Revised: October 2022 (1st version)

Standard Commodity Classification No. of Japan:
87314

Storage: 100 mg: Store at room temperature
500 mg: Store at a cold place
2 g: Store at a cold place
Expiration date: 3 years

Prescription drug

(Caution – Use only pursuant to the prescription issued of physician, etc.)

Vitamin C Injection
Japanese Pharmacopoeia (JP)

Ascorbic Acid Injection

Vitamin C Injection 100mg "FUSO"
Vitamin C Injection 500 mg "FUSO"
Vitamin C Injection 2g "FUSO"

	100 mg	500 mg	2 g
Approval No.	16100AMZ 02218	16100AMZ 02219	16100AMZ 02220
Date of Initial Marketing in Japan	June 1957		September 1981

3. COMPOSITION AND PRODUCT DESPRICTION

3.1 Composition and Product Description

Product name	Vitamin C Injection 100mg "FUSO"	
Volume	1 mL	
Active Ingredients	In one ampoule, JP Ascorbic acid	100 mg
Inactive Ingredients	In one ampoule, Sodium Thioglycolate Sodium Pyrosulfite Benzyl alcohol pH adjuster	1 mg 0.5 mg 10 mg
Dosage form	Aqueous injection	
Appearance	Clear and colorless liquid	
pH	5.6-7.4	
Osmotic pressure ratio (ratio to saline)	4.0-5.0	

Product name	Vitamin C Injection 500mg "FUSO"	
Volume	2 mL	
Active Ingredients	In one ampoule, JP Ascorbic acid	500 mg
Inactive Ingredients	In one ampoule, Sodium Thioglycolate Sodium Pyrosulfite pH adjuster	2 mg 2 mg
Dosage form	Aqueous injection	
Appearance	Clear and colorless liquid	
pH	5.6-7.4	
Osmotic pressure ratio (ratio to saline)	9.1-10.5	

Product name	Vitamin C Injection 2g "FUSO"	
Volume	10 mL	
Active Ingredients	In one ampoule, JP Ascorbic acid	2,000 mg
Inactive Ingredients	In one ampoule, Sodium Thioglycolate Sodium Pyrosulfite pH adjuster	10 mg 10 mg
Dosage form	Aqueous injection	
Appearance	Clear and colorless liquid	
pH	5.6-7.4	
Osmotic pressure ratio (ratio to saline)	7.3-8.5	

4. INDICATIONS

(1) Prevention and treatment of vitamin C deficiency (Scurvy, Möller-Barlow's disease)

(2) Supplementation of vitamin C when its demand increases and intake from meals is insufficient (Wasting disease, During pregnancy and delivery, nursing women, vigorous physical work, etc.)

(3) Vitamin C deficiency or metabolic disorder presumed to be involved in the following diseases:

- Capillary bleeding (epistaxis, gingival bleeding, hematuria, etc.)
- Drug poisoning
- Adrenocortical dysfunction
- Promotion of bone matrix formation/bone fusion for bone fracture
- Pigmentation due to chloasma, ephelis, or inflammation
- Photosensitive dermatitis

Vitamin C Injection "Fuso" should not be aimlessly administered for the above (3) cases when an effect is not achieved.

6. DOSAGE AND ADMINISTRATION

<Vitamin C Injection "Fuso" 100 mg>

Usually, for adults, administer 50 to 2,000 mg per day as ascorbic acid divided into one to several doses, by subcutaneous, intramuscular, or intravenous injection.
The dose may be increased or decreased according to age and symptom.

<Vitamin C Injection "Fuso" 500 mg, 2 g>

Usually, for adults, administer 50 to 2,000 mg per day as ascorbic acid divided into one to several doses, by intravenous injection.
The dose may be increased or decreased according to age and symptom.

9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUND

9.7 Pediatric Use

<Common to all three products>

9.7.1 Clinical trials have not been conducted in pediatric patients.

<Vitamin C Injection "Fuso" 100 mg>

9.7.2 Vitamin C Injection "Fuso" 100 mg: This product should be administered with care to low birth weight babies and newborn babies. [Toxic symptoms (gasping, acidosis, convulsion, etc.) were reported overseas in low birth weight babies after a large dose (99 – 234 mg/kg) of benzyl alcohol was administered. Vitamin C Injection "Fuso" 100 mg contains benzyl alcohol as an excipient.]

12. INFLUENCE ON LABORATORY TESTS

12.1 This product may interfere with the detection of urinary glucose in various urinary glucose tests.

12.2 This product may cause false negative results in various urinary test (occult blood, bilirubin, nitrite) and fecal occult blood reaction tests.

