PK-Merz®

Film-coated tablets
AMANTADINE SULPHATE

Direction for use, please read carefully!

Composition:
One film-coated tablet contains:
Active ingredient: Amantadine sulphate 100 mg.
Excipients: Lactose monohydrate, microcrystalline cellulose, potato starch, gelatine, povidone, talc, colloidal silicon dioxide, magnesium stearate, croscarmellose sodium, eudragit E, yellow-orange S and titanium dioxide.

Indications:
PK-Merz film-coated tablet is effective against all symptoms of Parkinson's disease such as rigidity, tremor and hypo- or akinesia as well as against residual symptoms and complaints after stereotactic operations.

Contra-indications:
PK-Merz film-coated tablets must not be used in patients with:
- hypersensitivity to amantadine or to any of the other constituents of the medicinal product,
- severe non compensated heart insufficiency (stage NYHA IV),
- cardiomyopathies and myocarditis (disease of the cardiac muscles),
- grade II or III AV-block,
- existing bradycardia under 55 beats/min,
- known prolonged QT interval (Bazett QTc > 420 ms) or discernible U-waves or congenital QT syndrome in the family anamnesis,
- history of serious ventricular arrhythmias including torsades de pointes and
- low blood level of potassium or magnesium.

PK-Merz film-coated tablets must not be used in patients simultaneous treatment with budipine or other drugs that prolong the QT interval (see interactions).
PK-Merz film-coated tablets should not be used in:
- severe renal impairment (creatinine clearance < 10 ml/min).

PK-Merz film-coated tablets may be used only with particular caution in patients with:
- prostate hypertrophy,
- narrow angle glaucoma,
- kidney failure (of varying severity; risk of accumulation due to deterioration in renal filtration performance,
- states of agitation or confusion and
- delirious syndromes or exogenous psychosis in the anamnesis.

PK-Merz film-coated tablets may be administered simultaneously with memantine with caution.
Pregnancy and lactation period:
During pregnancy, PK-Merz film-coated tablets should only be used after careful assessment of the risks and benefits and only where absolutely necessary.
Amantadine passes into breast milk. If use during breastfeeding is necessary, the infant should be monitored for possible side effects of the drug (skin rash, urinary retention, vomiting) and breastfeeding should be discontinued where necessary.
Children and older patients:
There is insufficient experience of it's use in children. In elderly patients, particularly those with states of agitation and confusion or delirious syndromes, the dose should be carefully selected.

Side effects:
The following table is used to explain this section:

Very common	More than 1 from 10 patients
Common	Less than 1 from 100 patients
Uncommon	Less than 1 from 1000 patients
Rare	Less than 1 from 10000 patients
Very rare	1 or less from 10000 patients and in very rare cases

Common:
Sleep disturbances, restlessness and agitation, and urinary retention in association with prostate hypertrophy may occur.
Paranoid exogenous psychoses accompanied by visual hallucinations may be triggered, particular in predisposed elderly patients. Adverse reactions of this type may occur with greater frequency when PK-Merz film-coated tablets is given in combination with other antiparkinsonian drugs (e.g. levodopa, bromocriptine, memantine).
Common:
The development of side effects sometimes accompanied by edema in the lower leg and ankle is commonly observed as a characteristic skin reaction for amantadine.
Common to uncommon:
Nausea, dizziness, dry mouth, and orthostatic dysregulation are observed.
Very rare to rarely:
Blurred vision.
Very rare:
Reports of cardiac dysrhythmias such as ventricular tachycardia, ventricular fibrillation, torsades de pointes, and QT prolongation. Most of these cases occurred after overdosage or in association with certain drugs or other risk factors for cardiac arrhythmias (see section "Contraindication and interaction").
Very rare:
Cases temporary loss of vision, increased photosensitivity, and heart rhythm disturbances with tachycardia have been reported. Epileptic fits have also been triggered in rare cases, usually after treatment in excess of the recommended dose.
If any other side effects not mentioned in this leaflet is observed please inform your doctor or pharmacist.

