(I) NOVARTIS

Flotac[®]

Anti-inflammatory and anti-rheumatic product. non-steroid, acetic acid derivative.

DESCRIPTION AND COMPOSITION Pharmaceutical form(s)

Hard gelatine capsules

Active substance(s) The active substance is diclofenac-cholestyram or [o[(2.6-dichlorophenyl)-amino]-phenyl]-acetate

resinate (= diclofenac resinate). Diclofenac is bound on resinate as an ion exchanger. Resinate is a basic ion exchanger sting of polymers of styrol and approx 2% divinylbenzene with groups of quaternary ammonium included in the net structure. One capsule contains 145 6 mg diclofenac resinate (corresponding to 75 mg diclofenac sodium).

Active moiety

Excipients Cansule content: Charcoal activated: weak cationic exchange resin (Cross linked polyacrylic acid resin); magnesium stearate.

Cansule shell content: gelatine: titanium dioxide (E171): iron oxide vellow (E172) and printing ink.

Printing ink: Shellac (E904); propylene glycol; onia solution, concentrated; potassium hydroxide: iron oxide black (F172)

INDICATIONS

- Acute arthritis (including acute attacks of gout)
- arthritis (chronic polyarthritis).

- Ankylosing spondylitis (Morbus Bechterew) and other inflammatory, rheumatoid
- and spondylarthritis, cervical syndrom, lumbalgia ischialgia)
- Inflammatory rheumatism of soft tissues. Painful post-traumatic or post-operative
- swelling and inflammation. Painful menstruation (dysmenorrhea without organic findings) Pain due to acute or subacute adnexitis
- (in general an antibiotic treatment is indicated as basic therapy). Pain caused by tumor, especially if the skeleton is affected or for inflammatory

peritumoral edema. DOSAGE AND ADMINISTRATION

As a general recommendation, the dose should he individually adjusted. Adverse effects may he minimized by using the lowest effective dose for the shortest duration necessary to control symptoms (see section WARNINGS AND

General target population

The recommended dose range for Flotac in adults is 1 to maximal 2 capsules per day, depending on the severity of the disorder.

If necessary, adults receive 2 x 1 capsule Flotac per day. The daily dose should be divided into 2 separate doses.

In milder cases, as well as for long-term therapy, 1 capsule per day is usually sufficient.

Special populations Pediatrics

Chronic arthritis, especially rheumatoid

No adjustment of the starting dose is required syndroms of the vertrebral column. for elderly patients (see section WARNINGS AND PRECAUTIONS) Irritation in degenerative diseases of the ioints or the vertebral column (active arthritis Established cardiovascular disease or significant cardiovascular risk factors

> recommended in nationts with established cardiovascular disease or uncontrolled

pertension. If needed, patients with established cardiovascular disease, uncontrolled hypertension or significant risk factors for ardiovascular disease should be treated with Flotac only after careful consideration and only at doses ≤ 100 mg daily if treated for more than 4 weeks (see section WARNINGS AND

Geriatrics (Patients aged 65 or above)

Treatment with Flotac is generally not

PRECAUTIONS). Renal impairment

Flotac is contraindicated in patients with renal failure (see section CONTRAINDICATIONS)

No specific studies have been carried out in patients with renal impairment, therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering Flotac to patients with mild to moderate renal impairment (see section WARNINGS AND

Hepatic impairment

Flotac is contraindicated in patients with hepatic failure (see section CONTRAINDICATIONS)

No specific studies have been carried out in patients with hepatic impairment, therefore, no specific dose adjustment recommendations can be made. Caution is advised when administe Voltaren Resinate to patients with mild to moderate hepatic impairment (see section WARNINGS AND PRECAUTIONS)

Method of administration

Because of their dosage strength and the lack of The cansules should be swallowed whole with possibility of individual dosing, Flotac capsules liquid, preferably during meals, and must not be are not suitable for children and adolescents.