14. PRECOUTIONS CONCERNING USE

14.1 Precautions Concerning Administration of the Drug

14.1.1 For Intravenous Injection

Since Angialgia may develop by intravenous administration, this product should be administered as slowly as possible.

14.1.2 For Intramuscular Injection

The following precautions should be taken before intramuscular injection to avoid any impact on tissues and nerves.

- Intramuscular injections should be given only when it is unavoidable, and only when necessary. Repeated injections to the same site should not be performed. Special care should be taken with birthweight infants, neonates, infants, young children, and children.
- Avoid areas where nerves run.
- If the patient complains of severe pain or regurgitation of blood when the needle is inserted, the needle should be removed immediately and the site should be changed for injection.

14.1.3 For Subcutaneously or Intramuscular Injection

Pain may occur at the injection site.

18. PHARMACOLOGY

18.1 Mechanism of Action

A typical deficiency of vitamin C is scurvy, which causes increased bleeding tendency, retardation of bone and tooth development, and decreased antibody production and wound healing. Administration of this drug is effective in these diseases and symptoms, but its physiological significance and action are not fully clear. Involvement in Collagen formation, improvement of bleeding tendency by increasing capillary resistance and shortening blood coagulation time, involvement in Adrenocortical function (prevention of stress response), and inhibition of melanin pigment production have been reported[1].

18.2 Collagen formation enhancement effect

Pathological findings of scurvy indicate the causes to be lowered collagen synthesis of the bone, teeth, and other connective tissues.[2,3]

An experiment in guinea pigs fed with a scurvy inducing diet was conducted to investigate the effect of ascorbic acid on connective tissue formation using skin regeneration as an index. Administration of ascorbic acid increased production of hydroxyproline and decreased non-collagen proline in tissue, and the result suggested conversion of a proline containing substance to collagen at the injury site.[4)]

Synthesis of epithelial basement membrane composed of a compound similar to collagen in the connective tissue was also dependent on ascorbic acid, and some signs of scurvy were caused by insufficient synthesis of basement membrane.[4)]

18.3 Adrenal defense mechanism

After loading stress to rats by epinephrine injection, the eosinophil count was decreased, and alarm reaction of the adrenal glands was suggested by histological images. In animals pretreated with ascorbic acid, the eosinophil count was significantly increased, and histological images of the adrenal glands were normal. Ascorbic acid was therefore suggested to have an adrenal defense mechanism.[6)]

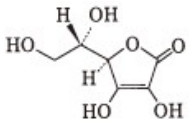
18.4 Impact on melanin synthesis

Results of *in vitro* experiments showed that ascorbic acid inhibited production of dopachrome based on its reduction mechanism for oxidization of dopaquinone to dopachrome. After administration of a large dose of ascorbic acid to guinea pigs and rabbits, the amount that might possibly inhibit dopachrome synthesis *in vitro* was distributed to the skin.[7)]

19. PHYSICOCHEMICAL PROPERTIES

Nonproprietary name : Ascorbic acid

Structural formula:



Molecular formula : $C_6H_8O_6$

Molecular weight : 176.12

Chemical name : L-*threo*-hex-2-enono-1,4-lactone

Description: This product occurs as white crystal or crystalline powder with no odor and acid taste. It is freely soluble in water, sparingly soluble in ethanol (95), and practically insoluble or insoluble in diethyl ether.

Melting point : About 190°C (decomposition)

22. PACKAGING

Vitamin C Injection "FUSO" 100 mg 1 mL, 50ampoules, Glass ampoule
Vitamin C Injection "FUSO" 500 mg 2 mL, 50ampoules, Glass ampoule
Vitamin C Injection "FUSO" 2 g 10 mL, 50 ampoules, Glass ampoule

23. REFERENCES

1) JP 18 Commentary, Hirokawa Shoten, 2021; C-95-100
2) Fullmer, H. M. et al., Ann. New York Acad. Sci., 1961; 92, 286-294
3) Kajiwara A, The Medical Frontline, 1962; 17: 1429-1446
4) Gould, B. S. et al., J. Biol. Chem., 1957; 226, 289-300
5) Priest, R. E., Nature, 1970; 225: 744-745
6) Bacchus, H. et al., Science, 1951; 113: 269-270
7) Takeuchi M et al., Vitamin, 1963; 28: 501-507

26. MARKETING AUTHORIZATION HOLDER, ETC

26.1 Marketing Authorization Holder,

FUSO PHARMACEUTICAL INDUSTRIES, LTD.
2-3-11, Morinomiya, Joto-ku, Osaka 536-8523, Japan