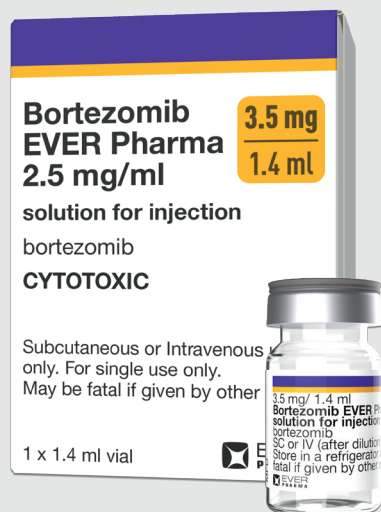


Bortezomib

Solution for Injection

MADE IN GERMANY



Bortezomib EVER Pharma is available as a ready-to-use liquid formulation for subcutaneous (SC) injection and for intravenous (IV) injection after dilution.

Indicated for the treatment of progressive or previously untreated multiple myeloma and of previously untreated mantle cell lymphoma.

- **Ready-to-use formulation** – no reconstitution required, simplifying preparation and reducing handling time.
- **Improved operational flexibility** – superior in-use stability compared with powder formulations.
- **Available in CytoWrap® protected vials** – ensuring safer handling and transportation



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IN-USE STABILITY OF 28 DAYS AT 25°C (protected from light)

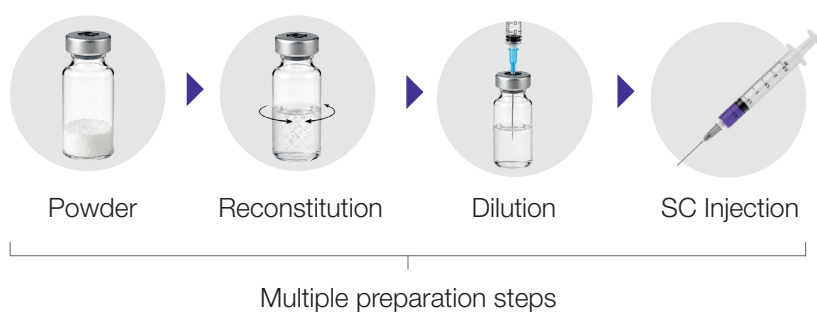
Indications	As monotherapy or in combination with pegylated liposomal doxorubicin or dexamethasone is indicated for the treatment of adult patients with progressive multiple myeloma who have received at least 1 prior therapy and who have already undergone or are unsuitable for haematopoietic stem cell transplantation. In combination with melphalan and prednisone is indicated for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for high-dose chemotherapy with haematopoietic stem cell transplantation. In combination with dexamethasone, or with dexamethasone and thalidomide, is indicated for the induction treatment of adult patients with previously untreated multiple myeloma who are eligible for high-dose chemotherapy with haematopoietic stem cell transplantation. In combination with rituximab, cyclo-phosphamide, doxorubicin and prednisone is indicated for the treatment of adult patients with previously untreated mantle cell lymphoma who are unsuitable for haematopoietic stem cell transplantation.
Active Ingredient	Bortezomib (as mannitol boronic ester)
Excipients	Mannitol (E421), Sodium chloride, Sodium hydroxide, Hydrochloric acid
Presentations	■ 3.5 mg/1.4 ml solution for injection
Strength	Each 1 ml of concentrate contains 2.5 mg Bortezomib (as a mannitol boronic ester).
Stability	■ Unopened: 3 years. Store in a refrigerator (2 °C to 8 °C). Protect from light. ■ In-use (undiluted): Chemical and physical in-use stability after first opening and/or dilution has been demonstrated for 8 hours at 25 °C when stored in the original vial and/or a polypropylene syringe. From a microbiological point of view the product should be used immediately; if not, in-use storage times are the responsibility of the user. The total storage time after first opening and/or dilution should not exceed 8 hours prior to administration.
Primary Packaging	Type I colourless glass vial with a rubber stopper, sealed with an aluminium cap, covered with a flip-off cap.
Pack Sizes	1 or 5 vials per pack. Vials may be sheathed in a protective sleeve.
Density	1.014 g/cm ³



NO RECONSTITUTION NECESSARY

- No reconstitution from powder required prior to preparing patient specific doses saving time and costs
- No dilution needed prior to SC injection - most patient doses are given SC as this route of administration has become a standard of care for patients with multiple myeloma. Can be used directly for SC injection or after dilution for intravenous injection.

