Paraplatin Injection (Carboplatin Injection) 50 mg

Pack size: 5mL/vial, 1vial/box

Active ingredient: Carboplatin

Name of drug classification

Antineoplastic agent

Approval etc.

Sales name: Paraplatin injection 50 mg

Approval / authorization number

European trademark name: PARAPLATIN INJECTION

Storage method · expiration date etc

Storage method: Shielding / room temperature preservation [see handling notes]

Expiration date: 2 years (The expiration date is stated on the outer box.)

Standard name

Japanese Pharmacopoeia
Carboplatin injection

Restriction classification

poison
Prescription drugs
Caution - To use by prescription such as doctor

composition

Amount in 1 vial: 5 mL
Ingredients · Content: Carboplatin 50 mg

Property

Color · formulation: Colorless to slightly yellow clear injection solution
pH: 5.0 to 7.0

Osmotic pressure ratio: Approximately 0.1 (ratio to daily saline physiological saline solution)

warning

1. Cancer chemotherapy including this drug should be performed only for cases where this therapy is deemed appropriate under a doctor who has sufficient knowledge and experience in cancer chemotherapy in a medical facility that can sufficiently respond in case of emergency about. Please carefully refer to the package insert of each concomitant medication when choosing an indication patient.Also, prior to the initiation of treatment, adequately explain the effectiveness and danger to the patient or his / her family, and give consent before administration.
2. Cancer chemotherapy for pediatric malignant solid tumor including this drug should be carried out under the doctor who has sufficient knowledge and experience for pediatric cancer chemotherapy.

Contraindication

(Do not take it for the next patient)

1. Patients with severe myelosuppression [Myelosuppression is a dose regulating factor, with infection or bleeding and can become severe.]
2. Patients with a history of severe hypersensitivity to this drug or other platinum-containing drugs
3. ** Pregnant women or women who may be pregnant (see "Administration to pregnant women, maternity women, lactating women, etc.")

Indication or effect

Head and neck cancer, lung small cell carcinoma, testicular tumor, ovarian cancer, cervical cancer, malignant lymphoma, non small cell lung carcinoma, breast cancer
Combination therapy with other antineoplastic agents against the following malignant tumors
Pediatric malignant solid tumor (neuroblastoma · retinoblastoma · hepatoblastoma · central nervous system germ cell tumor, recurrent or refractory Ewing sarcoma family tumor · nephroblastoma)

Dosage and dosage

1. In cases of head and neck cancer, small cell lung carcinoma, testicular tumor, ovarian cancer, cervical cancer, malignant lymphoma, non-small cell lung cancer

Usually, adults receive 300-400 mg / m^2 (body surface area) once a day as carboplatin and withdraw at least 4 weeks. Let this be one course and repeat dosing. The dosage may be increased or decreased according to age, disease, and symptoms.

2. In case of breast cancer

In combination with trastuzumab (genetical recombination) and a taxane antineoplastic agent, adults are usually administered 300 to 400 mg / m^2 (body surface area) once a day as carboplatin and withdraw for at least 3 weeks . Let this be one course and repeat dosing. The dose is appropriately reduced depending on the condition of the patient.

3. Combination with other antineoplastic agents against pediatric malignant solid tumors (neuroblastoma · retinoblastoma · hepatoblastoma · central nervous system germ cell tumor, recurrent or refractory Ewing sarcoma family tumor · nephroblastoma) In case of therapy

(1) Neuroblastoma / hepatoblastoma / central nervous system germ cell tumor, case of recurrent or refractory Ewing sarcoma family tumor · combination with other antineoplastic agents against renal blastoma

In the combination therapy of ifosfamide and etoposide, the dose and administration method of carboplatin was intravenous drip infusion of 635 mg / m^2 (body surface area) as carboplatin for one day or intravenous drip infusion of 400 mg / m^2 (body surface area) for 2 days , Rest for at least 3 to 4 weeks. Let this be one course and repeat dosing.

The dose and the number of administration days are appropriately reduced depending on the disease, symptoms, and other antineoplastic agents to be used in combination.

