

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use MATULANE safely and effectively. See full prescribing information for MATULANE.

MATULANE (procarbazine hydrochloride) capsules, for oral use
Initial U.S. Approval: 1969

INDICATIONS AND USAGE

MATULANE is an alkylating drug indicated for use in combination with other anticancer drugs for the treatment of Stage III or Stage IV Hodgkin Lymphoma. (1)

DOSAGE AND ADMINISTRATION

Recommended Dosage: 100 mg/m² orally once a day for adult and pediatric patients. (2.1)
See Full Prescribing Information for dosage modifications for adverse reactions (2.2)

DOSAGE FORMS AND STRENGTHS

Capsules: 50 mg of procarbazine hydrochloride (3)

CONTRAINDICATIONS

History of known hypersensitivity or anaphylaxis to the drug or drug components (4)

WARNINGS AND PRECAUTIONS

- Myelosuppression: Severe neutropenia, anemia, and thrombocytopenia can occur. Obtain complete blood counts prior to initiation of MATULANE (5.1)
- Secondary Malignancies: Lung cancer, myelodysplastic syndrome, acute myeloid leukemia, and non-Hodgkin lymphoma have been reported. Monitor patients for the development of secondary malignancies during and after treatment with MATULANE. (5.2)
- Use in Patients with Renal or Hepatic Impairment: Evaluate renal and hepatic function. Closely monitor for adverse reactions. (5.3)
- Risk of Disulfiram-like Reaction Due to Concomitant Use with Alcohol: Advise patients to avoid consumption of alcohol products containing propylene glycol before, after, and during

treatment with MATULANE. (5.4)

- Infertility: Male and female reproductive function and fertility may be impaired in patients treated with MATULANE. Advise patients on the potential risks for infertility. (5.5, 8.3)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential and males with female partners of reproductive potential of the potential risk to a fetus and to use effective contraception. (5.6, 8.1, 8.3)

ADVERSE REACTIONS

The most common adverse reactions are neutropenia, anemia, thrombocytopenia, nausea, and vomiting (6)

To report SUSPECTED ADVERSE REACTIONS, contact Leadiant Biosciences, Inc. at 1-888-393-4584 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Central nervous system depressants: monitor signs and symptoms of neurotoxicity. (7.1)
- Monoamine oxidase (MAO) inhibitors: avoid MAO inhibitors and other drugs with MAO inhibition activity within two weeks before and during treatment with MATULANE. (7.2)
- Alcohol: avoid consumption of alcohol or products containing propylene glycol before, after, and during therapy with MATULANE. (7.3)
- Tyramine-containing foods: avoid concomitant use. (7.4)

USE IN SPECIFIC POPULATIONS

- Lactation: Advise not to breastfeed. (8.2)
- Pediatric Use: Tremors, coma and convulsions, have occurred in pediatric patients treated with MATULANE. Dosage, therefore, should be individualized (2.1, 8.4)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 9/2026

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

MATULANE is indicated for use in combination with other anticancer drugs for the treatment of Stage III or Stage IV Hodgkin Lymphoma.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

The recommended dosage of MATULANE for adult and pediatric patients is 100 mg/m² orally once a day.

Use the patient's actual bodyweight for the recommended dosage, unless the patient is obese or experiencing weight gain due to edema, ascites, or abnormal fluid retention and then use estimated lean body mass.

Individualize the dose and dosing schedule of MATULANE based on the specific regimen administered, response to treatment, and patient risk factors.

Refer to the Prescribing Information for the agents used in combination for dosing information as appropriate.

