

Product Detail

Bicun

Mechanism of Action

Edaravone is a kind of cerebral protective agent (free radical scavenger). Clinical study indicates that N-acetylaspartate is a specific neuronal marker. In the early phase of cerebral infarction, N-acetylaspartate (NAA) decreases radically. Edaravone was given to patients with acute cerebral infarction, which can inhibit reduction of regional cerebral blood flow around infarction. 28 days later, NAA in the edaravone treatment group is much higher than that of control group. Clinical study suggests that edaravone intravenously administered to rats after ischemia-reperfusion injury can prevent the development of cerebral edema and cerebral infarction, attenuate neurogenic symptom and inhibit delayed neuronal death. Study suggests that edaravone can scavenge free radical, inhibit lipid peroxidation, and protect brain cell, endothelial cells and neuron against oxidative stress.

Genetic toxicity: Edaravone Ames test, CHL chromosome aberration test and mouse micronucleus test shows negative results.

Reproductive toxicity: In general reproductive toxicity test, rats were administered with edaravone at a dosage of 3 mg/kg, 20mg/kg and 200 mg/kg. Rats administered with edaravone at a dosage of 20 mg/kg and 200 mg/kg secrete brown urine, shed tears and reduce independent activities, with their mouth watering and weight and appetite loss. Average sexual cycle of female rats administered with edaravone at a dosage of 200 mg/kg prolongs. Reproductive capacity of female and male rats administered with edaravone at a dosage of 200mg/kg drops while residual ratio of fetal thymus rises. In a test conducted during the sensitive period to teratogenic agent, pregnant rats were intravenously administered with edaravone at a dosage of 3 mg/kg, 30 mg/kg and 300 mg/kg. Rats administered with edaravone at a dosage of 300mg/kg lost their appetite to a degree, was prostrate and shed tears, their gait being unstable, spontaneous movement and weight growth speed decreasing. Weight of male rat fetus administered with edaravone and female rat fetus administered with 300 mg/kg edaravone is lower than that of control group. Visceral teratogenic rate of fetus in the edaravone treatment group rises, with teratogenic auricle, eyelid opening, pendulous testicle and delayed vaginal opening. Pregnant New Zealand white rabbits were intravenously administered with edaravone at a dosage of 3mg/kg, 20mg/kg and 100mg/kg. Pregnant New Zealand white rabbits intravenously administered with 100mg/kg edaravone secreted brown urine and shed tears, with symptoms such as ataxic gait, miosis, respiratory disease and hind leg paralysis. Hyperaemia, edema, necrosis and inflammation occurred at injection position; Weight of placenta of white rabbits administered with edaravone at a dosage of 3mg/kg and 100mg/kg radically increases. In a toxicity test conducted during perinatal period, pregnant Wistar rats were intravenously administered with edaravone at a dosage of 3 mg/kg, 20mg/kg and 200mg/kg. Wistar rats administered with 200mg/kg edaravone lost their appetite to a degree, with weight growth speed decreasing, and symptoms such as head shaking, eye blinking, tears shedding and reduction of spontaneous movement. 20

days after neonatal rats were born, open field test shows that movement times of neonatal rats administered with 20mg/kg and 200mg/kg rises.

Pharmacokinetics

According to foreign literature report:

Plasma drug concentration: Healthy adult male volunteers (five cases) and healthy senile volunteers above 65 years of age (five cases) were intravenously administered with edaravone at a dosage of 0.5mg/kg twice a day (thirty minutes once) for two days. Two days later, parameters are calculated according to change in plasma drug concentration at the beginning of edaravone administration. Pharmacokinetics parameters: Healthy adult male volunteers (five cases) and healthy senile volunteers (five cases)

C_{max}(ng/ml) 888±171 1041±106

t_{1/2α}(h) 0.27±0.11 0.17±0.03

t_{1/2β}(h) 2.27±0.80 1.84±0.17

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(Mean± standard deviation)

Plasma edaravone concentration in healthy adult male volunteers and healthy senile volunteers seems to disappear without accumulation.

Serum protein binding rate: In vitro test suggests that rate of binding of edaravone to human serum protein and to human serum albumin is 92% and 89% to 91% respectively.

Metabolism: According to results of study conducted for healthy adult male volunteers and healthy senile volunteers, metabolites of edaravone in plasma include sulphate complex and glucuronic acid complex. Main metabolites of edaravone in urine include glucuronic acid complex and sulphate complex. Excretion: Healthy adult male volunteers and healthy senile volunteers were administered with edaravone injection at a dosage of 0.5mg/kg twice a day (thirty minutes once) for two days. Urine excreted 12 hours after the edaravone is given contains 0.7% to 0.9% of edaravone and 71.0% to 79.9% metabolites.

Indications

To relieve neurologic symptoms caused by acute cerebral infarction and enhance routine activity ability and alleviate functional disorders.

Safety

[Interactions]

1. When edaravone is used in combination with such antibiotics as cefazolin sodium, piperacillin sodium and cefotetan, there is a possibility of exacerbation of renal failure. Therefore, when edaravone is used in combination with these antibiotics, you have to detect and closely observe renal functions for many times.
2. Edaravone must be diluted with physiological saline on principle (When edaravone is diluted with liquid containing sugar, concentration of edaravone will be reduced).
3. Edaravone should not be intravenously administered in combination with high-octane liquid and amino acid preparation or through the same channel (Combined administration would reduce edaravone concentration).
4. Do not use edaravone in combination with antiepileptic drugs such as diazepam and phenytoin sodium (turbidity would occur).

