Katadolon® instructions

translated from original Russian instructions by Extrapharmacy Online Store
http://extrapharmacy.ru
Name in Cyrillic : КАТАДОЛОН

Active substance : Flupirtine
Pharmachologic effect : central analgesic, muscle relaxant
Pharmacodynamics:
Flupirtine is a selective neuronal potassium channel opener (SNEPCO) , it refers to opioid analgesics of central action.
Flupirtine activates the related G-protein neuronal K + channels internal straightening. The output of K + ions causes a stabilization of the resting potential and reduced excitability of neurons membranes. As a result, indirect inhibition of NMDA receptors (N-methyl-D-aspartate) occurs because NMDA receptors blockade by Mg2 + ions is maintained as long as the cell membrane depolarization occurs (indirect antagonistic effect on NMDA-receptors).
When a therapeutically relevant concentrations flupirtine does not bind to alpha 1, alfa2-, 5-HT1- (5-hydroxytryptophan), 5-HT2 serotonin, dopamine, benzodiazepine, opioid, central m- and n- holinoretseptors.
This central action of flupirtine leads to the implementation of the three main effects:

The analgesic effect

Due to the selective opening of voltage-gated K + channels of neurons with a concomitant yield of K + ions the potential of the neuron rest stabilizes. The neuron is less excitable.
Indirect flupirtine antagonism against NMDA-receptors protects neurons from entering Ca2 + ions. Thus, the sensitizing effect of increase the intracellular concentration of Ca2 + ions is mitigated.
Consequently, when excited neuron the upstream transmission of nociceptive impulses is inhibited.

Myorelaxation effect

Pharmacological effects described for analgesic effect, functionally supported by increasion of the absorption of Ca2 + ions by mitochondria, which takes place at therapeutically relevant concentrations.
Miorelaxing action arises as a result of concomitant inhibition of impulse transmission to motor neurons and corresponding effects of intercalary neurons. Thus, this effect is manifested mainly in respect of local muscle spasms, and not to the entire musculature in general.

Effect of chronification processes

Processes of chronification should be seen as processes of neuronal conduction due to the plasticity of neuronal functions. Through induction of intracellular processes elasticity neuronal function creates the conditions for the implementation of the inflation-type mechanisms, which involve gain response for each subsequent pulse. Running these changes is greatly facilitated by the NMDA-receptor (gene expression). Indirect blockade of these receptors by flupirtine leads to the suppression of these effects. This creates unfavorable conditions for clinically significant chronic pain, and in the case of chronic pain was present earlier - to erase the painful memory by stabilizing the membrane potential, which leads to a reduction in pain sensitivity.

Pharmacokinetics:
After oral administration flupirtine rapidly and almost completely (90%) absorbed from the gastrointestinal tract. Up to 75% of the dose is metabolized in the liver with the formation of metabolites M1 and M2. Active metabolite M1 (2-amino-3-acetamino-6- (4-fluoro) -benzilaminopiridin) formed by hydrolysis of the urethane structures (1st phase reaction) and subsequent acetylation (2nd reaction stage) and provides ~ 25 % analgesic activity of flupirtine. Another metabolite - M2 - is not biologically active, formed by the oxidation reaction (1st phase) of p-fluorobenzyl and conjugation (phase 2) of p-fluorobenzoic acid with glycine.
Research about what isoenzyme primarily involved in the oxidative degradation of the way, were not carried out. It is expected that flupirtine will only have a minor interoperability.
T1/2 of flupirtine from plasma is about 7 hours (10 hours for the base substance and metabolite M1), which is sufficient to provide an analgesic effect.
The concentration of flupirtine in the blood plasma proportional to doses. In the elderly (over 65 years) compared to young patients T1/2 of flupirtine is increased (up to 14 hours at a single dose and up to 18.6 hours when administered within 12 days) and Cmax of flupirtine in plasma is respectively 2- 2.5 times higher.
For the most part flupirtine is excreted by the kidneys (69%): 27% - unchanged, 28% - in the form of the M1 metabolite (acetyl metabolite), 12% - in the form of the M2 metabolite (para-ftorgippurovaya acid); 1/3 of the administered dose is excreted as metabolites of unknown structure. A small part of the dose excreted in the bile and feces.
Indications :

Treatment of acute pain of mild to moderate severity in adults.

Contraindications

Hypersensitivity to the active substance or to any other component of the drug;
the risk of developing hepatic encephalopathy and cholestasis because encephalopathy can develop or existing encephalopathy or ataxia can worsen;
myasthenia gravis due to the miorelaxing action of flupirtine;
related liver disease or alcoholism;
the simultaneous use of flupirtine with other drugs that may have hepatotoxic effects;
recently cured or existing tinnitus, due to the high risk of increase in liver enzymes;
Children up to age 18 years.

Precautions: renal impairment; hypoalbuminemia; older age (patients older than 65 years).

