TYFLOX

Ciprofloxacin

TYFLOX (Ciprofloxacin) is a fluorinated 4-quinolone antimicrobial agent. **TYFLOX** has broad spectrum activity. As antibacterial concentrations of Ciprofloxacin are obtained in serum and body tissues as well as in the urine following administration by mouth, **TYFLOX** has been suggested for use in the treatment of a wide range of infections caused by susceptible organisms including infections of the urinary, respiratory & gastrointestinal tracts, gonorrhoea and septicaemia.

The half-life of Ciprofloxacin is about 3.5 to 4.5 hours. About 30-50% of an oral dose of Ciproflaxacin is excreted in the urine within 24 hours as unchanged drug and biologically active metabolites.

COMPOSITION

TYFLOX 250 Tablet□: Each film coated tablet contains Ciprofloxacin USP 250 mg as □ □Hydrochloride Monohydrate.

TYFLOX 500 Tablet□: Each film coated tablet contains Ciprofloxacin USP 500 mg as □ □Hydrochloride Monohydrate.

TYFLOX 750 Tablet□: Each film coated tablet contains Ciprofloxacin USP 750 mg as □ □Hydrochloride Monohydrate.

TYFLOX Pellets for Suspension : When reconstituted each 5 ml suspension contains □ □ □ Ciprofloxacin USP 250 mg as Hydrochloride.

CLINICAL PHARMACOLOGY

In vitro studies have shown that the antibacterial action of Ciprofloxacin results from the inhibition of bacterial DNA gyrase. This mode of action differs from that of penicillins, cephalosporins, aminoglycosides and tetracyclines. Therefore, organisms resistant to these antibiotics are generally sensitive to Ciprofloxacin.

INDICATION

TYFLOX is indicated for the treatment of single infection or mixed infections caused by two or more susceptible organisms. **TYFLOX** can also be used for infections caused by organisms resistant to other antibiotics including aminoglycosides, penicillins and cephalosporins. The extensive tissue penetration of Ciprofloxacin combined with its enhanced antibacterial activity (including antipseudomonal activity), enables **TYFLOX** to be used alone (depending on sensitivity results) or in combination with an aminoglycoside or with beta-lactam antibiotics. For instance, when severe neutropenia is present or with an antibiotic active against anaerobes where the presence of *Bacteroides fragilis* is suspected. **TYFLOX** is indicated for the treatment of the following infections caused by sensitive bacteria: **Severe systemic infections**: Septicaemia, bacteremia, peritonitis, infections in immunosuppressed patients with hematological or solid tumors and in patients in intensive care with specific problems such as infected burns. **Respiratory tract infections**: Lobar and bronchopneumonia, acute and chronic bronchitis, acute exacerbation of cystic fibrosis, bronchiectasis, empyema. **Urinary tract infections**: Uncomplicated and complicated urethritis, cystitis, pyelonephritis, prostatitis, epididymitis. **Skin and soft tissue infections**: Infected ulcers, wound infections, abscesses, cellulitis, otitis externa, erysipelas, infected burns. **Gastro-intestinal infections**: Enteric fever, infective diarrhoea. **Infections of the biliary tract**: Cholangitis, cholecystitis, empyema of the gall bladder. **Intra-abdominal infections**: Peritonitis, intra-abdominal abscesses. **Bone and joint infections**: Osteomyelitis, septic arthritis. **Pelvic infections**: Salpingitis, endometritis, pelvic inflammatory diseases. **Eye, ear, nose and throat infections**: Otitis media, sinusitis, mastoiditis, tonsillitis. **Gonorrhoea**: Urethral, rectal and pharyngeal gonorrhoea caused by beta-lactamase producing organisms or organisms moderately sensitive to penicillins.

DOSAGE AND ADMINISTRATION

General dosage recommendations: The dosage of **TYFLOX** is determined by the sensitivity of the causative organism(s) and the age, weight and renal function of the patient. **Adolescents and children**: 20-30 mg/kg/day in 2 divided dosage. *Cystic fibrosis :* 20-40 mg/kg/day in 2 divided dosage.

Adults: The dosage range for adults is 250-750 mg twice daily.