CONVENTIONAL PREPARATION



READY-TO-USE FORMULATION



COMMON PATIENT DOSES

BSA m ²	1.3	1.4	1.5	1.6	1.7	1.8	1.9	2	2.1
Std Dose mg/m ²	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3
Patient Dose mg	1.69	1.82	1.95	2.08	2.21	2.34	2.47	2.6	2.73
Strength mg/ml	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
SC Injection volume ml	0.68	0.73	0.78	0.83	0.89	0.94	0.99	1.04	1.09
SC Injection volume ml (rounded) ¹	0.7	0.7	0.8	0.8	0.9	0.9	1.0	1.0	1.1

1. Injection volumes are rounded to the nearest 0.1 mL. Verify against the approved product information and local dosing protocol before administration.

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Plastic sleeving for safer handling

Bortezomib EVER Pharma 2.5 mg/ml solution for injection

Composition: One ml of solution contains 2.5 mg bortezomib (as mannitol boronic ester). List of excipients: Mannitol (E 421), Sodium chloride, Sodium hydroxide (for pH adjustment), Hydrochloric acid (for pH adjustment), Water for injections. Therapeutic indications: 1. as monotherapy or in combination with pegylated liposomal doxorubicin or dexamethasone is indicated for the treatment of adult patients with progressive multiple myeloma who have received at least 1 prior therapy and who have already undergone or are unsuitable for haematopoietic stem cell transplantation. 2. in combination with melphalan and prednisone is indicated for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for high-dose chemotherapy with haematopoietic stem cell transplantation. 3. in combination with dexamethasone, or with dexamethasone and thalidomide, is indicated for the induction treatment of adult patients with previously untreated multiple myeloma who are eligible for high-dose chemotherapy with haematopoietic stem cell transplantation. 4. in combination with rituximab, cyclophosphamide, doxorubicin and prednisone is indicated for the treatment of adult patients with previously untreated mantle cell lymphoma who are unsuitable for haematopoietic stem cell transplantation. Contraindications: Hypersensitivity to the active substance, to boron or to any of the excipients listed in section 6.1. Acute diffuse infiltrative pulmonary and pericardial disease Side effects: Multiple Myeloma: very common: Thrombocytopenia, Neutropenia, Anaemia, Decreased appetite, Neuropathies, Peripheral sensory neuropathy, Dysaesthesia, Neuralgia, Nausea and vomiting symptoms, Diarrhoea, Constipation, Musculoskeletal pain, Pyrexia, Fatigue, Asthenia, common: Herpes zoster (incl. disseminated & ophthalmic), Pneumonia, Herpes simplex, Fungal infection, Leukopenia, Lymphopenia, Dehydration, Hypokalaemia, Hyponatraemia, Blood glucose abnormal, Hypocalcaemia, Enzyme abnormality, Mood disorders and disturbances, Anxiety disorder, Sleep disorders and disturbances, Motor neuropathy, Loss of consciousness (incl. syncope), Dizziness, Dysgeusia, Lethargy, Headache, Eye swelling, Vision abnormal, Conjunctivitis, Vertigo, Hypotension, Orthostatic hypotension, Hypertension, Dyspnoea, Epistaxis, Upper/lower respiratory tract infection, Cough, Gastrointestinal haemorrhage (incl. mucosal), Dyspepsia, Stomatitis, Abdominal distension, Oropharyngeal pain, Abdominal pain (incl. gastrointestinal and splenic pain), Oral disorder, Flatulence, Hepatic enzyme abnormality, Rash, Pruritus, Erythema, Dry skin, Muscle spasms, Pain in extremity, Muscular weakness, Renal impairment, Oedema (incl. peripheral), Chills, Pain, Malaise, Weight decreased, uncommon: Infection, Bacterial infections, Viral infections, Sepsis (incl. septic shock), Bronchopneumonia, Herpes virus