

especially in those with hypertension, the use of nasal decongestants must be supervised by the physician. The prolonged use of preparations containing vasoconstrictive substances may alter the normal function of the nasal mucosa and of the paranasal sinuses, thus inducing drug addiction. Therefore, repeated applications for long periods may be harmful.

Rinofluimucil should be used with due caution in pediatrics, asthmatic patients, the elderly and subjects suffering from prostatic hypertrophy due to the risk of urinary retention.

Effects on the Ability to Drive or Operate Machinery: There is no evidence that Rinofluimucil can affect attention or reaction time.

**Use in pregnancy & lactation:** Rinofluimucil should be given to pregnant and lactating women only in case of real need, under medical supervision.

**ADVERSE REACTIONS:** Frequent administrations of Rinofluimucil at the highest dosage may cause adverse events of sympathomimetic nature eg, increase in excitability, cardiac palpitations, tremor, hypertension, headache and urination troubles.

**INTERACTIONS:** There is no evidence in literature of clinically significant interactions with the active ingredients of Rinofluimucil. The use of vasoconstrictors is not suggested during the treatment with tricyclic antidepressants.

**STORAGE:** Shelf-Life: 30 months. After first opening, Rinofluimucil can be used for a period not exceeding 20 days.

## SPEDIFEN

**CONTENTS:** \* Ibuprofen as arginine.

**PRESENTATION:** Tab 400 mg (film-coated) 5 x 6's.

**DESCRIPTION:** Ibuprofen arginine is a highly soluble salt formed by combining racemic ibuprofen with the amino acid L-arginine. The presence of arginine facilitates the dissolution of ibuprofen (in gastrointestinal tract), permitting more rapid absorption of ibuprofen. The principal effect of this product is more rapid onset of the analgesic and anti-inflammatory actions of ibuprofen.

**ACTIONS:** Spedifen has analgesic, antipyretic and prominent anti-inflammatory effects. The analgesic effects of ibuprofen are the result of both peripheral and central effects and are distinct from its anti-inflammatory properties.

Similar to other NSAIDs, Spedifen is potent, unspecific inhibitor of the isoenzymes cyclooxygenase-1 (COX-1) and -2 (COX-2) which results in a marked reduction in prostaglandin and thromboxane synthesis. In contrast to salicylates which irreversibly acetylate the cyclooxygenases, propionic derivatives compete with the precursor arachidonic acid at the active site of the enzymes in a reversible manner.

Besides the reduction of prostaglandin and thromboxane formation, ibuprofen arginine also partly inhibits the synthesis of several lipooxygenase products.

Analgesic, antipyretic and anti-inflammatory effects of the inhibition of prostaglandin synthesis prevent their hyperalgetic effect upon sensory nerves; reduction of vasodilator prostanoid formation (PGE<sub>2</sub>) diminishes vascularity and fluid transudation, which are main manifestations of inflammation.

**Pharmacokinetics:** Ibuprofen arginate and the analogous amino acid/ibuprofen salt formulation ibuprofen lysinate produce peak plasma levels considerably earlier and higher than ibuprofen acid, while bioavailability and elimination kinetics remain similar. Peak plasma levels are achieved 0.5-0.6 hr after administration of ibuprofen arginate and 0.55-0.75 hr after administration of ibuprofen lysinate. The systemic bioavailability of ibuprofen lysinate is complete.

**INDICATIONS:** \* Symptomatic relief of pain (eg, headache, toothache, dysmenorrhea, osteoarticular and muscular pain). Fever due to influenza.

**DOSAGE & ADMINISTRATION:** \* **Adults and Children >12 years:** 1 tab 3-4 times a day.

Do not exceed 4 tabs a day. Elderly, in particular, should use the lowest advised dose.

**CONTRAINDICATIONS:** \* Patients who have previously shown hypersensitivity to the components of Spedifen or to other antirheumatic drugs (acetylsalicylic acid, etc).

Patients with active or severe peptic ulceration or other gastropathies.

Patients with severe hepatic or renal impairment.

**Use in pregnancy & lactation:** Spedifen is contraindicated in pregnant and lactating women.

**WARNINGS:** After a short period of treatment without appreciable results, consult the physician. In patients whose activity requires surveillance should pay attention if somnolence, dizziness or depression occurs during ibuprofen treatment.

Spedifen cannot be used in haemorrhagic-fever patients.

**PRECAUTIONS:** \* In patients suffering from asthma, Spedifen must be administered only in case of real need and under physician's control.

**ADVERSE REACTIONS:** \* Sometimes cutaneous allergic reaction (erythema, urticaria and pruritus) may be experienced. The most frequent adverse events occurring with ibuprofen are gastrointestinal disturbances. These include dyspepsia, abdominal pain and, sometimes, constipation or diarrhoea. The frequency of nausea and vomiting is rare. Exceptionally, the appearance of ulcers has been reported. These may be accompanied by gastrointestinal bleeding. Such events quickly disappear upon suspension of treatment.

Consult the physician or pharmacist if adverse events, other than those previously mentioned occur.

**INTERACTIONS:** \* Interactions with coumarin-type anticoagulants should occur. Patients undergoing such therapy should consult the physician before treatment with Spedifen. In cases of any concomitant treatment with other drugs, it is advisable to consult the physician before starting with Spedifen.

## URFAMYCIN

**CONTENTS:** Thiamphenicol.

**PRESENTATION:** Cap 250 mg x 20's, 1000's. 500 mg x 5's, 500's. Vial 0.5 g x 1's, 100's. 0.75 g x 1's.

**DESCRIPTION:** Urfamycin capsule contains thiamphenicol while the injection contains thiamphenicol glycinate.

Thiamphenicol is D(+)-threo-2-dichloroacetamido-1-(4-methylsulfonylphenyl)propane-1,3-diol.