DOASAGE SCHEDULE OF TYFLOX

Indications □ □	Type of Severity □ □	Recommended □ Daily dose □	Length of Treatment
Urinary tract □ infections □	Mild to moderate □	250 mg b.i.d. □	7-14 days
	Severe & complicated □	500 mg b.i.d. □	7-14 days
Respiratory tract □ infections □	Mild to moderate □	500 mg b.i.d. □	7-14 days
	Severe & complicated □	750 mg b.i.d. □	7-14 days
Skin & soft tissue □ infections □	Mitd to moderate □	500 mg b.i.d. □	7-14 days
	Severe & complicated □	750 mg b.i.d. □	7-14 days
Bone & joint □ infections □	Mild to moderate □	500 mg b.i.d. □	≥ 4-6 weeks
	Severe & complicated □	750 mg b.i.d. □	≥ 4-6 weeks
Eye, ear, nose & □ throat infections □	Mild to moderate □	250 mg b.i.d. □	7-14 days
	Severe □	750 mg b.i.d. □	7-14 days
Infectious diarrhoea □	Mild, moderate & severe □	500 mg b.i.d. □	5-7 days
Enteric fever □	Mild, moderate & severe □	500 mg b.i.d. □	10 -14 days
Gonorrhoea □	□	250-500 mg Single dose □	1 day
Chancroid □	□	500 mg b.i.d.□	1-3 days

* Duration of treatment depends upon the severity of infections. For severe and complicated infections more prolonged therapy may be required.

Pediatric patients & adolescents (1 to 17 years of age):

Complicated Urinary Tract infections and Pyelonephritis due to *Escherichia coli.*

PEDIATRIC DOSAGE GUIDELINE

Infection	Route of Administraton	Dose(mg/kg)	Frequency	Total Duration
Complicated Urinary Tract or Pyelonephritis (patients from 1 to 17 years of age)	Oral	10 mg/kg to 20 mg/kg (maximum 750 mg per dose; not to be exceeded even in patients weighing >51 kg)	b.i.d	10-12 days
		6 to 10 mg/kg (maximum 10 mg/kg) (maximum 400 mg per dose)	Every 8 hours	

Cystic fibrosis: In adults with pseudomonal infections of the lower respiratory tract, the normal dose is 750 mg twice daily. As the pharmacokinetics of Ciprofloxacin remain unchanged in patients with cystic fibrosis, the low body weight of these patients would be taken into consideration when determining the dosage. Impaired renal function: Dosage adjustment is not usually required except in patients with severe renal impairment (serum creatinine> 265 micromol/l or creatinine clearance<20 ml/minute). If adjustment is necessary, this may be achieved by reducing the total daily dose by half, although monitoring of drug serum levels provide the most reliable basis for dose adjustment. *Elderly:* Although higher Ciprofloxacin serum levels are found in the elderly, no adjustment of dosage is necessary.

CONTRAINDICATION

Ciprofloxacin is contraindicated in patients who have shown hypersensitivity to Ciprofloxacin or other quinolones. Ciprofloxacin is also contraindicated in children and growing adolescents except where the benefits of treatment exceed the risks.

Use in pregnancy and lactation: Reproduction studies performed in mice, rats and rabbits using parenteral and oral administration did not reveal any evidence of teratogenicity, impairment of fertility or impairment of pre/post-natal development. However as with other quinolones, Ciprofloxacin has been shown to cause arthropathy in immature animals and therefore, its use during pregnancy is not recommended. Studies in rats have indicated that Ciprofloxacin is secreted in milk, thus administration to nursing mothers is not recommended.

WARNING AND PRECAUTION

Ciprofloxacin should be used with caution in patients with a history of convulsive disorders. Crystalluria related to the use of Ciprofloxacin has been observed only rarely. Patients receiving Ciprofloxacin should be well hydrated and excessive alkalinity of the urine should be avoided.

DRUG INTERACTION

Concurrent administration of Ciprofloxacin with theophylline may lead to elevated plasma concentrations of theophylline and prolongation of its elimination half-life. This may result in increased risk of theophylline-related adverse reactions. If concomitant use cannot be avoided plasma levels of theophylline should be monitored and dosage adjustments made as appropriate.