Also, consideration should be given to dosage for children under 1 year old or under 10 kg.

(2) case of combination therapy with retinoblastoma with other antineoplastic agent

In combination therapy with vincristine sulfate and etoposide, the dose and administration method of carboplatin is intravenously infused intravenously at 560 mg / m^2 (body surface area) as carboplatin for 1 day and withdraws for at least 3 to 4 weeks. Let this be one course and repeat dosing.

However, carboplatin should be 18.6 mg / kg for children under 36 months of age.

The dose and the number of administration days are appropriately reduced depending on the disease, symptoms, and other antineoplastic agents to be used in combination.

Four.

Upon administration of this drug, it is mixed with dextrose injection solution or physiological saline solution of 250 mL or more according to the dose, and intravenous drip infusion over 30 minutes.

Usage notes related to dosage and dose

1.

When this drug is administered to a patient with breast cancer, carefully read the package insert of another antineoplastic agent to be used in combination.

2. Particular attention should be paid to the development of bone marrow suppression, hearing disorder, renal disorder in patients with combination renal function in combination therapy with other antineoplastic agents against pediatric malignant solid tumor, paying attention to dosage and administration interval etc. Carefully administer while observing the patient's condition. Incidentally, it is desirable to select the dose in consideration of GFR (Glomerular filtration rate) or the like as an indicator of kidney function.

3. In combination therapy with pediatric malignant solid tumor with other antineoplastic agents, carefully read the related literature ("Anticancer agent report: Carboplatin (childhood)" etc.) and package inserts of concomitant drugs.

Usage notes

Careful Administration

(Carefully administer to the following patients)

1. Patients with bone marrow suppression [It may exacerbate myelosuppression.]
2. Patients with renal impairment [Since kidney function is declining, side effects may appear strongly.]
3. Patients with hepatic impairment [Since metabolic function etc. are declining, side effects may appear strongly.]

Four. Patients with complications of infection [Myelosuppression may exacerbate infections.]

Five. Chickenpox patients [There is a risk of fatal generalized disability appeared.]

6. Elderly (see "Administration to the elderly" section)
7. Children (see "Administration to children etc.")
8. Patients who are using for a long time [bone marrow suppression, etc. strongly appear and may be transient.]

Important basic attention

1.

Severe side effects **such** as **bone marrow suppression** may occur, so adequate observation of the condition of the patient, such as **clinical examination (blood test, liver function test, renal function test etc.)** should be performed as appropriate. If abnormality is found, appropriate measures such as weight loss, withdrawal, discontinuation should be taken. Bone marrow suppression may be strong in patients who have undergone pretreatment, especially cisplatin and have decreased renal function, so in these patients, we recommend reducing the initial dose appropriately and pay attention to the blood test value . Side effects may appear strongly when used over a long period of time, and it may change to prolonged behavior, so administer it carefully.

2. **Because** side effects **such** as **bone marrow suppression** may be enhanced, when using other antineoplastic agents, radiation irradiation together, observe the patient's condition, pay **attention** to **dosage such as weight loss** .

3. When administering this drug, consider appropriate use of G-CSF preparation etc.

4. Gastrointestinal symptoms such as nausea · vomiting, loss of appetite may occur, so observe the condition of the patient adequately and take appropriate measures.

5. Beware of **infectious disease, bleeding tendency** or exacerbation.

6. If it is necessary to administer to children and reproductive age patients, consider the effects on gonads.

7. Because it is reported that hepatic central venous occlusive disease (VOD) has developed due to the combined use of this drug with other antineoplastic agents and irradiation, be careful. [1)]

8. When using this drug for breast cancer, the relevant literature ("Report on the applicability of unapproved drugs with high medical necessity / Applicable Inspection Council Examination Application: Carboplatin (breast cancer)" etc.) etc. To peruse it carefully.

Interaction

Combined attention

(Be aware of combined use)
1. Drug name etc. Irradiation
Clinical symptoms and measures
Because side effects such as bone marrow suppression may be enhanced, when conducting combination therapy, pay attention to dosage such as weight loss while observing the patient's condition.
Mechanism / risk factor
Both have side effects such as bone marrow suppression.