CONTRAINDICATIONS

- Known hypersensitivity to the active
- substance or to any of the excipients Active gastric or intestinal ulcer bleeding AND PRECAUTIONS and ADVERSE DRUG REACTIONS).
- WOCBP, PREGNANCY, BREAST-FEEDING AND FERTILITY
- Hepatic failure
- Renal failure Severe cardiac failure (see section WARNINGS AND PRECAUTIONS)
- Like other non-steroidal anti-inflammatory drugs (NSAIDs), Flotac is also contraindicated in patients in whom attacks of asthma. urticaria, or acute rhinitis are precipitated by acetylsalicylic acid or other NSAIDs (see sections WARNINGS AND PRECAUTIONS and ADVERSE DRUG REACTIONS).

WARNINGS AND PRECAUTIONS Gastrointestinal effects

Gastrointestinal bleeding, ulceration or perforation, which can be fatal, have been reported with all NSAIDs, including diclofenac. and may occur at any time during treatment with or without warning symptoms or a previous history of serious gastrointestinal events. They nerally have more serious consequences n the elderly. If gastrointestinal bleeding or ulceration occurs in patients receiving Flotac the medicinal product should be withdrawn.

As with all NSAIDs, including diclofenac, close nedical surveillance is imperative and particular caution should be exercized when prescribing Flotac in patients with symptoms indicative of gastrointestinal (GI) disorders or with a history uggestive of gastric or intestinal ulceration. ng or perforation (see section ADVERSE DRUG REACTIONS) The risk of GI bleeding is higher with increasing NSAID doses and in patients with a history of ulcer, particularly if

complicated with hemorrhage or perforation and in the elderly.

To reduce the risk of GI toxicity in patients with a history of ulcer, particularly if complicated orrhage or perforation, and in the elderly the treatment should be initiated and maintained at the lowest effective dose.

Combination therapy with protective agents (e.g. proton pump inhibitors or misoprostol) should be considered for these patients, and also for patients requiring concomitant use of medicinal products containing low-dose acetylsalicylic acid (ASA) or other medicinal products likely to increase gastrointestinal risk

Patients with a history of GI toxicity, particularly the elderly, should report any unusual abdomina symptoms (especially GI bleeding). Caution is mmended in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as systematical corticosteroids, anticoagulants, anti-platelet agents or selective serotonin-reuptake inhibitors see section INTERACTIONS).

Close medical surveillance and caution should also be exercized in patients with ulcerative colitis or Crohn's disease, as their condition may be exacerbated (see section ADVERSE DRUG REACTIONS).

Cardiovascular effects

Treatment with NSAIDs including diclofenac particularly at high dose and in long term, may be associated with a small increased risk of serious cardiovascular thrombotic events (including myocardial infarction and stroke).

Treatment with Flotac is generally not recommended in patients with establishe cardiovascular disease (congestive heart failure, established ischemic heart disease peripheral arterial disease) or uncontrolled pertension. If needed, patients with established cardiovascular disease, uncontrolled hypertension or significant risk factors for

cardiovascular disease (e.g. hypertension nyperlipidemia, diabetes mellitus and smokin should be treated with Flotac only after careful consideration and only at doses < 100 mg laily when treatment continues for more than

As the cardiovascular risks of diclofenac may increase with dose and duration of exposure the lowest effective daily dose should be used for the shortest duration possible. The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically. especially when treatment continues for more than 4 weeks.

Patients should remain alert for the signs and symptoms of serious arteriothrom (e.g. chest pain, shortness of breath, weakness, slurring of speech), which can occur without warnings. Patients should be instructed to see a physician immediately in case of such an event.

