1.6.1 PRESCRIBING INFORMATION (SUMMARY OF PRODUCTS CHARACTERISTICS)

1. Name of the Medicinal Product

Kodoxy (Doxycycline Capsules BP 100mg)

1.1 Strength

100 mg

1.2 Pharmaceutical Form

Capsules

2. Qualitative and Quantitative Composition

2.1 Qualitative declaration:

Each Capsule contains:

Doxycycline Hyclate BP

Equivalent to Doxycycline……100mg

2.2 Quantitative declaration:

Composition of unit dose is given below:

Ingredients	Reference	Pharmaceutical Function	Quantity/ Tab (mg)	% w/w
Doxycycline Hyclate#	BP	Antibiotic	115.41	47.69
Hypromellose (HPMC E-15 Premium LV)	EP	Binder	12.00	4.96
Hypromellose (HPMC E-5 Premium LV)	BP	Binder	18.00	7.44
Sodium Lauryl Sulphate	BP	Solubility Enhancer	1.00	0.41
Microcrystalline Cellulose (PH 102)*	BP	Diluent	92.59	38.26
Magnesium stearate	BP	Lubricant	3.00	1.24
Green/Green size "2" hard gelatin capsules	IHS	Unit dose Holder	1 unit	-

BP-British Pharmacopoeia
EP- European Pharmacopoeia
IHS-In-house specification

Calculations:
Quantity of Doxycycline is based on the molecular weight of doxycycline Hyclate (Molecular weight is 512.9) equivalent to Doxycycline (Molecular weight 444.4)
To obtain label claim of 100mg Doxycycline 115.41mg of Doxycycline Hyclate is needed.
*Quantity of Microcrystalline Cellulose to be adjusted based on the actual quantity of Docycycline hyclate taken to achieve Total weight.

2.3 Salts and hydrates

Doxycycline Hyclate

2.4 Esters and pro-drugs

Not applicable

2.5 Oral Powders for solution or suspension

Not applicable

2.6 Parenterals excluding powders for reconstitution

Not applicable

2.7 Powders for reconstitution prior to parenteral administration

Not applicable

2.8 Concentrates

Not applicable

2.9 Transdermal patches

Not applicable

2.10 Multidose solid or semi-solid products

Not applicable

2.11 Biological medicinal products

Not applicable

3. Pharmaceutical form

Description: Hard Gelatin capsules Size "2" with green coloured cap and body, containing yellow granular powder.

4 Clinical Particulars

4.1 Therapeutic indications

KODOXY capsules are indicated for the treatment of following Infections due to sensitive Gram-positive and Gram-negative bacteria:

- Chronic prostatitis;
- Sinusitis;
- Syphilis;
- Pelvic inflammatory disease;
- Treatment and prophylaxis of anthrax;
- Malaria treatment and prophylaxis;
- Recurrentaphthous ulceration;
- Adjunct to gingival scaling and root planning for periodontitis;
- Oral herpes simplex;
- Rosacea;
- Acne vulgaris;
- Lyme disease.

4.2 Posology and Method of Administration

• 200mg on first day, then 100mg daily; severe infections (including refractory urinary-tract infections), 200mg daily

• Early syphilis, 100mg twice daily for 14 days; late latent syphilis, 100mg twice daily for 28 days; neurosyphilis, 200mg twice dailyfor28 days.

• Uncomplicated genital chlamydia, non-gonococcal urethritis, 100mg twice daily for 7 days (14 days in pelvic inflammatory disease)

- Lyme disease, 100mg twice daily for 10-14 days (28 days in Lyme arthritis)

• Anthrax (treatment or post-exposure prophylaxis), 100mg twice daily; CHILD (only if alternative antibacterial cannot be given), 5mg/kg daily in 2 divided doses (max. 200mg daily)

4.3 Method of Administration

Administration via Oral route. To be taken with a glass of water.

4.4 Contraindications

• Known hypersensitivity to doxycycline or other tetracyclines, or a history of a previous major allergic response to a tetracycline due to the possibility of cross sensitivity.