2.2 Dosage Modifications for Adverse Reactions

Monitor complete blood counts (CBCs) prior to initiation of, and as clinically indicated, during treatment with MATULANE [see *Warnings and Precautions* (5.1)]. If the following adverse reactions occur, permanently discontinue MATULANE:

- Anaphylaxis or other hypersensitivity reactions [see *Contraindications* (4)]

If any of the following adverse reactions occur, consider withholding until clinically stable or permanently discontinuing depending on adverse reaction severity:

- Grade 4 neutropenia, febrile neutropenia, or signs or symptoms of infection [see *Warnings and Precautions* (5.1)]
- Grade 4 thrombocytopenia, hemorrhage, or signs of bleeding [see *Warnings and Precautions* (5.1)]
- Central nervous system signs or symptoms such as paresthesia, neuropathies, or confusion [see *Adverse Reactions* (6)]
- Stomatitis (ulcerative or persistent pain) [see *Adverse Reactions* (6)]
- Diarrhea [see *Adverse Reactions* (6)]

2.3 Administration

MATULANE is a hazardous drug. Follow applicable handling and disposal procedures.¹

MATULANE can be administered with or without food.

Advise patients to avoid consumption of alcohol during treatment with MATULANE [see *Warnings and Precautions (5.3)*].

3 DOSAGE FORMS AND STRENGTHS

Capsules: 50 mg of procarbazine hydrochloride, ivory capsule, with “MATULANE LB213” imprint.

4 CONTRAINDICATIONS

MATULANE is contraindicated in patients with known hypersensitivity or anaphylaxis to the drug or drug components [see *Adverse Reactions (6)*].

5 WARNINGS AND PRECAUTIONS

5.1 Myelosuppression

Matulane can cause myelosuppression, including severe neutropenia, anemia, and thrombocytopenia.

Obtain complete blood counts prior to initiation of MATULANE and monitor patients during treatment for clinical complications due to myelosuppression. During treatment with MATULANE, monitor hemoglobin, hematocrit, white blood count (WBC) including differential, reticulocytes, and platelets weekly or as clinically necessary.

Myelosuppression often occurs 2 to 8 weeks after the start of MATULANE treatment. If severe myelosuppression occurs, withhold MATULANE until clinically stable, or permanently discontinue depending on severity [see *Dosage and Administration (2.2)*].

If radiation or a chemotherapeutic agent known to have myelosuppressive activity has been used, an interval of one month or longer without such therapy is recommended before starting treatment with MATULANE. The length of this interval may also be determined by evidence of bone marrow recovery based on successive bone marrow studies.

5.2 Secondary Malignancies

Secondary malignancies have been reported in patients treated with MATULANE when used in combination with other chemotherapy, including lung cancer, myelodysplastic syndrome, acute myeloid leukemia, and non-Hodgkin Lymphoma. The risks of secondary lung cancer from treatment appear to be increased by tobacco use.

Monitor patients for the development of secondary malignancies during and after treatment with MATULANE.

5.3 Use in Patients with Renal or Hepatic Impairment

Increased adverse reactions may occur if Matulane is used in patients with renal or hepatic impairment.

Evaluate renal and hepatic function prior to beginning therapy. Repeat urinalysis, transaminase, alkaline phosphatase and blood urea nitrogen tests at least weekly and as clinically indicated.

When appropriate, consider hospitalization for the initial course of treatment.

5.4 Risk of Disulfiram-like Reaction Due to Concomitant Use with Alcohol

MATULANE can cause a disulfiram-like reaction in patients who consume alcohol during treatment with MATULANE.

Advise patients to avoid consumption of alcohol or products containing propylene glycol before, after, and during treatment with MATULANE.

5.5 Infertility

Male and female reproductive function and fertility may be impaired in patients treated with MATULANE. Patients treated with MATULANE when used in combination with other chemotherapy have reported azoospermia and premature ovarian failure. Advise patients on the potential risks for infertility [see *Use in Specific Populations* (8.3)].

5.6 Embryo-Fetal Toxicity

Based on findings from human case reports and animal studies, MATULANE can cause fetal harm when administered to a pregnant woman. There are case reports of malformations in the offspring of women who were exposed to procarbazine hydrochloride in combination with other antineoplastic agents during pregnancy. In reproductive studies in rats, procarbazine hydrochloride caused adverse developmental outcomes including embryo-fetal mortality, structural abnormalities, and neurogenic tumors. Advise pregnant women and females of reproductive potential of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with MATULANE. Advise males with female partners of reproductive potential to use effective contraception during treatment with MATULANE [see *Use in Specific Populations* (8.1, 8.3)].

6 ADVERSE REACTIONS

The following adverse reactions are discussed in more detail elsewhere in the labeling.

