, it is necessary to include an interval as long as possible between the administration of these preparations and DOXY 200.

Phenobarbital, carbamazepine, primidone, phenytoin and alcohol may increase the metabolism of doxycycline (reduced half-life). The efficacy is however maintained if doxycycline is administered twice daily. An increase in the daily dosage of doxycycline should be considered.

In case of concomitant use of antibiotics with oestrogen-progestin oral contraceptive, the efficacy of oral contraceptives may be reduced. Unplanned pregnancy may occur with this combination.

The concomitant use of tetracyclines and methoxyflurane has been reported to increase the renal toxicity.

Isotretinoin should not be administered concomitantly with tetracyclines.

Concomitant administration of doxycycline with rifampicin may reduce the plasma levels of doxycycline, thereby decreasing its activity.

Concomitant administration with methotrexate may increase the risk of toxicity of methotrexate.

Laboratory test interactions
False elevations of urinary catecholamine levels may occur due to interference with the fluorescence test.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is no sufficient data related to the use of doxycycline in pregnant women to assess its potential toxicity.

Foetal plasma concentrations are equivalent to 30 % of plasma concentration observed in mother.
Tetracyclines class penetrate bones and teeth during development and may cause delayed growth, permanent discolouration of the teeth and potentially an increased risk of cavities.

Breast-feeding
Tetracyclines are present in the milk of lactating women who are taking this type of drug and should therefore not be used in nursing mothers. The concentration in breast milk corresponds to 30 to 40% of mother's plasmatic concentration. Doxycycline must not be administered during breast-feeding period.

4.7 Effects on ability to drive and use machines

The effect of doxycycline on the ability to drive and operate heavy machinery has not been studied. There is no evidence to suggest that doxycycline may effect these abilities.

4.8 Undesirable effects

The following frequencies of adverse events have been observed in patients treated with tetracyclines and specifically with doxycycline. They are ranked according to the following: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1000 to <1/100), rare (≥ 1/10000 to < 1/1000), very rare (< 1/10000; including isolated reports), not known (cannot be estimated from the available data).

System Organ Class	Very common (≥ 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1000 to <1/100)	Rare (≥ 1/10000 to < 1/1000)	Very rare (< 1/10000	Not known (cannot be estimated from the available data)
Blood and lymphatic system disorders				Haemolytic anaemia, thrombocytopenia, neutropenia, eosinophilia		
Immune system disorders		Anaphylactic reaction (including hypersensitivity, Schönlein-Henoch purpura, angioedema, exacerbation of disseminated lupus erythematosus, dyspnoea, serum		Medicine reactions with eosinophilia and systemic symptoms (DRESS)		Jarisch-Herxheimer reaction (see section 4.4)

		sickness, peripheral oedema, urticarial)				
Endocrine disorders				Brown-black microscopic discolouration of thyroid tissue		
Metabolism and nutrition disorders				Anorexia	Hypoglycaemia	
Nervous system disorders		Headache		Fontanelle bulging (in infants), benign intracranial hypertension in adults		
Ear and labyrinth disorders				Tinnitus		
Cardiac disorders				Pericarditis, tachycardia		
Vascular disorders				Flushing, hypotension		
Gastrointestinal disorders		Nausea, vomiting	Dyspepsia (pyrosis/gastritis)	Pancreatitis[a], pseudomembranous colitis, diarrhoea due to *C. difficile*, oesophageal ulceration, oesophagitis, enterocolitis, inflammatory lesions (with superinfection due to *C. difficile*) in the anogenital tract, abdominal pains, diarrhoea, dysphagia, glossitis		Teeth disolouration[b]
Hepatobiliary disorders				Hepatotoxicity, liver dysfunction, hepatitis		Rare
Skin and subcutaneous tissue disorders	Photosensitivity reaction	Rash (including maculopapular rash and		Exfoliative dermatitis, erythema multiforme,		

		erythematous rash)		Stevens-Johnson syndrome, toxic epidermal necrolysis, photo-onycholysis		
Musculoskeletal and connective tissue disorders				Myalgia, arthralgia		
Renal and urinary tract disorders				Increased blood level urea		
Reproductive system and breast disorders		Overgrowth of *Candida* that may cause candidiasis, vaginitis				

[a] This undesirable effect has been spontaneously reported during post-marketing surveillance and has not been observed during the clinical trials. The frequency was calculated using the following rule: the upper limit of the 95 % confidence interval of the frequency is lower of equal to 3/X, X being equal to 3833, the number of patients exposed during the clinical and epidemiological trials.
b A permanent reversible and superficial teeth discolouration has been reported with the use of doxycycline, but the frequency cannot be estimated based on the available data.

As with other tetracyclines, doxycycline forms a stable calcium complex in any bone-forming tissue. A decrease in fibula growth rate has been observed in premature children given oral tetracyclines in doses of 25 mg/kg every 6 hours. This reaction was shown to be reversible when the drug was discontinued (see section 4.4 and 4.6).