Hematologic effects During prolonged treatment with Flotac, as with other NSAIDs, monitoring of the blood count is

recommended Like other NSAIDs. Flotac may temporarily

inhibit platelet aggregation. Patients with defects of hemostasis should be carefully monitored. Respiratory effects (pre-existing asthma)

In patients with asthma, seasonal allergic rhinitis, swelling of the nasal mucosa (i.e. nasal polyps), chronic obstructive pulmonary diseases or chronic infections of the respiratory tract (especially if linked to allergic rhinitis-like symptoms), reactions on NSAIDs like asthma exacerbations (so-called intolerance to analgesics/analgesics-asthma), Quincke's edema or urticaria are more frequent than ir other patients. Therefore, special precaution s recommended in such patients (reading for emergency). This is applicable as well for patients who are allergic to other substances e.g. with skin reactions, pruritus or urticaria.

Henatohiliary effects

Close medical surveillance is required when rescribing Flotac to patients with impaired nenatic function, as their condition may be exacerbated.

As with other NSAIDs, including diclofenac, values of one or more liver enzymes may ncrease. During prolonged treatment with Flotac, regular monitoring of hepatic function is indicated as a precautionary measure. If abnormal liver function tests persist or worsen if clinical signs or symptoms consistent with iver disease develop, or if other manifestat occur (e.g. eosinophilia, rash) Flotac should be discontinued. Hepatitis may occur with use of diclofenac without prodromal symptoms.

Skin reactions

fatal, including exfoliative dermatitis Stevens-Johnson syndrome and toxic arely in association with the use of NSAIDs he majority of cases within the first month of

As with other NSAIDs, allergic reactions including anaphylactic/anaphylactoid reactions, can also occur in rare cases with diclofenac without earlier exposure to the drug

As fluid retention and edema have been reported in association with NSAID therapy, including diclofenac, particular caution is called for in patients with impaired cardiac or renal function,

therapy is usually followed by recovery to the pre-treatment state. **Geriatric patients** Caution is indicated in the elderly on

Caution is called for when using Flotac in patients with hepatic porphyria, since it may trigger an attack

Serious skin reactions, some of them

epidermal necrolysis, have been reported very including Flotac (see section ADVERSE DRUG REACTIONS). Patients appear to be at highest risk of these reactions early in the course of therapy the onset of the reaction occurring in treatment. Flotac should be discontinued at the first appearance of skin rash, mucosal lesions or any other sign of hypersensitivity.

Renal effects

receiving concomitant treatment with diuretics or medicinal products that can significantly

history of hypertension, the elderly nationts

impact renal function, and in those patients ith substantial extracellular volume depletion from any cause, e.g. before or after major surgery (see section CONTRAINDICATIONS) oring of renal function is recommended as a precautionary measure when using Flotac in such cases Discontinuation of

basic medical grounds. In particular it is recommended that the lowest effective dose be used in frail elderly patients or those with a low hody weight Interaction with other NSAIDs

ne concomitant use of Flotac with systemic NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided due to the potential for additive undesirable effects (see section INTERACTIONS).

Masking signs of infections Like other NSAIDs, Flotac may mask the signs and symptoms of infection due to its

pharmacodynamic properties. ADVERSE DRUG REACTIONS

Tabulated summary of adverse drug

Adverse drug reactions from clinical trials and/or spontaneous or literature reports (Table 1) are listed by MedDRA system organ class. Within each system organ class, the adverse drug reactions are ranked by frequency, with the most frequent reactions first. Within each frequency grouping, adverse drug reactions are presented in order of decreasing seriousness. In addition the corresponding frequency category for each adverse drug reaction is based on the following convention (CIOMS III): very common (>1/10)

common ($> 1/100 \text{ to } < 1/10) \cdot \text{uncommon}$ $(\geq 1/1,000 \text{ to } < 1/100)$; rare $(\geq 1/10,000 \text{ to})$ <1/1.000); very rare (<1/10.000).

The following undesirable effects include those reported with Flotac capsules and/or other pharmaceutical forms of diclofenac, with either short-term or long-term use.