- Myelosuppression [see *Warnings and Precautions* (5.1)].
- Secondary Malignancies [see *Warnings and Precautions* (5.2)].
- Risk of Disulfiram-like Reaction Due to Concomitant Use with Alcohol [see *Warnings and Precautions* (5.3)].
- Infertility [see *Warnings and Precautions* (5.4)].

The following adverse reactions associated with the use of MATULANE were identified in clinical studies or post-marketing reports. Because some of these reactions were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

The most common adverse reactions for MATULANE are neutropenia, anemia, thrombocytopenia, nausea, and vomiting.

Other adverse reactions are:

Hematologic: Pancytopenia, eosinophilia, hemolytic anemia

Vascular: Petechiae, purpura, epistaxis, hemoptysis

Hepatobiliary: Hepatic dysfunction, jaundice

Gastrointestinal: Stomatitis, hematemesis, melena, diarrhea, dysphagia, anorexia, abdominal pain, constipation, dry mouth

Neurologic: Coma, convulsions, neuropathy, ataxia, paresthesia, nystagmus, diminished reflexes, falling, foot drop, headache, dizziness, unsteadiness, slurred speech

Cardiovascular: Hypotension, tachycardia, syncope

Ophthalmic: Retinal hemorrhage, papilledema, photophobia, diplopia, inability to focus

Respiratory: Pneumonitis, pleural effusion, cough, hoarseness

Dermatologic: Herpes, dermatitis, pruritus, alopecia, hyperpigmentation, rash, urticaria, flushing

Allergic: Generalized allergic reactions

Genitourinary: Hematuria, urinary frequency, nocturia

Musculoskeletal: Pain including myalgia and arthralgia, tremors

Psychiatric: Hallucinations, depression, apprehension, nervousness, confusion, nightmares, insomnia

Endocrine: Gynecomastia in prepubertal and early pubertal boys

Miscellaneous: Intercurrent infections, hearing loss

General: Pyrexia, diaphoresis, lethargy, weakness, fatigue, edema, chills, drowsiness

Neoplasms: Secondary lung cancer, acute myelocytic leukemia, myelodysplastic syndrome, malignant myelosclerosis

7 DRUG INTERACTIONS

7.1 Central Nervous System Depressants

Monitor signs and symptoms of neurotoxicity with concomitant use of MATULANE and other central nervous system (CNS) depressing agents. Concomitant use of MATULANE with other CNS depressing agents may result in potentiation of CNS depression with MATULANE.

7.2 Monoamine Oxidase Inhibitors

Avoid monoamine oxidase (MAO) inhibitors and other drugs with MAO inhibition activity within two weeks before, and during treatment with MATULANE. MATULANE exhibits MAO inhibitory activity. Concomitant use of MATULANE with other MAO inhibitors may increase the risk of a hypertensive crisis.

7.3 Alcohol

Avoid consumption of alcohol or products containing propylene glycol before, after, and during therapy with MATULANE [see *Warnings and Precautions* (5.3)]. Use of MATULANE is associated with a disulfiram-like reaction to alcohol, including abdominal cramps, nausea, vomiting, headaches, and flushing.

7.4 Tyramine-containing Foods

Avoid tyramine-containing foods during therapy with MATULANE. Concurrent ingestion of foods rich in tyramine may cause sudden and severe high blood pressure in patients receiving MATULANE.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on findings from human case reports and animal studies, MATULANE can cause fetal harm when administered to a pregnant woman (see *Data*). In reproductive studies in rats, procarbazine hydrochloride caused adverse developmental outcomes including embryo-fetal mortality, structural abnormalities, and neurogenic tumors.

Advise pregnant women and females of reproductive potential of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with MATULANE.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20% respectively.

Data

Human

There are case reports of malformations in the offspring of women exposed to procarbazine hydrochloride in combination with other antineoplastic agents during pregnancy.

Animal

Procarbazine hydrochloride caused embryo-fetal mortality and structural abnormalities in rats when administered intraperitoneally at doses approximately 1.5 to 4.5 times the maximum recommended human therapeutic dose of 100 mg/m² based on body surface area.