infection, Meningoencephalitis herpetic, Bacteraemia (incl. staphylococcal), Hordeolum, Influenza, Cellulitis, Device related infection, Skin infection, Ear infection, Staphylococcal infection, Tooth infection, Pancytopenia, Febrile neutropenia, Coagulopathy, Leukocytosis, Lymphadenopathy, Haemolytic anaemia, Angioedema, Hypersensitivity, Cushing's syndrome, Hyperthyroidism, Inappropriate antidiuretic hormone secretion, Tumour lysis syndrome, Failure to thrive, Hypomagnesaemia, Hypophosphataemia, Hyperkalaemia, Hypercalcaemia, Hypernatraemia, Uric acid abnormal, Diabetes mellitus, Fluid retention, Mental disorder, Hallucination, Psychotic disorder, Confusion, Restlessness, Tremor, Peripheral sensorimotor neuropathy, Dyskinesia, Cerebellar coordination and balance disturbances, Memory loss (exc. dementia), Encephalopathy, Posterior Reversible Encephalopathy Syndrome, Neurotoxicity, Seizure disorders, Post herpetic neuralgia, Speech disorder, Restless legs syndrome, Migraine, Sciatica, Disturbance in attention, Reflexes abnormal, Parosmia, Eye haemorrhage, Eyelid infection, Chalazion, Blepharitis, Eye inflammation, Diplopia, Dry eye, Eye irritation, Eye pain, Lacrimation increased, Eye discharge, Dysacusis (incl. tinnitus), Hearing impaired (up to and incl. deafness), Ear discomfort, Cardiac tamponade, Cardio-pulmonary arrest, Cardiac fibrillation (incl. atrial), Cardiac failure (incl. left and right ventricular), Arrhythmia, Tachycardia, Palpitations, Angina pectoris, Pericarditis (incl. pericardial effusion), Cardiomyopathy, Ventricular dysfunction, Bradycardia, Cerebrovascular accident, Deep vein thrombosis, Haemorrhage, Thrombophlebitis (incl. superficial), Circulatory collapse (incl. hypovolaemic shock), Phlebitis, Flushing, Haematoma (incl. perirenal), Poor peripheral circulation, Vasculitis, Hyperaemia (incl. ocular), Pulmonary embolism, Pleural effusion, Pulmonary oedema (incl. acute), Pulmonary alveolar haemorrhage, Bronchospasm, Chronic obstructive pulmonary disease, Hypoxaemia, Respiratory tract congestion, Hypoxia, Pleurisy, Hiccups, Rhinorrhoea, Dysphonia, Wheezing, Pancreatitis (incl. chronic), Haematemesis, Lip swelling, Gastrointestinal obstruction (incl. small intestinal obstruction, ileus), Abdominal discomfort, Oral ulceration, Enteritis, Gastritis, Gingival bleeding, Gastroesophageal reflux disease, Colitis (incl. clostridium difficile), Colitis ischaemic, Gastrointestinal inflammation, Dysphagia, Irritable bowel syndrome, Gastrointestinal disorder, Tongue coated, Gastrointestinal motility disorder, Salivary gland disorder, Hepatotoxicity (incl. liver disorder), Hepatitis, Cholestasis, Erythema multiforme, Urticaria, Acute febrile neutrophilic dermatosis, Toxic skin eruption, Toxic epidermal necrolysis, Stevens-Johnson syndrome, Dermatitis, Hair disorder, Petechiae, Ecchymosis, Skin lesion, Purpura, Skin mass, Psoriasis, Hyperhidrosis, Night sweats, Decubitus ulcer, Acne, Blister, Pigmentation disorder, Muscle twitching, Joint swelling, Arthritis, Joint stiffness, Myopathies, Sensation of heaviness, Renal failure acute, Renal failure chronic, Urinary tract infection, Urinary tract signs and symptoms, Haematuria, Urinary retention, Micturition disorder, Proteinuria, Azotaemia, Oliguria, Pollakisuria, Vaginal haemorrhage, Genital pain, Erectile dysfunction, General physical health deterioration, Face oedema, Injection site reaction, Mucosal disorder, Chest pain, Gait disturbance, Feeling cold, Extravasation, Catheter related complication, Change in thirst, Chest discomfort, Feeling of body temperature change, Injection site pain, Hyperbilirubinaemia, Protein