The use of drugs of tetracycline class during tooth development (pregnancy, infancy and childhood to the age of 8 years) may cause permanent discolouration of the teeth (yellow-grey-brown). The adverse reaction is more common during long-term use of the drugs but has been observed following repeated short-term courses. Enamel hypoplasia has also been reported (see section 4.4 and 4.6).

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

4.9 Overdose

Treatment
In the event of over dosage, discontinue the medication and symptomatic treatment plus appropriate supportive treatment is indicated. Dialysis does not alter serum half-life and thus would not be of benefit in treating cases of over dosage.

5. PHARMACOLOGICAL PROPERTIES

Doxycycline is a broad spectrum antibiotic synthetically derived from oxytetracycline. the chemical name of this light yellow crystalline powder is 6-deoxy-5-oxytetracycline. Doxycycline has a high degree of lipid solubility and a low affinity for calcium. It is highly stable in normal human serum. Doxycycline will not degrade into an epianhydro form.

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antibacterials for systemic use, Tetracyclines, ATC code: J01AA02

Doxycycline inhibits the bacterial protein synthesis, binding the bacterial 30S ribosomal subunit. It also affects the pseudo-bacterial protein synthesis of the infracellular plastids of some protozoans. Doxycycline is bacteriostatic. It is active against a broad panel of Gram positive and Gram negative bacteria, including atypical and obligate intracellular bacteria (spirochetes, rickettsia, chlamydia mollicutes) and some protozoans.

Resistance
Resistance to tetracyclines is generally due to ribosomal protection (by linkage to ribosome of proteins that are normally soluble) and efflux mechanisms. Inactivation of tetracyclines may happen in some organisms as *Bacteroides* spp.

Threshold of sensitivity trials
The thresholds of the *European Committee on Antimicrobial Susceptibility Testing* (EUCAST – version 5.0, 2015) for the sensitivity trials are presented below.

Organisms	**Thresholds (CMI (mg/l)**	
	Sensitive (≤ S)	**Resistant (R >)**
Staphylococcus spp.	1	2
Streptococcus pneumoniae	1	2
Streptococcus of A, B, C, G groups	1	2
Haemophilius influenzae	1	2
Moraxella catarrhalis	1	2
Campylobacter jejuni and *coli*	--[1]	--[1]

[1]Tetracycline (S ≤ 2 mg/1 ; R > 2 mg/l) may be used to determine the sensitivity to doxycycline.

Organisms	**Thresholds of zone diameters (mm)**	
	Sensitive (≤ S)	**Resistant (R >)**
Staphylococcus spp.	23	20
Streptococcus pneumoniae	--[A]	--[A]
Streptococcus of A, B, C, G groups	23	20
Haemophilius influenzae	--[A]	--[A]
Moraxella catarrhalis	--[A]	--[A]
Campylobacter jejuni and *coli*	--[1]	--[1]

[A]Tetracycline sensitive isolates (S ≤ 25 mm ; R > 22 mm) are equally sensitive to doxycycline, but some tetracycline resistant isolates might be sensitive to doxycycline. Tetracycline resistant isolates should be tested for sensitivity to doxycycline using the CMI determination method.

[1] Tetracycline (S ≥ 30 mm; R < 30 mm) may be used to determine the sensitivity to doxycycline.

Relation pharmacokinetics/pharmacodynamics
The relation between the area under the concentration-time of the medicine in the circulation curve and the minimal inhibitory concentration of the medicine for the pathogen organism is the parameter that gives the best correlation with the efficacy of doxycycline.

Clinical efficacy again specific pathogens
The efficacy has been demonstrated during clinical trials against the pathogens enumerated under each sensitive to doxycycline *in vitro* indication

Respiratory tract infections
Atypical microorganisms
- *Mycoplsma pneumoniae*

Gram positive microorganisms
- *Streptococcus pneumoniae*

Gram negative microorganisms
- *Haemophilius influenzae*
- *Klebsiella pneumoniae*

Genito-urinary infections
Atypical microorganisms
- *Chlamydia trachomatis*
- *Ureaplasma urealytium*

Gram negative microorganisms
- *Nesseria gonorrhoeae*
- *Treponema pallidum*
- *Haemophilius ducreyi*
- *Klebsiella granulomatis*

Gram negative and Gram positive anaerobia microorganisms

Dermatological microorganisms
Gram positive microorganisms
- *Propionibacterium acnes*

Gastrointestinal infections
Gram negative microorganisms
- *Vibrio cholera*

Vectorial transmission and zoonotic infections
Gram negative microorganisms
- *Borrelia burgdorferi*
- *Leptospira* spp.