Procarbazine hydrochloride has not been adequately studied in animals for its effects on peri- and postnatal development. However, neurogenic tumors developed in the offspring of rats that were intravenously administered procarbazine hydrochloride on day 22 of gestation at a dose approximately 7.5 times the maximum recommended human therapeutic dose of 100 mg/m² based on body surface area.

8.2 Lactation

Risk Summary

There are no data on the presence of MATULANE or its metabolites in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious

adverse reactions, including tumorigenicity in the breastfed child, advise women not to breastfeed during treatment with MATULANE.

8.3 Females and Males of Reproductive Potential

MATULANE can cause fetal harm when administered to a pregnant woman [*see Use in Specific Populations (8.1)*].

Pregnancy Testing

Verify pregnancy status of females of reproductive potential prior to initiating MATULANE.

Contraception

Females

Advise females of reproductive potential to use effective contraception during treatment with MATULANE.

Males

Advise males with female partners of reproductive potential to use effective contraception during treatment with MATULANE.

Infertility

Females

MATULANE administered in combination with other chemotherapeutic agents can cause premature ovarian failure and infertility based on human clinical studies.

Males

MATULANE administered in combination with other chemotherapeutic agents can cause azoospermia and infertility based on human clinical studies. Based on findings in animals, procarbazine hydrochloride may impair male fertility [*see Nonclinical Toxicology (13.1)*].

8.4 Pediatric Use

Tremors, coma, and convulsions have occurred in pediatric patients treated with MATULANE. Pediatric patients should be closely monitored. Individualize the dosage based on the incidence and severity of adverse reactions [*see Dosage and Administration (2.2)*].

8.5 Geriatric Use

Clinical studies of MATULANE did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger patients.

10 OVERDOSAGE

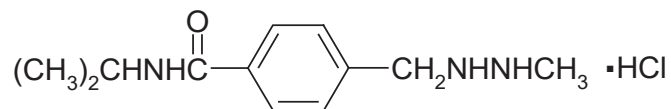
Adverse reactions due to overdosage with MATULANE are anticipated to be nausea, vomiting, enteritis, diarrhea, hypotension, tremors, convulsions and coma.

As treatment, administer either an emetic or gastric lavage. Use general supportive measures such as intravenous fluids. Since the major toxicity of procarbazine hydrochloride is hematologic and hepatic, conduct frequent complete blood counts and liver function tests throughout the

period of recovery and for a minimum of two weeks thereafter. Provide immediate supportive care to manage adverse reactions as clinically indicated.

11 DESCRIPTION

Procarbazine hydrochloride is an alkylating drug and hydrazine derivative. The chemical name is *N*-isopropyl- α -(2-methylhydrazino)-*p*-toluamide monohydrochloride. It is soluble but unstable in water or aqueous solutions. The molecular weight of procarbazine hydrochloride is 257.76 and the structural formula is:



MATULANE (procarbazine hydrochloride) capsules are for oral use. Each capsule contains approximately 58 mg of procarbazine hydrochloride, equivalent to 50 mg of procarbazine free base. Inactive ingredients in MATULANE are cornstarch, mannitol and talc. Gelatin capsule shells contain titanium dioxide, FD&C Yellow No. 6 and D&C Yellow No. 10.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The precise mode of cytotoxic action of procarbazine has not been clearly defined. After metabolic activation, procarbazine may inhibit the transmethylation of methyl groups of methionine into transfer RNA (t-RNA). The unavailability of t-RNA prevents protein synthesis, and consequently prevents DNA and RNA synthesis. Procarbazine may also undergo auto-oxidation, resulting in the formation of cytotoxic free radicals which directly damage DNA through an alkylation reaction.

12.2 Pharmacodynamics

Procarbazine exposure-response relationships and the time course of pharmacodynamic responses have not been fully characterized.

12.3 Pharmacokinetics

Absorption

Procarbazine is rapidly and completely absorbed. Following oral administration of 30 mg of ¹⁴C-labeled procarbazine, maximum peak plasma radioactive concentrations were reached within 60 minutes.