Interaction with other drugs:
The simultaneous use of amantadine and drugs known to cause prolongation of the QT interval is contra-indicated. Examples are:
- certain class I A antiarrhythmics (e.g. quinidine, disopyramide, procainamide) and class III (e.g. amiodarone, sotalol),
- certain antipsychotics (e.g. thioridazine, chlorpromazine, haloperidol, pimozide),
- certain tricyclic and tetracyclic antidepressants (e.g. amitriptyline),
- certain antihistamines (e.g. astemizole, terfenadine),
- certain macrolide antibiotics (e.g. erythromycin, clarithromycin),
- certain gyrase inhibitors (e.g. sparfloxacin) and
- azole antimycotics and other drugs such as budipine, halofantrine, co-trimoxazole, pentamidine, cisapride, and bepridil.

This list may be in-exhaustive. Before commencing use of another drug concomitantly with amantadine, this patients information leaflet should be thoroughly checked for potential interactions between the drug and amantadine caused by QT prolongation.
Use of PK-Merz film-coated tablets in combination with other antiparkinsonian drugs is possible. To avoid side effects (such as psychotic reactions), it may be necessary to reduce the dosage of the other drug or of the combination.
There have been no specific studies on the occurrence of interactions after administration of PK-Merz film-coated tablets concomitantly with other antiparkinsonian

drugs (e.g. levodopa, bromocriptine, trihexyphenidyl, etc.) or memantine (take note of side effects).
Simultaneous treatment with PK-Merz film-coated tablets and any of the drug types or active substances listed below may lead to the following interactions:
Anticholinergics: The side effects (confusion and hallucinations) of anticholinergics (e.g. trihexyphenidyl, benztropine, scopolamine, biperiden, orphenadrine, etc.) may be intensified if they are administered concomitantly with PK-Merz film-coated tablets.
Indirectly CNS-active sympathomimetics: Potentiation of the central effects of amantadine.
Alcohol: Lowering of alcohol tolerance.
Levodopa (antiparkinsonian drug): Mutual potentiation of the therapeutic action. Levodopa can therefore be given concomitantly PK-Merz film-coated tablets.
Memantine: Memantine can potentiate the effect and side effects of PK-Merz film-coated tablets.
Other drugs: The simultaneous use of diuretics of the triamterene/hydrochlorothiazide type can result in a decrease in the plasma clearance of amantadine, leading to toxic plasma concentrations. Simultaneous use should therefore be avoided.
Precautionary measures for application and warning:
An ECG (50 mm/s) should be recorded before and 1 and 3 weeks after commencing treatment and the Bazett frequency-corrected QT time (QTc) determined manually. Such an ECG should also be recorded before and 2 weeks after any subsequent increase in dose. Further ECG check-ups should then take place at least once a year. Treatment must be avoided or discontinued in patients who show baseline QTc values above 420 ms, an increase in QTc of more than 60 ms under treatment with PK-Merz film-coated tablets, or a QTc time in excess of 480 ms under treatment with PK-Merz, and in patients who show discernible U waves.
Patients at risk of electrolyte imbalances, owing e.g. to treatment with diuretics, frequent vomiting and/or diarrhoea, use of insulin in emergency situations, or renal or anorectic conditions must undergo adequate monitoring of laboratory parameters and appropriate electrolyte replacement, particularly for potassium and magnesium.
In the event of symptoms such as palpitations, dizziness, or syncope, treatment with PK-Merz film-coated tablets must be immediately discontinued and the patient checked within 24 hours for QT prolongation. If no QT prolongation is present, the treatment with PK-Merz film-coated tablets can be recommenced, taking into account the contra-indications and interactions.
In the case of patients with cardiac pacemakers, exact determination of QT times is not possible, therefore the decision on use of PK-Merz film-coated tablets must be made on an individual basis in consultation with the patient's cardiologist.
Supplementary administration of amantadine for prophylaxis and treatment of influenza virus A infection is inadvisable and should be avoided on account of the danger of overdose.
This product contains the colouring agent E 110 (yellow-orange S), which in hypersensitive individuals can trigger allergic reactions including asthma. This allergy is more common in persons allergic to acetylsalicylic acid.
Patients treated simultaneously with neuroleptic drugs and PK-Merz film-coated tablets are at risk of developing life-threatening malignant neuroleptic syndrome if PK-Merz film-coated tablets therapy is discontinued abruptly.
Effects on vigilance and accommodation, particularly in association with the effects of other drugs used to treat Parkinson's syndrome cannot be ruled out. On commencement of treatment there may consequently be a further deterioration in the ability to drive and operate machinery over and above any impairment caused by the condition itself. Please note that this impairment is further intensified in combination with alcohol. Avoid the use of alcoholic drinks and beverages because they might reduce the tolerability of PK-Merz film-coated tablets.

