** Revised: May 2010 (9th version, section of Contact Information on Request for Literature and Product Information)
* Revised: June 2008

Analgesic and anti-inflammatory agent

Prescription drug Note 1)

ZALTIRON® INJECTION

《Sodium salicylate and Chondroitin sulfate sodium injection》

Storage: Store at room temperature.

Expiration date:
Indicated on the package and ampoule.

Standard Commodity Classification No. of Japan 871149		
Approval No.	Date of listing in the NHI reimbursement price	Date of initial marketing in Japan
20900AMZ00094	July 1997	July 1997

Note 1) Caution – Use only pursuant to the prescription of a physician, etc.

CONTRAINDICATIONS (Zaltiron is contraindicated in the following patients.)

1) Patients with a history of hypersensitivity to the product or salicylic acid compounds (aspirin, etc.) or chondroitin sulfate
2) Pregnant women or women who may possibly be pregnant (See "Use during Pregnancy, Delivery or Lactation".)

* DESCRIPTION

Content per ampoule	10 mL
Active ingredient	Chondroitin sulfate sodium..... 200 mg Sodium salicylate (JP)..... 400 mg
Inactive] Ingredients	Sodium Bisulfite..... 5 mg Isotonic agent (Sodium Chloride), pH adjusting agent (Sodium Hydroxide, Hydrochloric Acid)
Description	Colorless to pale yellowish brown, slightly viscous, clear solution with a bitter taste and without an odor.
pH	5.6 - 7.0
Osmotic pressure ratio	Approx. 2 (ratio to isotonic sodium chloride solution)

INDICATIONS

Symptomatic neuralgia, lumbago

DOSAGE AND ADMINISTRATION

The usual adult dose is a single 10 mL intravenous injection slowly over 3 minutes or longer. The dosage may be adjusted according to the patient's age and symptoms.
The product should be used only if the patient is unable to receive oral analgesics or need immediate improvement of symptoms.

PRECAUTIONS

1. Careful Administration (Zaltiron should be administered with care in the following patients.)

1) If patients or their parents or siblings have allergy, urticaria, bronchial asthma, allergic rhinitis, food allergy, etc. due to other drugs.
2) Patients with liver or renal disorder [Liver or renal disorder may be aggravated.]
3) Patients with bleeding tendency [Abnormal platelet function may occur.]
4) Patients with peptic ulcer [Peptic ulcer may be aggravated.]
5) Patients with ulcerative colitis [It has been reported that ulcerative colitis is aggravated with other nonsteroidal anti-inflammatory analgesic drugs.]
6) Patients with Crohn's disease [It has been reported that Crohn's disease is aggravated with other nonsteroidal anti-inflammatory analgesic drugs.]
7) Elderly patients [See "Use in the Elderly"]

2. Important Precautions

1) Although there is a different use status of salicylic acid preparations from Japan, some epidemiological surveys in the U.S. have reported relationships between salicylic acid preparations and Reye's syndrome. Therefore, in principle, the product **should not be used in patients under 15 years with varicella or influenza**, but if it is inevitable to use, the product should be administered with care, and the patient's conditions should be closely observed after administration. [**Reye's syndrome**: It is a disease with high mortality rate and extremely rarely associated with symptoms such as severe vomiting, consciousness disturbed, convulsion (acute brain oedema), fat deposit in liver and other organs, mitochondrial deformation, acute increase in AST (GOT), ALT (GPT), LDH and CK (CPK), hyperammonaemia, hypoprothrombinaemia, hypoglycaemia, etc. which occur for a short time following viral diseases such as varicella, influenza, etc.]
2) **Shock** may occur. Treatment with the product should be considered only if it the patient is unable to receive oral administration or immediate analgesic or immediately needs analgesic treatment. It is advisable to prepare to take emergency measures prior to use of the product.
3) The patients should be fully interviewed to predict responses to the product such as shock.
4) In infants, children, and elderly with hyperthermia or those with debilitating diseases, effects of the product may rapidly appear, leading to excessive body temperature decreased, collapse, cold extremities, etc. If it is necessary to administer the product in these patients, their conditions should be closely observed after administration.
5) Patients should be kept at rest for at least 10 minutes after administration, and be closely observed.

6) Long-term repeated administration of the product should be avoided.

3. Drug Interactions

Precautions for coadministration (Zaltiron should be administered with care when coadministered with the following drugs.)

Drugs	Signs, Symptoms and Treatment	Mechanism and Risk Factors
Coumarin anticoagulants Warfarin	The effects of coumarin anticoagulants may be enhanced. This product should be administered with care by reduction of dosage or other measures.	Salicylic acid preparations (such as aspirin) have hemorrhagic effects due to platelet antiaggregating effects. Salicylic acid preparations are replaced with coumarin anticoagulants binding to plasma proteins to release these drugs.
Diabetic drugs Insulin preparations Tolbutamide, etc.	The effects of diabetic drugs may be enhanced. This product should be administered with care by reduction of dosage or other measures.	Salicylic acid preparations (such as aspirin) are replaced with diabetic drugs binding to plasma proteins to release these drugs.