Table 1 Adverse drug reactions

Blood and lymphatic system disorders Very rare: Thrombocytopenia, leukopenia anemia (including hemolytic and aplastic anemia), agranulocytosis mune system disorders

Rare: Hypersensitivity, anaphylactic

and anaphylactoid reactions (including hypotension and Angioedema (including face Very rare:

Psychiatric disorders Verv rare:

insomnia, nightmare, irritability, psychotic disorder. ervous system disorders Headache, dizziness, Somnolence

Paresthesia, memory

aseptic, dysgeusia,

impairment, convulsio

anxiety tremor meningitis

cerebrovascular accident.

Disorientation, depression

Eve disorders

Very rare:

Visual impairment, vision Very rare: blurred, diplopia.

Ear and labyrinth disorders Common: Vertigo.

Tinnitus, hearing impaired. Very rare. Cardiac disorders

Uncommon*: Myocardial infarction, cardiac failure nalpitations chest pair

Vascular disorders

Very rare: Hypertension, vasculitis Respiratory, thoracic and mediastinal disorders

Asthma (including dyspnea) Rare: Very rare:

Gastrointestinal disorders Common: Nausea, vomiting, diarrhea

dyspensia, abdominal pain. flatulence, decreased appeti Gastritis, gastrointestinal hemorrhage hematemesis melena, gastrointestinal ulce (with or without bleeding or

Colitis (including hemorrhagi colitis and exacerbation of ulcerative colitis or Crohn's disease) constination

stomatitis, glossitis, intestinal diaphragm disease

pancreatitis. epatobiliary disorders

Rare: Hepatitis, jaundice, liver Henatitis fulminant henatic Very rare: necrosis henatic failure

Skin and subcutaneous tissue disorders

Rash. Rare: Urticaria. Very rare:

Dermatitis bullous, eczema, erythema, erythema multiforme. Stevens-Johnso syndrome, toxic epidermal necrolysis (Lyell's syndrome) dermatitis exfoliative, alopecia photosensitivity reaction, purpura, Henoch-Schonlein purpura, pruritus,

Renal and urinary disorders Renal failure acute, hematur Very rare: proteinuria nephrotic syndrome, tubulointerstitial nephritis, renal papillary

General disorders and administration site

Rare:

* The frequency reflects data from long-term treatment with a high dose (150 mg daily).

Description of selected adverse drug

Arteriothrombotic events Meta-analysis and pharmacoepidemiological data point towards a small increased risk of arteriothromhotic events (for example myocardial infarction) associated with the use of diclofenac, particularly at a high dose (150 mg daily) and during long-term treatment (see section WARNINGS AND PRECAUTIONS).

INTERACTIONS

The following interactions include those observed with Flotac capsules and/or other pharmaceutical forms of diclofenac.

Observed interactions to be considered **Potent CYP2C9 inhibitors:** Caution is recommended when co-prescribing diclofena

with potent CYP2C9 inhibitors (such as voriconazole), which could result in a significant increase in peak plasma concentrations and xposure to diclofenac due to inhibition of diclofenac metabolism

Lithium: If used concomitantly, diclofenac may raise plasma concentrations of lithium Monitoring of the serum lithium level is

Digoxin: If used concomitantly, diclofenac nay raise plasma concentrations of digoxin Monitoring of the serum digoxin level is

Diuretics and antihypertensive agents: Like other NSAIDs, concomitant use of diclofenac beta-blockers, angiotensin converting enzyme (ACE) inhibitors) may cause a decrease in their antihypertensive effect. Therefore, the combination should be administered with caution and patients, especially the elderly should have their blood pressure periodically monitored Patients should be adequately

section WARNINGS AND PRECAUTIONS) it should be given at doses lower than those

Drugs known to cause hyperkalemia: may be associated with increased serum. potassium levels, which should therefore be