Side effects

Hepatobiliary system: very often - increase in liver transaminases;
Immune system: rarely - hypersensitivity to the drug, allergic reactions (in some cases accompanied by increased body temperature, skin rash, urticaria, pruritus).
Metabolism: often - a lack of appetite.
Nervous system: often - insomnia, depression, anxiety / nervousness, dizziness, tremors, headache; rare - confusion.
Organs of vision: rarely - visual impairment.
Digestive tract: often - indigestion, nausea, vomiting, stomach pain, constipation, abdominal pain, dryness of the oral mucosa, flatulence, diarrhea.
Skin and subcutaneous tissue disorders: often - sweating.
Other: often - fatigue / weakness (15% of patients), especially in early treatment.
Side effects are mainly dependent on the dose (except allergic reactions). In many cases they disappear on their own or after the end of treatment.

Interaction

It enhances the effect of alcohol, sedatives and muscle relaxants. Due to the fact that flupirtine associates with proteins, one should consider the possibility of interaction with other simultaneously taken drugs (such as acetylsalicylic acid, benzylpenicillin, digoxin, glibenclamide, propranolol, clonidine, warfarin and diazepam) which can be displaced by flupirtine from connection with proteins, that can lead to an increase in their activity. Especially this effect can be expressed while taking warfarin or diazepam with flupirtine.
When administration of flupirtine is accompanied with coumarin derivatives should regularly monitor the prothrombin index to timely adjust the dose of coumarin. There is no data on the interaction with other anticoagulants or antiplatelet (including aspirin) . If simultaneous use of flupirtine with drugs that are metabolized in the liver, regular monitoring of liver enzymes is required. Avoid combined use of flupirtine and medicines containing paracetamol and carbamazepine.

Dosing and Administration

Swallow without chewing, squeezed small amounts of liquid (preferably water). If possible take the drug in an upright position.
In exceptional cases, the capsule of Katadolon® can be opened and taken in / enter through the probe only the contents of the capsule. In the case of ingestion of the capsule contents the some meal, such as a banana is recommended to neutralize the bitter taste.
Usual dose is 100 mg 3-4 times a day, possibly at regular intervals between doses. When expressed pain - 200 mg 3 times a day. The maximum daily dose - 600 mg
The dose is adjusted depending on the intensity of pain and individual tolerability. It should apply the minimum effective dose for the shortest possible period of time. Duration of treatment should not exceed 2 weeks.
Elderly patients over 65 years: in the beginning of treatment used, 100 mg 2 times a day, morning and evening.
Patients with severe renal impairment or hypoalbuminemia: should monitor the concentration of creatinine in the blood plasma. The maximum daily dose should not exceed 300 mg. If necessary to use a higher dose- patients should be supervised by a doctor.
Patients with mild to moderate renal insufficiency: creatinine concentration in plasma must be monitored, dose adjustment is not required.

Overdose

Treatment is symptomatic. The specific antidote is unknown.

Pregnancy and breast-feeding

The data on the use of flupirtine in pregnancy is insufficient. In experimental animal studies flupirtine has

shown reproductive toxicity, but not teratogenicity. The potential risk for humans is unknown. Katadolon drug should not be used during pregnancy, except in those cases where the benefit to the mother outweighs the potential risk to the fetus.
According to studies, flupirtine in small amounts into breast milk. Therefore Katadolon® not be used during breast-feeding, except when taking the drug there is an urgent need. If necessary, use Katadolon® during lactation should stop breastfeeding.

Special instructions
Katadolon should be used if treatment with other analgesics (eg NSAIDs or light opioids) is contraindicated.
In patients with reduced kidney function should monitor the concentration of creatinine in the blood plasma.
In patients older than 65 years or with severe renal insufficiency or hypoalbuminemia - dose adjustment is required.
Patients should be warned that during treatment with Katadolon they need to pay attention to any symptoms of liver injury (such as lack of appetite, nausea, vomiting, stomach pain, fatigue, dark urine, jaundice, pruritus). If you notice any of these symptoms should stop taking the Katadolon and urgently seek medical advice.
In the treatment of flupirtine possible false positive reactions with diagnostic test strips for bilirubin, urobilinogen and protein in urine. A similar reaction is possible for the quantitative determination of bilirubin concentration in the blood plasma.
In applying the drug in high doses, in some cases there may be a urine stain in the green, which is not a clinical sign of any disease.

Effects on ability to drive vehicles and management mechanisms:
When using Katadolon should refrain from driving motor vehicles and machinery handling, due to the fact that patients may develop drowsiness and dizziness, which could affect the concentration of attention and speed of psychomotor reactions. It is especially important to remember this while drinking alcohol.
Manufacturer
TEVA, Poland
Reliable supplier with fast Worldwide shipping
Extrapharmacy Online Store
http://extrapharmacy.ru
Storage
The temperature is not above 25 ° C.
Keep out of the reach of children.
Shelf-life of the drug is 5 years.