5. Do not use edaravone in combination with canrenoate potassium (turbidity would occur).

Adverse Reactions

According to observation of 569 patients in Japan, adverse reactions were found in 26 patients (4.57%). Main adverse reactions include abnormal liver functions found in 16 patients (2.81%) and tetter found in 4 patients (0.70%). Abnormal change in clinical detection results were found in 122 patients (21.4%). AST (aspartate aminotransferase) rise was found in 43 in 558 patients (7.71%) and ALT (alanine aminotransferase) rise was found in 46 in 559 patients (8.23%).

Severe adverse reactions include:

1. Acute renal failure (degree of renal failure is unknown). you have to detect and observe renal functions for many times during the administration of edaravone; cease giving edaravone to patients and handle the situation immediately after decline in renal functions or oliguria is found.
2. Abnormal liver functions and icterus accompanied with rise in AST, ALT, ALP, γ -GT and LDH (degree of abnormal liver functions and icterus is still unknown). You have to detect and closely observe liver functions during the administration of edaravone. Cease giving earavone to patients and handle the situation immediately after abnormal liver functions and icterus are found.
3. Thrombocytopenia (degree is unknown). There is symptom of thrombocytopenia. You have to closely observe during the administration of edaravone. Cease giving edaravone and handle the situation immediately after abnormalities are found.
4. Disseminated intravascular coagulation (degree is unknown). Periodically detect the symptoms of disseminated intravascular coagulation during the administration of edaravone. Cease giving edaravone and handle the situation immediately after laboratory manifestation and clinical symptom of disseminated intravascular coagulation is found.

Other adverse reactions (incidence) and their symptoms include:

1. Allergy (incidence ranges from 0.1% to 5%): main allergic symptoms include tetter, flush, tumefaction, herpes and pruritus.
2. Blood cell system (incidence ranges from 0.1% to 5%): Main symptoms include hypocythaemia, leucocytosis, leukocytopenia, hematocrit drop, hypochromia, thrombocytosis and thrombocytopenia;
3. Injection position (incidence ranges from 0.1% to 5%): Main symptoms include tetter and tumefaction in the injection position.
4. Liver (incidence is more than 5%): Main symptoms include rise in AST (aspartate aminotransferase), ALT (alanine aminotransferase), LDH (lactate dehydrogenase), ALP (alkaline phosphatase) and γ -GT (γ -glutamyl transferase). (Incidence ranges from 0.1% to 5%): rise in total bilirubin, positive urobilinogen and bilirubinuria.
5. Kidney (incidence ranges from 0.1% to 5%): Main symptoms include rise in BUN (blood urea nitrogen) and serum uric acid and drop in serum uric acid, proteinuria, hematuria and creatinine rise (degree is unknown).
6. Digestive system (incidence ranges from 0.1% to 5%): Belching.
7. Others (incidence ranges from 0.1% to 5%): fever, blood pressure rise, serum cholesterol rise or drop, triglyceride rise, serum total protein drop, CK (creatine kinase) or

CPK (creatin phosphokinase) rise or drop, serum potassium drop and serum calcium drop.

Precaution

[Contraindication]

1. Patients with severe renal failure (there is a possibility of exacerbating renal failure if edaravone injection is administered).
2. Patients who are allergic to edaravone.

[Precaution]

1. Edaravone injection should be used in patients with mild or moderate renal insufficiency with caution (there is a possibility of exacerbating renal failure).
2. Edaravone injection should be used in patients with liver failure with caution (there is a possibility of exacerbating liver failure).
3. Edaravone injection should be used in patients with cardiac disease with caution (there is a possibility of exacerbating cardiac disease or renal insufficiency).
4. Edaravone injection should be used in senile patients with caution (there were reports on senile patients' death caused by edaravone injection).

As there are cases of death caused by exacerbation of acute renal insufficiency or renal failure, so you have to detect renal functions for many times during the administration of edaravone; and you have to continue to closely observe after edaravone is administered; cease giving edaravone to patients (senile patients in particular) and handle the situation immediately after decline in renal functions or oliguria is found. Special attention should be paid to senile patients as there are reports on senile patients' death caused by the administration of edaravone (Most of these senile patients are above 80 years of age).

[Pregnancy and lactation]

1. Edaravone injection is contraindicated in women who are or may become pregnant (Whether the administration of edaravone injection during lactation is safe is still unknown).
2. Edaravone injection should not be given to women during lactation. If women during lactation have to employ edaravone injection, the women should cease lactating when edaravone injection is administered (Animal experiment reports distribution of edaravone in milk).

[Children]

Edaravone injection should not be given to children (As we have no related experience, so whether it is safe to administer children with edaravone injection is still unknown).

[Senile patients]

Cease giving edaravone injection and handle the situation immediately after adverse reaction occurs because physiological functions of the senile patients degenerates. Generally speaking, edaravone injection should be used in senile patients (above 80 years of age) with caution.

Administration and Dosage

Patient is intravenously administered with 30 mg edaravone injection twice a day in combination with physiological saline (30 minutes once). One course of treatment should be less than 14 days. Patients should be intravenously administered with edaravone injection within 24 hours after onset of the disease

Description

Edaravone injection is a kind of colorless transparent liquid.

Specification

5ml:10mg

Package

Easy-to-break retort ampoule, 6 bottles/box.

Price

468 RMB/box

Characteristics

Another specification is 20 ml: 30 mg, with price of 724 RMB/box.

(3-Methyl-1-phenyl-2-pyrazolin-5-one) Main component of this product is edaravone.

Chemical name of edaravone is 3-Methyl-1-phenyl-2-pyrazolin-5-one.

Molecular formula: C₁₀H₁₀N₂O Molecular weight: 174.20