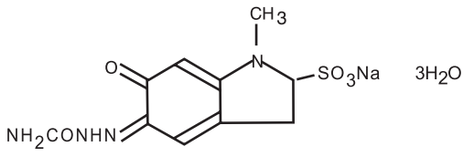
VASOTROPIC AGENT

ADONA-FORTE® Tablet (30 mg)
ADONA (AC-17)® Tablet (10 mg)
ADONA (AC-17)® Injection

Mitsubishi Tanabe Pharma

COMPOSITION AND DESCRIPTION

- Generic name : Carbazochrome sodium sulfonate
- Chemical name : Sodium 1-methyl-5-semicarbazono-6-oxo-2,3,5,6-tetrahydroindole-2-sulfonate trihydrate



$C_{10}H_{11}NaN_4O_5S \cdot 3H_2O$: 376.32

- Carbazochrome sodium sulfonate is odorless and consist of orange yellow crystals or crystalline powder.
- It is slightly soluble in water, very slightly soluble in absolute alcohol and practically in soluble in acetone and ether.
- Melting point : about 210°C (with decomposition).

Product's names	Reg.No.	Content of Carbazochrome sodium sulfonate	Description of the product
ADONA-FORTE® Tablet (30 mg)	DKL7625201810B1	30 mg per tablet	Orange yellow to orange yellow brown plain tablet
ADONA (AC-17)® Tablet (10 mg)	DKL7225201810A1	10 mg per tablet	Orange yellow plain tablet
ADONA (AC-17)® Injection (intravenous)	DKL7225201743A1	25 mg per ampoule (5 mL)	Orange yellow clear liquid pH : 5.5-6.2 Osmotic pressure ratio : About 2.0
	DKL7225201743A1	50 mg per ampoule (10 mL)	

ACTIONS

PHARMACOLOGICAL ACTIONS :

Carbazochrome sodium sulfonate inhibits the increasing permeability of the capillary and reinforces its resistance.
Carbazochrome sodium sulfonate has an action to shorten the bleeding time (hemostatic action), but it has no effect on blood coagulation or fibrinolytic systems.

1. Inhibitory action on capillary permeability :
   - The intramuscular administration of 5 and 10 mg/kg Carbazochrome sodium sulfonate to rabbit inhibits the Kallikrein-induced capillary permeability by 20% and 30% respectively, one hour after administration.
   - The intravenous administration of 0.5, 2.5 and 5.0 mg/kg Carbazochrome sodium sulfonate inhibits the hyaluronidase-induced capillary permeability in rabbits by 28%, 40% and 65% respectively.
2. Increasing action on capillary resistance value :
   - The intraperitoneal administration of 0.5 mg/kg Carbazochrome sodium sulfonate increases the capillary resistance value (by negative pressure method) with 41.9 mmHg at maximum in guinea pigs and the effect last for about 5 hours.
   - The intramuscular administration of 10 mg/kg Carbazochrome sodium sulfonate increases the capillary resistance of nictitating membrane by 1.3 times in rabbits, one hour after administration.
3. Shortening action on bleeding time :
   - By the intravenous administration of 2.5 and 5.0 mg/kg Carbazochrome sodium sulfonate to rabbits, the bleeding time shortened in 18% and 42% respectively, 1 hour later. The action sustains for more than 3 hours.
4. Action on blood platelets and coagulation system :
   - The intravenous administration of 5.0 mg/kg Carbazochrome sodium sulfonate has no effect on number of platelets in rabbit.
   - The intramuscular administration of 4.0% Carbazochrome sodium sulfonate has no effect on blood coagulation time in rabbit.
5. Action on respiration and circulation :
   - Neither respiration nor blood pressure of rabbits is affected by the intravenous administration of 5.0, 10.0 mg/kg of Carbazochrome sodium sulfonate
   - Carbazochrome sodium sulfonate solution does not elicit any vasoconstrictive action when perfused as solution of 4% into the ear vein or as solution of 5×10^{-4} into the mesenteric blood vessel in rabbits.

ABSORPTION AND EXCRETION :

After the oral administration of 25 mg/kg of this compound, about 20% and 45% are absorbed in 2 and 6 hours respectively in ddY strain mice. Distribution into each tissue reaches its peak 2 - 4 hours later. The double amount of compound is found in urine as compared with that in feces and more than 90% of the administered dose are excreted in 48 hours. After administration of 25 mg/kg Carbazochrome sodium sulfonate to ddY strain mice intravenously, this compound is distributed to whole body except central nervous system, and its concentration reaches its peak just shortly after administration (10 - 30 minutes after intramuscular administration) and decreases with lapse of time. This compound is excreted about 63% in urine in 1 hour, and about 91% in urine and 5% in feces in 24 hours.