Quinolone antibacterials: There have been isolated reports of convulsions which may have been due to concomitant use of quinolones and

exchanger, generally an inhibition of absorption of other orally given medicinal products has to he taken into account Anticipated interactions to be considered

Concomitant administration of diclofenac and

other systemic NSAIDs or corticosteroids may

increase the frequency of gastrointestinal

Due to the fact that resinate is a basic ion.

with diuretics or antihypertensive agents (e.g. hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy and periodically thereafter particularly for diuretics and ACE inhibitors due to the increased risk of nephrotoxicity (see

Ciclosporin: Diclofenac, like other NSAIDs, may increase the nephrotoxicity of ciclosporin due to the effect on renal prostaglandins. Therefore, that would be used in patients not receiving

Concomitant treatment with notassium-sparing diuretics, ciclosporin, tacrolimus or trimethoprim ently (see section WARNINGS AND PRECAUTIONS)

Methotrexate: Caution is recommended when Other NSAIDs and corticosteroids:

undesirable effects (see section WARNINGS AND PRECAUTIONS). Concomitant administration of acetylsalicylic acid decreases the plasma concentration of diclofenac, without

Anticoagulants and anti-platelet agents: Caution is recommended since cond administration could increase the risk of bleeding (see section WARNINGS AND PRECAUTIONS) Although clinical investigation do not appear to indicate that diclofenac affects the action of anticoagulants, there are isolated reports of an increased risk of hemorrhage in patients receiving diclofenac and anticoagulants

is therefore recommended Selective serotonin reuptake inhibitors (\$\$R(s): Concomitant administration of systemic NSAIDs, including diclofenac, and SSRIs may increase the risk of gastrointest bleeding (see section WARNINGS AND

vperglycemic effects necessitating changes n the dosage of the antidiabetic agents during concomitant therapy.

Phenytoin: When using phenytoin concomitantly with diclofenac, monitoring of phenytoin plasma concentrations is exposure to phenytoin

compromising clinical efficacy.

concomitantly. Close monitoring of such patients

Antidiabetics: Clinical studies have show that diclofenac can be given together with oral antidiabetic agents without influencing their clinical effect. However, there have b isolated reports of both hypoglycemic and during treatment with diclofenac. For this reason, monitoring of the blood glucose level is recommended as a precautionary measure

mended due to an expected increase in

NSAIDs, including diclofenac, are administered

less than 24 hours before or after treatment

should not be administered during breast feedin

of methotrexate may rise and the toxicity of this substance be increased

WOMEN OF CHILD-REARING POTENTIAL PREGNANCY BREAST-FEEDING AND FERTILITY Women of child-bearing potential There are no data to suggest any recommendations for women of child-bearing potential.

There are insufficient data on the use of diclofenac in pregnant women. Therefore Flotac should not be used during the first two

and NON-CLINICAL SAFETY DATA). **Breast-feeding**Like other NSAIDs, diclofenac passes into the breast milk in small amounts. Therefore, Flotac

arteriosus (see sections CONTRAINDICATIONS

in order to avoid undesirable effects in the infant As with other NSAIDs, the use of Flotac may impair female fertility and is not recomn in women attempting to conceive. In women who have difficulties conceiving or who are

OVERDOSAGE

of Flotac should be considered.

here is no typical clinical picture resulting from diclofenac overdosage. Overdosage can cause symptoms such as vomiting, gastrointestinal hemorrhage, diarrhea, dizziness, tinnitus or convulsions. In the event of significant poisoning, acute renal failure and liver damage

Therapeutic measures

Management of acute poisoning with NSAIDs including diclofenac, essentially consists of supportive measures and symptomatic treatment. Supportive measures and symptomatic treatment should be given for complications such as hypotension, renal failure, convulsions, gastrointestinal disorder,

Activated charcoal may be considered after ingestion of a potentially toxic overdose,

and gastric decontamination (e.g. vomitir

CLINICAL PHARMACOLOGY

Diclofenac, the active substance of Flotac, is a non-steroidal compound with pronounced mechanism of action. Prostaglandins play a major role in causing inflammation, pain and

Diclofenac in vitro does not suppress proteoglycan biosynthesis in cartilage at concentrations equivalent to those reached in humans.