Antacids containing Magnesium hydroxide or Aluminium hydroxide may interfere with the absorption of Ciprofloxacin resulting in serum and urine levels lower than desired. So, concurrent administration of these agents with Ciprofloxacin should be avoided. Probenecid interferes with renal tubular secretion of Ciprofloxacin and produces an increase in the level of Ciprofloxacin in the serum. This should be considered if patients are receiving both drugs concomitantly.

As with other broad spectrum antibiotics, prolonged use of Ciprofloxacin may result In overgrowth of non susceptible organisms. Repeated evaluation of the patient's condition and microbial susceptibility testing is essential. If superinfection occurs during therapy, appropriate measures should be taken.

SIDE EFFECT

Gastrointestinal disturbances: Nausea, diarrhoea, vomiting, dyspepsia, abdominal pain. *Disturbance of the central nervous system:* Dizziness, headache, tiredness, confusion, convulsions.

HYPERSENSITIVITY REACTION

Skin rashes, pruritus and possible systemic reactions. *Other reactions:* Joint pain, mild photosensitivity and transient increase in liver enzymes (particulariy in patients with previous liver damage) serum bilirubin, urea or creatinine levels.

OVERDOSAGE

No information on overdose is available. In case of overdose routine measures such as gastric lavage should be performed as soon as possible after ingestion of Ciprofloxacin tablets. Serum levels of Ciprofloxacin are reduced by dialysis.

INFORMATION TO THE PATIENT

Patients should be advised that Ciprofloxacin may be taken with or without meals. The preferred time of dosing is two hours after a meal. Patients should also be advised to drink fluids liberally and not to take antacids containing Magnesium or Aluminium concomitantly or within two hours after dosing. Ciprofloxacin may cause dizziness and light-headedness, therefore patients should know how they react to this drug before they operate an automobile or machinery or engage in activities requiring mental alertness or coordination.

The tablet should be swallowed whole with water or fruit juice. Medicine should be kept in a cool, dry place, away from light and out of reach of children.

PACKAGING

TYFLOX 250 Tablet: Box containing 3 x 10's tablet in blister pack.

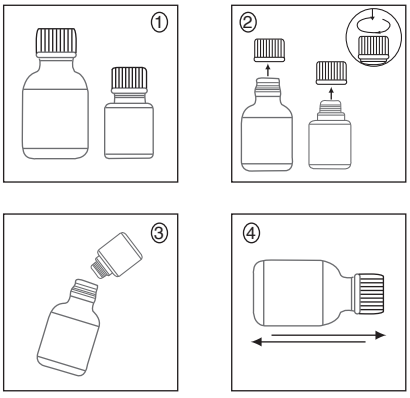
TYFLOX 500 Tablet: Box containing 3X10's tablet in blister pack.

TYFLOX 750 Tablet: Box containing 1X10's tablet in blister pack.

TYFLOX Pellets for Suspension: Small bottle contains pellets and large bottle contains diluent.

Special instruction for Tyflox Pellets for Suspension.

DIRECTION OF PREPARATION:



As per above figure-

1. Small glass bottle contains Ciprofloxacin pellets and large PET bottle contains diluent
2. Open the cap of both the bottles
3. Pour the Ciprofloxacin pellets completely into the large bottle of diluent. Do not add □water to the suspension
4. Tight the cap of large bottle completely and shake vigorously until it is propery mixed. Now the suspension is ready for use.

Prepared suspension is to be consumed within 14 days of preparation if kept in room temperature or in a refrigerator.

Appropriate dosing volumes of the Tyflox Pellets for Suspension:
250 mg Ciprofloxacin is equivalent to 1 tea-spoonful (5 ml) suspension
500 mg Ciprofloxacin is equivalent to 2 tea-spoonful (10 ml) suspension
750 mg Ciprofloxacin is equivalent to 3 tea-spoonful (15 ml) suspension

Manufactured by
SOMATEC PHARMACEUTICALS LTD.
SARULIA, DEMRA, DHAKA, BANGLADESH.