• Deposition of tetracyclines in growing bone and teeth (by binding to calcium) causes staining and occasionally dental hypoplasia, and they should not be given to children under 12 years.

• Doxycycline should not be given to patients with acute porphyria.

4.5 Special warnings and precautions for use

Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines, including doxycycline. Patients likely to be exposed to direct sunlight or ultraviolet light should be advised that this reaction can occur with tetracycline drugs and treatment should be discontinued at the first evidence of skin erythema.

The use of antibiotics may occasionally result in over-growth of non-susceptible organisms, including Candida. If a resistant organism appears, the antibiotic should be discontinued and appropriate therapy instituted. Pseudomembranous colitis has been reported with nearly all antibacterial agents, including doxycycline, and has ranged in severity from mild to life-threatening. It is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents. Bulging fontanelles in infants and benign intracranial hypertension in juveniles and adults have been reported in individuals receiving full therapeutic drugs. These conditions disappeared rapidly when the drug was discontinued. Due to a potential for weak neuromuscular blockade, care should be taken in administering tetracyclines to patients with myasthenia gravis.Tetracyclines can cause exacerbation of systemic lupus erythematosus (SLE). Caution is advised in administering tetracyclines with methoxyflurane.

4.7 Interactions with other medicinal products and other forms of interactions • Antibacterials: Plasma concentration of doxycycline reduced by rifampicin-consider increasing dose of doxycycline;

- Antiepileptics: Metabolism of doxycycline accelerated by carbamazepine (reduced effect); metabolism of doxycycline accelerated by phenobarbital and phenytoin (reduced plasma concentration);
- Cytotoxics: Doxycycline increases risk of methotrexate toxicity;
- Iron: Absorption of tetracyclines reduced by oral iron, also absorption of oral iron reduced by tetracyclines;
- Retinoids: Possible increased risk of benign intracranial hypertension when tetracyclines given with retinoids (avoid concomitant use)
- Zinc: Absorption of tetracyclines reduced by zinc, also absorption of zinc reduced by tetracyclines.
- Alcohol: Decreases half-life of doxycycline

4.8 Pregnancy and Lactation

Doxycycline should not be administered to pregnant and lactating mothers.

4.9 Effects on ability to drive and use machine

Doxycycline may have a minor influence on the ability to drive and use machines. Dizziness (including visual disturbances and blurring of vision) may occur following administration of doxycycline.

4.10 Undesirable effects

Common:Nasopharyngitis, Sinusitis, Fungal infection, Anxiety, Sinus headache, Hypertension, Diarrhoea,Abdominal pain (upper), Dry mouth, Back pain; Rare: Thrombocytopenia, neutropenia, eosinophilia, Hypersensitivity reactions including anaphylaxis, Anaphylactoid purpura, Benign intracranial hypertension, Pericarditis,hypotension, tachycardia, Nausea, vomiting, anorexia, Hepatotoxicity, Maculopapular and erythematous rashes, skin photosensitivity, urticaria; Very rare: Anogenital candidiasis, Haemolytic anaemia, Brown-black microscopic discolouration of thyroid tissue, Bulging fontanelle in infants, angioneurotic oedema, Glossitis,

dysphagia,dyspnoea, enterocolitis, Oesophagitis and oesophageal ulceration, Exfoliative dermatitis, angioneurotic oedema, Stevens-Johnson syndrome, Exacerbation of systemic lupus erythematosus..

4.11 Overdose and antidote

Symptoms of overdose may be from those listed in side effects . Treatment of overdose / Emergency Measures: In case of overdose, Doxycycline must be discontinued. Gastric lavage and supportive treatment initiated, which includes measures to accelerate elimination and symptomatic treatment of adverse reaclions. Dialysis does not alter serum half-life and thus would not be of benefit in treating cases of overdosage .