CV. DUTA WARNA	PRINT OUT ARTWORK			
TGL. : 04 April 2019	NO. REVISI AW :	BAHAN : HVS 60 gr		JUMLAH WARNA : 1/1 KET. WARNA : - HITAM
PEMESAN : TANABE INDONESIA	NO. WO : AF11173	UKURAN : 165X300 MM		
JENIS & NAMA BARANG : BROSUR ADONA TABLET (MTP) MEPRO REV.7		PRINT OUT : 100%		
KETERANGAN REV : 16-5-2018 : - Perubahan teks "PT. TANABE INDONESIA" menjadi PT. MITSUBISHI TANABE PHARMA INDONESIA - Logo Tanabe "lingkaran" menjadi "Logo Biru" 28-9-2018 : Penulisan nama perusahaan menjadi PT Mitsubishi Tanabe Pharma Indonesia, font Frutiger 45 light 18-12-2018 : - 2 Logo MTPC pada alamat dihilangkan dan tambahkan logo MTP baru hitam sebelah kanan atas bagian depan 19-12-2018 : - 2 Logo MTPC pada alamat For .. dan Under .... dihilangkan 2-2-2019 : - Adona (AC-17) injection 2 ml dihilangkan satu kolom/baris di bag depan, Dosage, Presentations 4-4-2019 : Teks "the" terakhir dihilangkan pada Actions bagian 2 dot ke dua		OPERATOR : DSK		
		KASIE D/F :	KABAG PENJ :	PEMESAN :

DISETUJUI OLEH BPOM : 02/03/2023 ID : EREG10002812300026

TOXICOLOGICAL AND TERATOLOGICAL ACTIONS :

1. Acute toxicity (LD_{50}) : over 600 mg/kg (i.v.) (♂, ♀), 10,000 mg/kg (p.o.) (♂, ♀) in Wistar-KBL strain rats.
   Over 600 mg/kg (i.v.) (♂, ♀), 5,000 mg/kg (p.o.) (♂, ♀) in beagle dogs.
2. Subacute and Chronic Toxicity : The 30 days subacute toxicity studies at the dose of 50, 100, 200, 500 mg/kg/day (i.p.) and 180 days chronic toxicity tests at the dose 750, 1,500, 3,000 mg/kg/day (p.o.) both in Wistar-strain rats disclose no significant difference in general condition, hematological, urinary, pathohistological findings between the control and the drug-treated groups.
3. Teratogenesis : When the fetal toxic effect of the drug was studied in ICR-JCL strain mice and Wistar strain rats in accordance with the guidelines for the safety test of drugs, issued by the Japanese Ministry of Health and Welfare, teratogenic action is not observed between drug-treated and the control groups.

INDICATIONS

1. Hemorrhagic tendency (purpura etc.) due to decreased capillary resistance and increased capillary permeability.
2. Hemorrhage from skin, mucous membrane and internal membrane, hemorrhage at eyeground, nephrotic hemorrhage and metrorrhagia.
3. Abnormal bleeding during and after operation due to decrease of capillary resistance.

CONTRAINDICATION

Patients who have known hypersensitivity to this drug.

DOSAGE AND ADMINISTRATION

- ADONA-FORTE® Tablet and ADONA (AC-17)® Tablet
  The usual adult daily dose 30 - 90 mg is orally administered in 3 divided doses.
  The dose may be increased or decreased depending on the age and symptoms.
- ADONA (AC-17)® intravenous injection : 5 mL and 10 mL ampoule.
  Usually administer 25 - 100 mg or one ampoule of 5 mL to two ampoules of 10 mL (single dose for adult) of Carbazochrome sodium sulfonate intravenously or intravenously by drip.
  The dose may be increased or decreased depending on the age and symptoms.

PRECAUTIONS

(1) Careful attention should be paid in administration to the following patients :
Patients having history of hypersensitiveness to this drug.

(2) Adverse Reactions :
1. Hypersensitiveness : When hypersensitiveness like eruption appears, discontinue the administration.
2. Gastrointestinal system : Occasionally loss of appetite and disagreeable sensation of stomach may be encountered after oral administration

(3) Effect on Laboratory values :
It is possible that urobilinogen test becomes positive due to the metabolite of Carbazochrome sodium sulfonate.

(4) Precaution on Administration :
1. Induration and pain at injection site may be encountered occasionally.
2. In case of the subcutaneous and intramuscular administration, carefully inject not to hurt the nerves and blood vessels. When it is necessary to inject repeatedly, it is preferable to change the site of injection. Especially to infant and small children, careful attention should be paid.
3. To prevent glass splinters dropping into the ampoule during cutting, wipe the ampoule neck with cotton soaked in ethanol before breaking.

CAUTION ON HANDLING

The color of the product changes to brown by being exposed to direct light or kept in a hot place for a long time.
Do not use the deteriorated product.

ADONA (AC-17)® & ADONA-FORTE® Tablet : Store at below 30°C, away from direct light.
ADONA (AC-17)® Injection : Store at below 15°C, away from direct light.

PRESENTATIONS

ADONA-FORTE® Tablet	: Box of 10 blisters of 10 tablets
ADONA (AC-17)® Tablet	: Box of 10 blisters of 10 tablets
ADONA (AC-17)® Injection (intravenous)	: Box of 10 X 5 mL ampoules Box of 10 X 10 mL ampoules

ON DOCTOR'S PRESCRIPTION ONLY
HARUS DENGAN RESEP DOKTER

ADONA FORTE® Tablet, box of 10 blisters of 10 tablets
ADONA (AC-17)® Tablet, box of 10 blisters of 10 tablets

Manufactured by
PT Mitsubishi Tanabe Pharma Indonesia
Bandung, Indonesia

Under License from
Mitsubishi Tanabe Pharma Corporation
Osaka, Japan

ADONA (AC-17)® Injection (intravenous)
Box of 10 X 5 mL ampoules
Box of 10 X 10 mL ampoules

Manufactured by
PT. Meprofarm
Bandung, Indonesia

For
PT Mitsubishi Tanabe Pharma Indonesia
Bandung, Indonesia

Under License from
Mitsubishi Tanabe Pharma Corporation
Osaka, Japan

C/DW/PI/AC17/09-2016/03

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