2. Drug name etc. Irradiation
Clinical symptoms and measures
There are reports that severe esophagitis or pneumonitis has developed when irradiation to the chest is used in combination. In case of simultaneous use, pay attention to the condition of the patient, when esophagitis or pulmonary shadow etc. appears, administration of this drug and radiation should be immediately stopped and appropriate measures should be taken.
Mechanism / risk factor
Although the mechanism is unknown, an increase in radiosensitivity by this drug is observed in animal test (mouse).
3. Drug name etc. Antineoplastic agent
Clinical symptoms and measures
Because side effects such as bone marrow suppression may be enhanced, when conducting combination therapy, pay attention to dosage such as weight loss while observing the patient's condition.
Mechanism / risk factor
Both have side effects such as bone marrow suppression.
Four. Drug name etc. drugs with nephrotoxicity and ototoxicity aminoglycoside antibiotics etc.
Clinical symptoms and measures
Renal disorder and hearing loss may be enhanced, so when using combination therapy, you should administer it carefully.
Mechanism / risk factor
Both have renal impairment and hearing loss.

Side effect

Outline of development status of side effects etc.

(Aggregation till the end of re-examination)
The incidence of adverse reactions and laboratory test abnormalities in 6,218 cases (620 cases at the time of approval and 5, 598 cases of use results) was 86.02%, the main ones were nausea · vomiting 50.45%, anorexia 45.43%, general malaise 18.64%, depilation 18.25%, fever 5.74%, leucocytopenia 56.42%, thrombocytopenia 42.67%, hemoglobin decrease 40.10%, red blood cell loss 36.14%, hematocrit decrease 31.65%, ALT (GPT) increase 10.15%, AST (GOT) 9.18%, neutropenia reduction 7.40%, BUN increase 5.05%, creatinine · clearance value decrease 3.57%, serum creatinine increase 2.57%, etc.

Serious side effects

1. **Myelosuppression such as pancytopenia** (<0.1%) **etc** :
Pancytopenia, anemia (hemoglobin reduction, red blood cell reduction, decrease in hematocrit value), leukocytopenia, neutropenia, thrombocytopenia, bleeding, etc. may occur, so observation of peripheral blood is performed sufficiently, abnormality

is observed If appropriate, take appropriate measures such as weight loss, withdrawal, discontinuation.

2. **Shock, anaphylaxis** (<0.1%):

Shock and anaphylaxis may occur, so observe thoroughly, cyanosis, difficulty breathing, anguish in the chest, blood pressure decrease, bronchospasm, etc. should be discontinued and appropriate measures should be taken. Incidentally, there is also a tendency that the frequency of occurrence of shock and anaphylaxis tends to increase when the administration frequency of this drug is repeated (see other cautions).

Interstitial pneumonia (0.1%):

Interstitial pneumonia accompanied by fever, cough, dyspnea, chest X-ray abnormality, etc. may occur, so observe thoroughly and if abnormality is found, administration is discontinued and administration of adrenocortical hormone drug Appropriate measures should be taken.

4. * **Acute kidney injury** (<0.1%), **Fancony syndrome** (frequency unknown):

Acute kidney injury , Fanconi syndrome, etc. may occur, so observe thoroughly and if abnormality is found in BUN, serum creatinine, creatinine · clearance value etc, discontinue administration and take appropriate measures about.

5. **Liver failure, liver dysfunction, jaundice** (frequency unknown in any case):

Liver failure, liver function disorder, jaundice may appear, so observe thoroughly, such as by conducting regular inspections, if abnormalities are observed, discontinue administration and take appropriate measures.

6. **Gastrointestinal tract necrosis, gastrointestinal perforation, gastrointestinal bleeding, gastrointestinal ulcer** (frequency unknown in any case):

Gastrointestinal necrosis, gastrointestinal perforation, gastrointestinal bleeding, gastrointestinal ulcer may occur, so observe thoroughly and if abnormalities are observed discontinue administration and take appropriate measures.