Dosage and mode of application:
Unless prescribed otherwise, it is recommended that treatment be started with 1 tablet/day on the first three days to be increased to a regular dosage of 2 tablets/day. It is possible to raise the dosage by weekly increases of 1 tablet/day. In special cases, and under medical supervision the dosage may be increased to 5 ± 6 tablets/day. The maximum daily dosage of 6 tablets (600 mg amantadine sulphate) should not be exceeded. In combination treatment with other antiparkinson drugs the dosage must be adjusted to the need of the individual patient. The last daily dose should be taken in the afternoon.
In elderly patients, especially those who are suffering from agitation and confusion, predelirious and delirious conditions, the dosage must be carefully stabilised. The use of PK-Merz film-coated tablets must not be discontinued abruptly, as this might result in a sudden deterioration of the patient's condition.

Overdosage and misuse:
Inform your physician and be admitted to a hospital, when such symptoms of intoxication occur like nausea, vomiting, hyper-excitability, tremor, ataxia, blurred vision, lethargy, depression, dysarthria, and convulsions (a malignant cardiac arrhythmia was observed).
Acute toxic psychoses in the form of states of confusion with visual hallucinations up to and including coma and myoclonus have been observed after simultaneous administration of amantadine and other antiparkinsonian drugs.
There is no known specific drug treatment or antidote. In the event of intoxication with PK-Merz film-coated tablets, vomiting should be induced and/or gastric lavage performed. Because of the low dialysability of amantadine (approx. 5 %), hemodialysis is not reasonable.
In the event of life-threatening intoxication, intensive care is necessary. Therapeutic measures to be considered include fluid intake and acidification of the urine for more rapid excretion of the substance, and possibly sedation, anticonvulsive measures, and antiarrhythmics (lido-caine i.v.).
For the treatment of neurotoxic symptoms (such as those described above), intravenous administration of physostigmine can be tried in adults at a dose of 1–2 mg every 2 hours and in children 2 x 0.5 mg at intervals of 5–10 minutes up to a maximum dose of 2 mg. Your physician would conduct an ECG to check for symptoms that favour QT prolongation e.g. electrolyte imbalances (potassium and magnesium) and when necessary bradycadia.
If you find you have forgotten to take your dose of PK-Merz film-coated tablets, wait and take your next dose at the usual time. Do not take a double dose to make up for the forgotten dose.
Patients must not discontinue treatment unilaterally. Inform your physician, if you wish to discontinue the therapy due to side effects or good health.

Note:
Do not store above 25°C.
Do not use PK-Merz film-coated tablets after the expiry date stated on the carton and the blister.

Keep all drugs out of the reach of children!
Marketing Authorisation Holder:
Merz Pharmaceuticals GmbH, 60318 Frankfurt/Main, Germany.

Manufacturer:
Merz Pharma GmbH & Co. KGaA, 60318 Frankfurt/Main, Germany.

Presentation and package size:
Packs of 30 and 100 film-coated tablets.

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