Resinate is a basic ion exchanger on which diclofenac is bound as anion. The resinate part of Flotac is not absorbed from the gastrointestinal tract and is eliminated via the faeces. The dosage of resinate per capsule Flotac is approx. 100 to 200 times lower than the dosage recommended for therapy of various forms of lipodystrophia

Pharmacodynamics (PD) In rheumatic diseases, the anti-inflammatory and analgesic properties of diclofenac elicit a clinical response characterized by marked relief from signs and symptoms such as pain at rest, pain on movement, morning stiffness and swelling of the joints, as well as by an

relieves both spontaneous pain and pain on

bleeding in primary dysmenorrhea. Pharmacokinetics (PK)

Absorption The special galenic properties of Flotac result in

After single administration of a Flotac cansule diclofenac concentrations can be measured in the plasma (mear 0.3 micrograms/mL [0.96 micromol/L1) after 20 minutes. Peak plasma concentrations (C_{max}) of 0.7 \pm 0.22 micrograms/mL $(2.2 \pm 0.7 \text{ micromol/L})$ are attained within 1.25 hours (SD 0.33 to 2 hours) and are about one third of those achieved following administration of Voltaren Dragées

In comparison with the equivalent dosag of Voltaren gastro-resistant tablets. Flota shows a quicker absorption of the active substance lower neak plasma concentration longer measurable plasma level as well as

er interindividual differences of the peak

plasma concentrations and the area under the

concentration curve.

Comparison of the plasma concentrations

In nost-traumatic and nost-operative inflammatory conditions, diclofenac rapidly

relieving the pain and reducing the extent of

of diclofenac from the resinate.

(gastro-resistant tablets).

mother. The estimated amount ingested by an infant consuming breast milk is equivalent to a

after i.v. resp oral administration of radioactive narked diclofenac show that also after oral administration the whole dose of the substance

is available systemically. Out of this up to

substance, the rest consists of partially active

approx. 54% consist of unchanged active

metabolites (first-pass-metabolism) (see

section CLINICAL PHARMACOLOGY subsection Pharmacodynamics (PD)). In comparison with Voltaren 50 gastro-resistant tablets the bioavailability of diclofenac from

after repeated administration. No accumulation occurs provided the recommended dosage intervals are observed

0.17 L/kg. Diclofenac enters the synovial fluid, where naximum concentrations are measured 2 to 4 hours after neak plasma values have been

e plasma, and they remain higher for up to 12 hours

Diclofenac was detected in a low concentration

(100 ng/ml) in breast milk in one nursing

Flotac capsules reaches a mean value of $78 \pm 18\%$ (SD: 62 to 117%). Pharmacokinetic behaviour does not change

99.7% diclofenac is bound to serum proteins. mainly to albumin (99.4%). The apparent volume of distribution calculated is 0.12 to

attained. The apparent half-life for elimination from the synovial fluid is 3 to 6 hours. Two hours after reaching peak plasma values, concentrations of the active substance are already higher in the synovial fluid than in

0.03 mg/kg/day dose Biotransformation/metabolism

partly by glucuronidation of the intact molecule but mainly by single and multiple hydroxylation

ones, also have short plasma half-lives of 1 to 3 hours. One metabolite, 3'-hydroxy-4'-metho However, this metabolite is virtually inactive. About 60% of the dose absorbed is excreted in the urine as the glucuronide conjugate of the intact molecule and as metabolites, most of which are also converted to glucuronide conjugates. Less than 1% is excreted as

Four of the metabolites, including the two active

Linearity/non-linearity C_{max} as well as the area under the concentratio

the faeces

Special populations No relevant age-dependent differences in the drug's absorption, metabolism, or excretion

impairment show that an accumulation of the unchanged active substance following a single-dose i.v. administration is unlikel ver, based on the results from these studies, elevated plasma levels of the hydrox expected in natients suffering from severe renal impairment. According to the actual status of knowledge, this is not clinically relevant.

non-decompensated cirrhosis, the kinetics and

metabolism of diclofenac are the same as in patients without liver disease CLINICAL STUDIES

In natients with chronic henatitis or

Flotac is a well established product.