7. **Hemorrhagic enteritis, pseudomembranous colitis** (frequency unknown):

Hemorrhagic enteritis, pseudomembranous colitis and the like may occur, so observe thoroughly and if severe abdominal pain / diarrhea etc. appears, administration should be stopped and appropriate measures should be taken.

8. **Paralytic ileus** (<0.1%):

Because of intestinal paralysis (loss of appetite, nausea / vomiting, remarkable constipation, abdominal pain, abdominal distension or relaxation, stasis of intestinal contents, etc.) and may shift to paralytic ileus, when intestinal paralysis appears Discontinue administration and take appropriate measures such as intestinal decompression.

9. **Cerebral infarction** (less than 0.1%), **pulmonary infarction** (frequency unknown):

Cerebral infarction, pulmonary infarction may occur, so observe thoroughly, if abnormalities are observed discontinue administration and take appropriate measures.

10. **Thrombus · embolism** (Frequency unknown):

Thrombosis · Embolism (pulmonary embolism, cerebral thrombosis, other arterial or venous thrombosis, etc.) may occur, so observe thoroughly, if abnormality is found discontinue administration and take appropriate measures about.

11. **Myocardial infarction, congestive heart failure** (Frequency unknown):

Myocardial infarction and congestive heart failure may occur. If abnormalities are observed, administration should be discontinued and appropriate measures should be taken.

12. **Hemolytic uremic syndrome** (frequency unknown):
    Hemolytic uremic syndrome, which is characterized by thrombocytopenia, hemolytic anemia and renal failure, may appear, so observe thoroughly by regularly conducting blood tests (platelets, erythrocytes, etc.) and renal function tests, If abnormality is observed, discontinue administration and take appropriate measures.
13. **Acute Respiratory Distress Syndrome** (Frequency Unknown):
    Acute respiratory distress syndrome may appear, so observe thoroughly, and if chest X-ray abnormality such as breathing difficulty, hypoxia, bilateral diffuse diffuse lung infiltration shadow etc. which progress rapidly is observed etc, administration should be performed Discontinue and take appropriate measures.
14. **Disseminated intravascular coagulation syndrome (DIC)** (Frequency unknown):
    Disseminated intravascular coagulation syndrome (DIC) may occur, so observe thoroughly and if abnormality is found in blood test such as platelet count, serum FDP value, plasma fibrinogen concentration etc, discontinue administration, Appropriate measures should be taken.
15. **Acute pancreatitis** (frequency unknown):
    As acute pancreatitis may appear, administration should be discontinued if observation is sufficiently performed and abnormality is observed in serum amylase value, serum lipase value, etc.
16. **Hearing loss** (<0.1%):
    Hearing loss, tinnitus, etc. may occur, so if you observe well enough, if abnormalities are observed discontinue administration and take appropriate measures.
17. **White matter encephalopathy (including reversible posterior leukoencephalopathy syndrome)** (Frequency unknown):
    As white matter encephalopathy (including reversible posterior leukoencephalopathy syndrome) may appear, administration is discontinued when walking wobble, tongue entanglement, convulsions, headache, confusion, vision disorder etc. are observed To carry out Do treatment.
18. **Tumor collapse syndrome** (frequency unknown):
    Tumor collapse syndrome may appear, so observe patient condition sufficiently, such as serum electrolyte concentration and renal function test. When abnormality is observed, administration is discontinued, appropriate treatment (administration of physiological saline, hyperuricemia treatment, etc., dialysis etc.) is carried out, and the state of the patient is sufficiently observed until the symptoms recover To do.

Serious side effects (drugs)

1. **Stasis papilla, retrobulbar optic neuritis, cortical blindness** :
    Cisplatin, in rare cases visual impairment such as congestive papilla, retrobulbar optic neuritis, cortical blindness etc. may appear, so if abnormalities are found, discontinue administration.

2. **Hemolytic anemia** :
   Because coombs-positive hemolytic anemia may appear in cisplatin, administration should be discontinued if abnormality is observed.