5.0 Pharmacological properties

5.1 Pharmacodynamic properties

Doxycycline is a tetracycline antibiotic with bacteriostatic mode of action. Doxycycline reversibly binds to the 30 S ribosomal subunits and possibly the 50S ribosomal subunit(s), blocking the binding of aminoacyl tRNA to the mRNAand inhibiting bacterial protein synthesis. Doxycycline prevents the normal function of the apicoplast of Plasmodium falciparum, a malaria causing organism.

SPECTRUM OF ACTIVITY:

The following microorganisms are susceptible to doxycycline under in vivo conditions: Streptococcus pneumoniae, Haemophi/us influenzae, Kfebsie/fa pneumoniae, Mycopfasma pneumoniae, K/ebsie/fa species, Escherichia coli, Streptococcus faecalis, Chlamydia trachomatis, Ureaplasma urealyficum (T-mycoplasma),susceptible strains of staphylococci, gonococci, Borreliasp., Bacillusanthracis, Treponemapallidum

5.2 Pharmacokinetic properties

Absorption:

Absorption is rapid (effective concentrations are attained as from the first hour), and the peak serum concentration (3 µg/ml) occurs after 2 to 4 hours. Almost all of the product is absorbed in the upper part of the digestive tract. Absorption is not modified by administration with meals, and milk has little effect.

Distribution:

In adults, an oral dose of 200 mg results in residual concentration of more than 1 µg/ml after 24 hours, protein binding varying between 82 and 93% (labile binding) intra- and extracellular diffusion is good. With usual dosages, effective concentrations are found in the ovaries, uterine tubes, uterus, placenta, testicles, prostate, bladder, kidneys, lung tissue, skin, muscles, lymph glands, sinus secretions, maxillary sinus, nasal polyps, tonsils, liver, hepatic and gallbladder bile, gallbladder, stomach, appendix, intestine, omentum, saliva and gingival fluid. Doxycycline is transferred into breast milk.

Metabolism:

No significant metabolism occurs

Elimination:

Doxycycline is cleared intact by renal and biliary mechanisms. The antibiotic is concentrated in the bile. About 40% of the administered dose is eliminated in 3 days in active form in the urine and about 32% in the faeces.Urinary concentrations are roughly 10 times higher than plasma concentrations at the same time. In the presence of impaired renal function, urinary elimination decreases, faecal elimination increases and the half-life remains unchanged. The half-life is not affected by haemodialysis.

5.3 Pre-clinical 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 antibacterial drugs, oxytetracycline (adrenal and pituitary tumours) and minocycline (thyroid tumors).

No studies on mutagenicity of doxycycline have been conducted. Positive results in *in vitro* mammalian cell assays have been reported for related antibacterial drugs (tetracycline, oxytetracycline).

Doxycycline administered orally at dosage levels as high as 250mg/kg/day had no apparent effect on the fertility of female rats. Effect on male fertility has not been studied.

6 Pharmaceutical Particulars

6.1 List of Excipients-

Ingredients	Reference
Hypromellose (HPMC E-15 Premium LV)	EP
Hypromellose (HPMC E-5 Premium LV)	BP
Sodium Lauryl Sulphate	BP
Microcrystalline Cellulose (PH 102)	BP
Magnesium stearate	BP
Green/Green size "2" hard gelatin capsules	IHS

BP-British Pharmacopoeia
EP- European Pharmacopoeia
IHS-In-house specification

6.2 Incompatibilities:

None

6.3 Shelf life:

Proposed shelf life: 36 Months (3 years)

6.4 Special precautions for storage:

Store below 30°C in a dry place. Protect from light.

6.5 Nature and contents of container

Alu/ PVC blister of 10x10

6.6 Special precautions for disposal and other handling

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

7. Marketing authorization holder.

KOPRAN LIMITED

Village Savroli, Taluka Khalapur,

District-Raigad-410202

India

8. Marketing authorization registration number(s).

Not applicable

9. Date of first authorization registration/renewal of the authorization:

Not applicable

10. Date of revision (if any) of this text.

Not applicable

11. DOSIMETRY (IF APPLICABLE)

Not applicable

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE)

Not applicable