4. Adverse Reactions

No investigation such as a drug use investigation clearly showing the incidence of adverse reactions has been conducted.

1) Clinically significant adverse reactions (incidence unknown)

(1) **Shock:** Shock may occur. Patients should be carefully monitored, and if any abnormalities such as distressed feeling of chest, decreased blood pressure, facial pallor, abnormal pulse, dyspnoea, etc. are observed, administration of this product should be discontinued and appropriate measures should be taken.

(2) **Oculomucocutaneous syndrome (Stevens-Johnson syndrome), erythroderma (dermatitis exfoliative):** Oculomucocutaneous syndrome (Stevens-Johnson syndrome), erythroderma (dermatitis exfoliative), etc. may occur. Patients should be carefully monitored, and if any abnormalities are observed, administration of this product should be discontinued and appropriate measures should be taken.

(3) **Aplastic anaemia:** Aplastic anaemia may occur. Patients should be carefully monitored, and if any abnormalities are observed, administration of this product should be discontinued and appropriate measures should be taken.

2) Other adverse reactions

	Incidence unknown
Hypersensitivity Note 2)	Rash, oedema, rhinitis-like symptoms, conjunctivitis, etc.
Hematologic Note 2)	Leukopenia, thrombocytopenia, anaemia, etc.
Psychoneurologic Note 3)	Tinnitus, deafness, dizziness
Hepatic Note 2)	Jaundice, AST (GOT) increased, ALT (GPT) increased, Al-P increased
Renal Note 2)	Renal disorder
Gastrointestinal	Stomachache, anorexia, queasy, vomiting, gastrointestinal haemorrhage
Injection site	Vascular pain, numbness, redness, pruritus, swelling, etc.

Note 2) If any of these symptoms is observed, administration of the product should be discontinued.

Note 3) If any of these symptoms is observed, appropriate measures such as dose reduction, treatment cessation, etc. should be taken.

5. Use in the Elderly

Elderly patients should be carefully observed for adverse reactions, and the product should be administered with care by starting administration at lower doses, etc. (See "Important Precautions".)

6. Use during Pregnancy, Delivery or Lactation

1) The product should not be used in pregnant women or women who may possibly be pregnant. [It has been reported in animal studies that sodium salicylate has a teratogenic effect.]
2) When sodium salicylate (aspirin) was administered to rats during late pregnancy, weak foetal ductus arteriosus systole was reported.

7. Precautions concerning Use

1. **Administration routes**: Zaltiron is for intravenous use only.
2. **During administration**: Patients' general physical conditions should be closely monitored for prophylaxis against adverse reactions.
3. **Administration rates**: Careful attention should be paid to injection methods; e.g., an ampoule of this product is injected as slowly as possible (over a period of ≥ 3 minutes) while the patient is in a recumbent position.
4. **Ampoule cutting**: The product is supplied as a one-point-cut-ampoule. Wipe the ampoule with ethanol before opening to avoid contamination at the time of ampoule-cut.

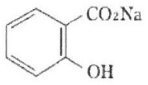
8. Other Precautions

Temporary infertility has been reported in female patients on a long-term administration of nonsteroidal anti-inflammatory analgesics.

*PHYSICOCHEMISTRY

1. Sodium salicylate

Structural formula:



Nonproprietary name: Sodium Salicylate
Chemical Name: Monosodium 2-hydroxybenzoate
Molecular formula: $C_7H_5NaO_3$
Molecular weight: 160.10
Description: Sodium salicylate occurs as a white crystal or crystalline powder. It is very soluble in water, freely soluble in acetic acid (100), and soluble in ethanol (95). It is gradually colored by light.

2. Chondroitin sulfate sodium

Nonproprietary name: Chondroitin Sulfate Sodium
Another name: Sodium Chondroitin Sulfate
Description: Chondroitin Sulfate sodium occurs as a white to pale yellow-brown powder with no odor or faint peculiar odor and taste. It is freely soluble in water, and practically insoluble in ethanol (95), acetone or diethyl ether. pH of solution (1→100) is 5.5 to 7.5. It is hygroscopic.

**PRECAUTIONS FOR HANDLING

1. Precautions

The product is kept in a one-point-cut-ampoule. To open, break downwards while keeping the circular mark •on top facing upwards.

**2. Stability test

In an accelerated test using final packaging products (at 40°C for 6 months), ZALTIRON INJECTION was estimated to be stable for 3 years under normal distribution conditions[1)] in the market.

PACKAGING

ZALTIRON INJECTION: 10 mL × 10 ampoules
10 mL × 50 ampoules

**REFERENCES

**1) Internal data of TOWA PHARMACEUTICAL CO., LTD.: Stability study

Manufactured and Distributed by:
TOWA PHARMACEUTICAL CO., LTD.
2-11, Shinbashi-cho, Kadoma, Osaka
571-8580, Japan