Rickettsia
Protozonans
- *Plasmodium falciparum*

5.2 Pharmacokinetic properties

a.) Absorption

Doxycycline is completely absorbed after oral administration. Studies reported to date indicate that the absorption of doxycycline, unlike certain other tetracyclines, is not notably influenced by the ingestion of food or milk. Its absorption is not significantly affected by the presence of food or milk.
Tetracyclines form biologically inactive chelates with metals. Consequently, concomitant administration with antacids and irons salts preparations should be avoided.
Following a 200 mg dose the first day, followed by a 100 mg dose daily, the peak serum concentration varies between 1.5 to 3 micrograms/ml of doxycycline. Two hours following the administration, the peak serum levels vary between 2.6 to 3.0 micrograms/ml.
The mean serum level 24 hours after dosing was 1.5 micrograms/ml.
The table below indicates the mean serum levels (µg/ml) after administration of respectively:

(1) 100 mg doxycycline every 12 hours the first day and then 50 mg, every 12 hours the following days
(2) 100 mg doxycycline every 12 hours the first day and then 100 mg, every 24 hours the following days
(3) 100 mg doxycycline every 12 hours

Dosage	**Serum concentration (µg/ml) after**								
	1 h	2 h	8 h	12 h*	24 h*	48 h*	72 h*	96 h*	144 h*
(1)	1,346	1,440	1,061	0,876	1,250	1,124	N.D.	1,294	1,279
(2)	1,374	1,302	1,027	0,887	1,515	1,042	N.D.	0,711	0,714
(3)	1,413	1,107	0,936	1,005	1,831	N.D.	2,651	N.D.	2,519

* Before the dosage
N.D.: Not Determined

b.) Distribution
At pH= 7.4, the protein binding varies between 89.1 ± 3 % (n = 47, dialysis method) and 91.1 ± 4.6 % (n = 16, ultracentrifugation method). After the administration of repeated doses, the half-life of doxycycline varies from18 to 22 hours. The volume of distribution represents 158 % of the body weight, 1.58 l/kg of body weight.
After absorption, doxycycline is well distributed in tissues.
As other tetracyclines, doxycycline does not cross the haemato-encephalic barrier in significant quantity.

c.) Metabolism
Generally, no significant metabolism occurs and doxycycline is cleared intact by renal and biliary mechanisms. In case of concomitant administration of doxycycline with hepatic enzyme inducers, a decrease of the half-life of doxycycline has been observed.

d.) Excretion
Excretion of doxycycline by the kidney is about 40 % in 72 hours in individuals with normal function (creatinine clearance above 75 ml/min).

Linearity/Non-linearity
Doxycycline seems to exhibit a linear pharmacokinetics

Kidney damage
This percentage excretion may fall as low as 1 to 5 % in 72 hours in individuals with severe renal insufficiency (creatinine clearance below 10 ml/min). Studies have shown no significant difference in serum half-life of doxycycline in individuals with normal and with severely impaired renal function.
The fraction of drug not eliminated with urine is mainly excreted in the faeces.

Haemodialysis does not alter serum half-life.

Liver damage
No pharmacokinetics study has been carried out in patients with liver failure.

Elderly
No data available on pharmacokinetics parameters in elderly people.

5.3 Preclinical safety data

Long-term studies in animals to evaluate carcinogenic potential of doxycycline have not been conducted. However, there has been evidence of oncogenic activity in rats in studies with the related antibiotics, oxytetracycline (adrenal and pituitary tumours) and minocycline (thyroid tumours).
Likewise, although mutagenicity studies of doxycycline have not been conducted, positive results in *in-vitro* mammalian cell assays have been reported for related antibiotics (tetracycline, oxytetracycline).
The oral administration of 250mg/kg/day in female rats has no effect on the reproductive process. No study was conducted to assess the potential effect of doxycycline of the reproductive process in male rats.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch, microcrystalline cellulose, sodium methyl parahydroxybenzoate (E219), sodium propyl parahydroxybenzoate (E217), sodium lauryl sulphate, colloidal anhydrous silica, magnesium stearate, talc.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Keep out of the sight and reach of children.
Store in the original package, protect from heat, light and moisture.
Store below 30°C.

6.5 Nature and contents of container

Box of 8 scored tablets in blister pack (PVC-Aluminium).

6.6 Special precautions for disposal and other handling

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

7. MARKETING AUTHORISATION HOLDER

Exphar sa
Zoning Industriel de Nivelles Sud - Zone II
Avenue Thomas Edison 105
1402 Thines, Belgium
Phone +32 (0)67 68 84 05
Fax +32 (0)67 68 84 19

8. CATEGORY OF DISTRIBUTION

☐ Over-the counter medicine ☒ Prescription only medicines
List I

9. MANUFACTURER

Gracure Pharmaceuticals Ltd., E-1105,
Industrial Area, Phase-III, Bhiwadi,
District Alwar (Raj.) INDIA
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10. DATE OF REVISION OF THE TEXT

09/2019