Empirical Formula: C<sub>12</sub>H<sub>15</sub>Cl<sub>2</sub>NO<sub>5</sub>S.

Molecular Weight: 356.24.

Thiamphenicol is a white crystalline, odorless powder with a slightly bitter taste. The substance used in therapy is one of the optically active isomers of the compound having the configuration D-threo. The rotation of polarized light varies according to the solvent. It is (+) in alcohol and (-) in dimethylformamide.

Thiamphenicol glycinate is D(+)-threo-2-dichloroacetamido-3-aminoacetoxy-1-(4-methylsulfonylphenyl)-propane-1-ol.

Empirical Formula:  $C_{14}H_{19}Cl_2N_2O_6S$ .

Molecular Weight: 449.74.

Thiamphenicol glycinate HCl is a white crystalline, practically odorless, insipid powder. Each gram is equivalent to thiamphenicol 0.792 g. It is the highly water-soluble derivative of thiamphenicol obtained by esterification of the primary alcoholic hydroxy group of thiamphenicol with glycine and successive salification with hydrochloric acid. After introduction in the organism, the cleavage of the ester bond is accelerated by the combined effect of the increase in pH and the tissue esterases, thus ensuring a rapid and complete liberation of thiamphenicol.

**ACTIONS:** Broad-spectrum antibiotic.

**Pharmacology:** Bacteriostatic and Bactericidal Activities: Urfamycin has primarily a bacteriostatic action. It becomes bactericidal only at concentrations that are many times superior to the minimum effect in inhibiting bacterial growth.

There exist, nevertheless, a certain number of bacteria on which Urfamycin has a bactericidal action at concentrations that are equal or only a few times superior to the bacteriostatic ones. In this group, we find bacteria of considerable clinical importance belonging to the genera *Diplococcus*, *Streptococcus*, *Neisseria*, *Klebsiella* and *Brucella*.

**Microbiology:** The antibacterial action of Urfamycin consists in the inhibition of protein synthesis within the bacterial cell. This inhibition does not concern the activation of the amino acids, their association with the molecules of soluble-RNA and the synthesis of messenger-RNA, rather, it presumably consists in blocking the attachment of messenger-RNA on the ribosomes, thus impeding their function.

**Pharmacokinetics:** Urfamycin is readily absorbed by the oral as well as the parenteral route. Once absorbed, it is effectively available at the various sites of infection as it is not inactivated by metabolic processes, is not bound to the plasma proteins, freely diffuses into the interstitial fluids and the cells of the different tissues, and is excreted in high active concentrations in the urine and the bile.

Upon topical application, Urfamycin glycinate acts directly because of its rapid hydrolysis which does not require preliminary absorption. When applied to structures capable of absorption, it penetrates deeply in them, thus providing tissue levels which are effective against certain localized infections and not simply a superficial antibacterial effect.

**INDICATIONS:** Urfamycin is a synthetic antibiotic with a broad antibacterial spectrum against both gram-positive and gram-negative organisms, which seldom provokes antibacterial resistance. It is also active against several species of rickettsiae and some protozoa, but it seems devoid of antimycotic or antiviral activity. Urfamycin, for its characteristics of absorption, diffusion and absence of inactivation in the body, ensures high antibacterial concentrations in the blood, tissues and, above all, in the excretory ways (urinary, hepatobiliary, enteric tracts), that permits very satisfactory therapeutic results in several infections. Urfamycin glycinate is used for injections, aerosols and bronchial instillations.

For Systemic Use: Infections of the urogenital, hepatobiliary, enteric tracts; typhoid, paratyphoid fever and other salmonellosis; brucellosis; respiratory infections and, in general, all the infections caused by organisms sensitive to Urfamycin.

For Topical Use: Laryngotracheitis, pertussis, bronchitis, bronchiectasis, tonsillitis, lung abscess, empyema, sinusitis, rhinitis, rhinopharyngitis, otitis, mastoiditis, peritonitis, etc.

**DOSAGE & ADMINISTRATION:** *Capsule, Injection (IM, IV):*

**Adults:** Average daily dose is 1.5 g (500 mg every 8 hrs).

**Children:** The average oral and parenteral dose is 20-30 mg/kg body weight/day.

During the 1st week of treatment, these daily doses may be increased by the physician up to 3 g for adults and 50 mg/kg body weight for children in typhoid fever and other salmonellosis.

The duration of treatment may vary from a few days to 2-3 weeks, according to the infection and clinical response.

Urfamycin by the IV use must be injected slowly.

**CONTRAINDICATIONS:** Hematopoietic disorders, anuria and severe hepatic insufficiency.

**WARNINGS:** In pregnant women and infants, Urfamycin is to be used only under medical supervision. In mild renal insufficiency (creatinine clearance = 50 to 20 mL/min) and in elderly patients of >65 years, the dose should be reduced to 0.5 g thiamphenicol, twice a day; in severe renal insufficiency (creatinine clearance = 20 to 5 mL/min), the dose should not exceed 0.5 g once a day, in order to avoid accumulation. In prolonged treatments and when high doses are needed, it is advisable to perform periodical blood examinations.

**ADVERSE REACTIONS:** The symptomatic side effects which are mentioned in the clinical therapeutic studies on thiamphenicol were common disturbances of the gastrointestinal tract, skin and mucous membrane or of mild general nature, while symptoms of neurological, hematopoietic, hepatic or renal interference were completely absent.