Other side effects

1. **digestive tract**
   10% or more or Frequency unknown
   Nausea · vomiting Note 1), anorexia
2. **Gastrointestinal**
   Less than 1 to 10%
   Diarrhea, stomatitis, abdominal pain, constipation
3. **Gastrointestinal**
   Less than 1%
   Thirst
4. **Kidney**
   Less than 1 to 10%
   Hematuria, proteinuria
5. **Kidney**
   Less than 1%
   Oliguria
6. **Hypersensitivity** Note 2)
   10% or more or Frequency unknown
   Hives *
7. **Hypersensitivity** Note 2)
   Less than 1 to 10%
   rash
8. **Hypersensitivity** Note 2)
   Less than 1%
   Itching sensation
9. **Psychoneurotic system**
   Less than 1 to 10%
   Peripheral neuropathy (numbness etc.), headache
10. **Psychic nervous system**
    Less than 1%
    Tinnitus, hearing loss, vision disorder, vertigo, convulsions, abnormal sensation, dysgeusia, nervousness, anxiety, insomnia
11. **Liver**
    10% or more or Frequency unknown
    ALT (GPT) rise
12. **Liver**
    Less than 1 to 10%
    AST (GOT) increase, Al - P increase, bilirubin increase, LDH increase, γ - GTP increase
13. **Cardiotomy**
    Less than 1%

Electrocardiogram abnormality (extrasystole), palpitation, blood pressure increase, blood pressure decrease, arrhythmia (tachycardia, bradycardia, atrial fibrillation, atrial flutter, atrioventricular block)

14. **Electrolyte**
    Less than 1 to 10%
    Abnormalities such as serum sodium, potassium, crawl, calcium, phosphorus, magnesium etc.
15. **Electrolyte**
    Less than 1%
    Antidiuretic hormone secretory abnormality syndrome
16. **Skin**
    10% or more or Frequency unknown
    Depilation
17. **Skin**
    Less than 1%
    Pigmentation, nail discoloration, skin disease
18. **Other**
    10% or more or Frequency unknown
    General malaise, asthenia *, uric acid increase *, chills *, dehydration *, weight loss *, albumin decrease *, dyspnea ※
19. **Other**
    Less than 1 to 10%
    Fever
20. **Other**
    Less than 1%
    Pain, flushing, hot flashes, chest discomfort, stasis, injection site reaction (redness, swelling, pain, necrosis, induration etc.), hypoproteinemia
    ※ : Frequency unknown
    Note 1: As an action, administration of an antiemetic agent etc. is carried out.
    Note 2: In case of such symptoms appear, discontinue administration.

Administration to the elderly

As elderly people generally have physiological functions (bone marrow function, liver function, kidney function, etc.) declining, careful administration should be made while observing the patient's condition, taking notice of dosage and administration interval.

Administration to pregnant women, maternity women, nursing women, etc.

1.
** Do not administer to pregnant women or women who may be pregnant. Also, for women who are likely to become pregnant, be instructed to give proper contraception during the administration of this drug and for a certain period after

administration. [Teratogenic effects and fetal lethal effects are reported in animal experiments (rats).]

2.

** Men who are likely to become pregnant by partner should be instructed to take proper contraceptive during the administration of this drug and for a certain period after the administration. [Genotoxicity has been reported in revertive mutation test using bacteria, chromosomal aberration test using mammalian cultured cells and micronucleus test using mouse.]

3.

When feeding to a nursing woman, stop breast-feeding. [Animal experiment (rat) has reported the transition into milk.]

Administration to children etc.

In combination therapy with other antineoplastic agents against pediatric malignant solid tumors (neuroblastoma / retinoblastoma / hepatoblastoma / central nervous system germ cell tumor, recurrent or refractory Ewing sarcoma family tumor · nephroblastoma) Pay particular attention to the development of kidney disorders such as bone marrow suppression, hearing loss, Fancony syndrome, and carefully administer it while observing the condition of the patient, taking notice of dose and administration interval. In addition, there are reports that clinically significant hearing loss occurs in pediatric patients when using this drug in a high dose in a foreign country together with a drug having other ototoxicity.