NON-CLINICAL SAFETY DATA Preclinical data from acute and repeated dose toxicity studies, as well as from genotoxicity mutagenicity, and carcinogenicity studies with diclofenac revealed no specific hazard for nans at the intended therapeutic doses. In standard preclinical animal studies, there was no evidence that diclofenac had a teratogenic

Diclofenac had no influence on the fertility of parent animals in rats. Except for minimal fetal effects at maternally toxic doses, the prenatal perinatal and postnatal development of the offspring was not affected. Administration of NSAIDs (including

potential in mice, rats or rabbits.

diclofenac) inhibited ovulation in the rabbit and implantation and placentation in the rat and led to premature closure of the ductus arteriosus in the pregnant rat. Maternally toxic doses of diclofenac were associated with dystocia, prolonged gestation, decreased fetal in rats. The slight effects of diclofenac on reproduction parameters and delivery as well as constriction of the ductus arteriosus in utero are pharmacologic consequences of this class of prostaglandin synthesis inhibitors (see sections CONTRAINDICATIONS and WOCBP, PREGNANCY, BREAST-FEEDING AND FERTILITY).

STORAGE See folding box

Store in the original package in order to protect from moisture Flotac capsules should not be used after the date marked "EXP" on the pack.

Flotac cansules must be kent out of the reach and sight of children. INSTRUCTIONS FOR USE AND HANDLING

No special requirements Manufacturer-See folding box.

(R) = registered trademark

International Package Leaflet

Information issued: September 2013

Novartis Pharma AG Basle - Switzerland





trimesters of pregnancy unless the expected benefits to the mother outweigh the risks to the fetus. As with other NSAIDs, use of diclofenac during the third trimester of pregnancy is dicated owing to the possibility of utering nertia and/or premature closure of the ductus

ing investigation of infertility, withdrawal

and respiratory depression.

Special measures such as forced diuresis dialysis or hemoperfusion are probably of no help in eliminating NSAIDs, including diclofenac due to the high protein binding and extensive

gastric lavage) after ingestion of a potentially

Mechanism of action (MOA) antirheumatic, anti-inflammatory, analgesic and antipyretic properties. Inhibition of prostaglandin thesis, which has been demonstrated in periments, is considered fundamental to its

improvement in function.

movement and reduces inflammatory swelling and wound edema. In addition, the active substance is canable of

a quick onset as well as in a long-lasting release

Plasma levels can be measured up to 12 hours after administration of Flotac.

Biotransformation of diclofenac is quick and almost complete. The metabolites are known. Biotransformation of diclofenac takes place

ation, resulting in several phenolic metabolites (3'-hydroxy- 4'-hydroxy -hydroxy-, 4',5-dihydroxy- and 3'-hydroxy-4'-methoxy-diclofenac), most of which are converted to glucuronide conjugates. Two of e phenolic metabolites are biologically active, but to a much smaller extent than

Total systemic clearance of diclofenac from plasma is 263 \pm 56 mL/min (mean value \pm SD) The terminal half-life in plasma is 1 to 2 hours.

diclofenac has a much longer plasma half-life. unchanged substance. The rest of the dose is

eliminated as metabolites through the bile in

curve (AUC) are linearly related to the size of the administered dose.

have been observed. Trials in natients suffering from renal INCOMPATIBILITIES

Not applicable

Novartis Pharma AG, Basel, Switzerland