Procarbazine crosses the blood-brain barrier and rapidly equilibrates between plasma and cerebrospinal fluid after oral administration.

Elimination

After intravenous injection, the plasma half-life of procarbazine is approximately 10 minutes.

Metabolism

Procarbazine is metabolized primarily in the liver and kidneys. The drug appears to be auto-oxidized to the azo derivative with the release of hydrogen peroxide. The azo derivative isomerizes to the hydrazone, and following hydrolysis splits into a benzylaldehyde derivative and methylhydrazine. The methylhydrazine is further degraded to CO₂ and CH₄ and possibly hydrazine, whereas the aldehyde is oxidized to *N*-isopropylterephthalamic acid.

Excretion

Approximately 70% of the drug is excreted in the urine as *N*-isopropylterephthalamic acid within 24 hours following both oral and intravenous administration of ¹⁴C-labeled procarbazine.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Procarbazine hydrochloride was carcinogenic in mice, rats, and monkeys.

Procarbazine hydrochloride was mutagenic and clastogenic in a variety of in vitro and in vivo test systems.

Compounds which inhibit DNA, RNA and/or protein synthesis might be expected to have adverse effects on gametogenesis. In animal studies, procarbazine hydrochloride caused unscheduled DNA synthesis in the testis of rabbits and decreased fertility in male mice.

15 REFERENCES

1. OSHA Hazardous Drugs. OSHA. <https://www.osha.gov/hazardous-drugs>

16 HOW SUPPLIED/STORAGE AND HANDLING

MATULANE (procarbazine hydrochloride) capsules: ivory, in bottles of 100 (NDC 54482-054-01). Imprint on capsules: MATULANE LB213.

Store at 25°C (77°F); excursions permitted to 15°C–30°C (59°F–86°F) [see USP Controlled Room Temperature].

Dispense in light-resistant container as defined in USP/NF.

MATULANE is a hazardous drug. Follow applicable special handling and disposal procedures.¹

17 PATIENT COUNSELING INFORMATION

Myelosuppression

Inform the patient that MATULANE can cause severe myelosuppression. Advise the patient to immediately report signs or symptoms such as bleeding, easy bruising, symptoms of infection (fever, chills, cough, pain, or burning during urination), fatigue, or shortness of breath to their healthcare provider [see *Warnings and Precautions* (5.1)].

Secondary Malignancies

Advise patients of the increased risk of secondary malignancies [*see Warnings and Precautions (5.2)*].

Risk of Disulfiram-like Reaction Due to Concomitant Use with Alcohol

Inform patients that MATULANE may cause a disulfiram-like reaction when consuming alcohol during treatment. Advise patients to avoid consumption of alcohol during treatment with MATULANE before, after and during therapy with MATULANE [*see Warnings and Precautions (5.4) and Drug Interactions (7.3)*].

Embryo-Fetal Toxicity

Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females to inform their healthcare provider of a known or suspected pregnancy [*see Warnings and Precautions (5.6) and Use in Specific Populations (8.1, 8.3)*].

Advise females of reproductive potential to use effective contraception during treatment with MATULANE [*see Use in Specific Populations (8.3)*].

Advise males with female partners of reproductive potential to use effective contraception during treatment with MATULANE [*see Use in Specific Populations (8.3)*].

Lactation

Advise women not to breastfeed during treatment with MATULANE [*see Use in Specific Populations (8.2)*].

Infertility

Advise patients of reproductive potential of the potential for reduced fertility from MATULANE [*see Use in Specific Populations (8.3), Nonclinical Toxicology (13.1)*].

Drug Interactions

Advise patients to discontinue consumption of alcohol or products containing propylene glycol before, after and during therapy with MATULANE [*see Warnings and Precautions (5.4) and Drug Interactions (7.3)*].

Advise patients to avoid foods with known high tyramine content. [*see Drug Interactions (7.4)*]

Administration

Instruct patients to follow applicable handling and disposal procedures since Matulane is a hazardous drug.

Advise the patient that Matulane may be taken with or without food.

Manufactured by

Alcami Corporation

1726 North 23rd St.

Wilmington, NC 28405

for:



MAT13