Overdosage

There are reports that visual impairment including blindness appeared when this drug was administered at a high dose.

Application note

1. At **preparation**

(1)

This product should be mixed with these amino acid infusions because degradation occurs in the amino acid (methionine and cystine) infusion containing sulfur.

(2)

Since this agent reacts with aluminum to form a precipitate and its activity declines, do not use medical equipment containing aluminum for use.

(3)

Since this drug is a complex compound, it should not be mixed with other antineoplastic agents.

(Four)

Because this drug is cytotoxic, it is desirable to wear gloves during preparation. If chemicals adhere to the skin, rinse thoroughly with plenty of running water immediately.

2. On **administration**

(1)

When this drug is mixed with an infusion solution containing inorganic salts such as physiological saline (NaCl, KCl, $CaCl_2$, etc.), administration should be completed within 8 hours.

(2)

In case of intravenous administration, leakage of drug solution out of the blood vessel may result in induration / necrosis etc. at the injection site, so careful administration should be made so that the drug solution does not leak out of the blood vessel.

3. When **saved**

As this product is decomposed by light and heat, avoid direct sunlight and high temperature.

Other notes

1.

For this drug, efficacy was not recognized for cases in which no effect was observed by administration of cisplatin.

2.

This product has mutagenicity to bacteria and human lymphoblastoid cells and chromosome abnormality induction to hamsters is recognized.

3.

There are reports that adenocarcinoma of the parotid gland and mammary gland and precancerous lesion of the prostate occurred due to the chronic toxicity test (intravenous administration) of rats.

4.

There are reports that acute leukemia (sometimes accompanying the preleukemic phase) and myelodysplastic syndrome (MDS) occurred by combination of this drug and other antineoplastic agents.

5.

There is a tendency that the frequency of occurrence of shock and anaphylaxis tends to be high when the administration frequency of this drug is repeated, and there is a report that the tendency becomes remarkable especially when the administration number of platinum preparations exceeds 8 times.

Pharmacokinetics

1. **blood concentration** [2) to 4)]

Changes in the blood concentration when intravenous drip infusion of paraplatin as carboplatin once into a cancer patient by intravenous infusion showed a decay curve of 3 phase, the half life of α phase was 0.16 to 0.32 hours, the β phase was 1.29 to 1.69 hours, the γ phase was 22 to 32 hours, most of the carboplatin rapidly disappeared after administration and slowly disappeared from the blood with the lapse of time.

Note: Approved dose of this drug is 300 ~ 400 mg / m^2 .

2. **excretion** [2) to 4)]

Urinary excretion of this drug in cancer patients was relatively fast after administration and 57 to 82% was excreted 24 hours after administration.

Plasma platinum concentration after carboplatin administration

Clinical results

1. **Domestic clinical test results** [5) to 15)]

(1) Head and neck cancer (number of cases analyzed 67)

Effective (CR): 1, effective (PR): 13, invariable (NC): 35, progression (PD): 18, response rate% (CR + PR): 20.9

(2) Small cell lung cancer (Number of cases subject to analysis 116)

Effective (CR): 1, effective (PR): 30, invariant (NC): 56, progression (PD): 29, response rate% (CR + PR): 26.7

(3) Testicular tumor (number of cases analyzed 21)

Effective (CR): 1, effective (PR): 9, invariant (NC): 7, progression (PD): 4, response rate% (CR + PR): 47.6

(4) Ovarian cancer (number of cases to be analyzed 50)

Effective (CR): 5, effective (PR): 14, invariant (NC): 22, progression (PD): 9, response rate% (CR + PR): 38.0

(5) Cervical cancer (number of cases analyzed 32)

Effective (CR): 2, effective (PR): 5, invariant (NC): 16, progression (PD): 9, response rate% (CR + PR): 21.9

(6) Malignant lymphoma (number of cases analyzed 33)

Effective (CR): 2, effective (PR): 11, invariable (NC) · Progressive (PD): 20, response rate% (CR + PR): 39.4

※) Effective = complete remission, effective = incomplete remission, invariant · progress = no response

Disease-specific response rate (remission rate) was 20.9% of head and neck cancer (14/67), small cell carcinoma of lung 26.7% (31/116), testicular tumor 47.6% (10/21), ovarian cancer 38.0% (19 / 50), cervical cancer 21.9% (7/32), malignant lymphoma 39.4% (13/33). In addition, the efficacy of this drug is also recognized in comparison with cisplatin for head and neck cancer and ovarian cancer.

Paraplatin has no statistically significant difference in response rate compared with cisplatin clinical phase II study results, but patients who can not tolerate treatment of cisplatin (patients with reduced renal function, large amounts of Patients with disorders of cardiac and circulatory system due to moisture loading, patients with obstructive disorder in the urinary route of the kidney, urinary tract, bladder, patients with obstructive disorder, patients with gastrointestinal symptoms such as nausea and vomiting strongly emerging and hinder treatment) Administration was possible, and the incidence of peripheral neuropathy and ototoxicity was lower than that of cisplatin.

2. **Overseas clinical study results** [16) ~ 20)]

Response efficiency and survival time of this drug alone monotherapy for non-small cell lung cancer abroad are as follows.

1)

Researcher: Kreisman et al. [16] Number of cases analyzed: 70, Response example (CR + PR): 11, Response efficiency (%): 16, Survival time (median): 6.5 months

2)

Researcher: Kramer et al. [17] , number of cases analyzed: 50, response example (CR + PR): 6, response rate (%): 12, survival time (median)

3)

Researcher: Bonomi et al. [18] , Number of cases analyzed: 88, Response example (CR + PR): 8, Response efficiency (%): 9, Survival time (median): 31.7 weeks

In addition, combination chemotherapy containing this drug has been widely used for non-small cell lung cancer in recent years, and the response rate and the survival time in these combination chemotherapy are as follows.

1)

Combination therapy: carboplatin + etoposide [19] , number of cases analyzed: 102, response (CR + PR): 16, response rate (%): 16, survival time (median): 27 weeks

2)

Combination therapy: carboplatin + paclitaxel [20] , number of cases analyzed: 190, response (CR + PR): 43, response rate (%): 23, survival time (median): 233 days

Medicinal pharmacology

1. **Antitumor effect** [21) to 27)]

Antitumor effect was observed in murine L1210 leukemia, P388 leukemia, B16 melanoma, colon 26 colon cancer, M5076 ovarian cancer, Lewis lung cancer. Carboplatin showed cross-tolerance to cisplatin-resistant ovarian cancer cell lines KFr and TYK-nu (R) cells, but the degree was 1/2 or 1/4 of that of cisplatin.

2. **Mechanism of action** [28) - 30)]

It is believed to bind DNA strands within cancer cells and inhibit DNA synthesis and subsequent division of cancer cells.

Physicochemical knowledge on active ingredients

common name: Carboplatin (Carboplatin)
Chemical name: (*SP* -4-2) -Diammine [cyclobutan-1, 1-dicarboxylato (2 -) - *O* , *O* '] platinum
Structural formula:

Molecular formula: $C_6H_{12}N_2O_4Pt$
Molecular weight: 371.25
Property: Carboplatin is a white crystal or a crystalline powder.
It is slightly soluble in water and very insoluble in ethanol (99.5).

Handling Precautions

1. This product should be used as soon as possible after mixing with infusion.
2. Store the vial in a box after opening the package.
3. In refrigerator storage, crystals may precipitate.

Packaging

Paraplatin injection 50 mg: 5 mL (containing carboplatin 50 mg) 1 vial

Name or name and address of manufacturer / distributor etc

Market Authorisation Holder

Bristol-Myers Squibb Co., Ltd.
6-5-1 Nishi-Shinjuku, Shinjuku-ku, Tokyo
Japan

Manufacturer

Bristol-Myers Squibb Co., Ltd.
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