analyses abnormal, Weight increased, Blood test abnormal, C-reactive protein increased, Fall, Contusion, rare: Meningitis (incl. bacterial), Epstein-Barr virus infection, Genital herpes, Tonsillitis, Mastoiditis, Post viral fatigue syndrome, Neoplasm malignant, Leukaemia plasmacytic, Renal cell carcinoma, Mass, Mycosis fungoides, Neoplasm benign, Disseminated intravascular coagulation, Thrombocytosis, Hyperviscosity syndrome, Platelet disorder, Thrombotic microangiopathy (including Thrombotic thrombocytopenic purpura), Blood disorder, Haemorrhagic diathesis, Lymphocytic infiltration, Anaphylactic shock, Amyloidosis, Type III immune complex mediated reaction, Hypothyroidism, Hypermagnesaemia, Acidosis, Electrolyte imbalance, Fluid overload, Hypochloreaemia, Hypovolaemia, Hyperchloreaemia, Hyperphosphataemia, Metabolic disorder, Vitamin B complex deficiency, Vitamin B12 deficiency, Gout, Increased appetite, Alcohol intolerance, Suicidal ideation, Adjustment disorder, Delirium, Libido decreased, Cerebral haemorrhage, Haemorrhage intracranial (incl. subarachnoid), Brain oedema, Transient ischaemic attack, Coma, Autonomic nervous system imbalance, Autonomic neuropathy, Cranial palsy, Paralysis, Paresis, Presyncope, Brain stem syndrome, Cerebrovascular disorder, Nerve root lesion, Psychomotor hyperactivity, Spinal cord compression, Cognitive disorder, Motor dysfunction, Nervous system disorder, Radiculitis, Drooling, Hypotonia, Guillain-Barré syndrome, Demyelinating polyneuropathy, Corneal lesion, Exophthalmos, Peritonitis, Scotoma, Eye disorder (incl. eyelid), Dacryoadenitis acquired, Photophobia, Photopsia, Optic neuropathy, Different degrees of visual impairment (up to blindness), Ear haemorrhage, Vestibular neuronitis, Ear disorder, Atrial flutter, Myocardial infarction, Atrioventricular block, Cardiovascular disorder (incl. cardiogenic shock), Torsade de pointes, Angina unstable, Cardiac valve disorders, Coronary artery insufficiency, Sinus arrest, Peripheral embolism, Lymphoedema, Pallor, Erythromelalgia, Vasodilatation, Vein discoloration, Venous insufficiency, Respiratory failure, Acute respiratory distress syndrome, Apnoea, Pneumothorax, Atelectasis, Pulmonary hypertension, Haemoptysis, Hyperventilation, Orthopnoea, Pneumonitis, Respiratory alkalosis, Tachypnoea, Pulmonary fibrosis, Bronchial disorder, Hypocapnia, Interstitial lung disease, Lung infiltration, Throat tightness, Dry throat, Increased upper airway secretion, Throat irritation, Upper-airway cough syndrome, Pancreatitis acute, Peritonitis, Tongue oedema, Ascites, Oesophagitis, Chelitis, Faecal incontinence, Anal sphincter atony, Faecaloma, Gastrointestinal ulceration and perforation, Gingival hypertrophy, Megacolon, Rectal discharge, Oropharyngeal blistering, Lip pain, Periodontitis, Anal fissure, Change of bowel habit, Proctalgia, Abnormal faeces, Hepatic failure, Hepatomegaly, Budd-Chiari syndrome, Cytomegalovirus hepatitis, Hepatic haemorrhage, Cholelithiasis, Skin reaction, Jessner's lymphocytic infiltration, Palmar-plantar erythrodysesthesia syndrome, Haemorrhage subcutaneous, Livedo reticularis, Skin induration, Papule, Photosensitivity reaction, Seborrhoea, Cold sweat, Skin disorder, Erythrosis, Skin ulcer, Nail disorder, Rhabdomyolysis, Temporomandibular joint syndrome, Fistula, Joint effusion, Pain in jaw, Bone disorder, Musculoskeletal and connective tissue infections and inflammations, Synovial cyst, Bladder irritation, Testicular disorder, Prostatitis, Breast disorder female, Epididymal tenderness, Epididymitis, Pelvic pain, Vulval ulceration, Aplasia, Gastrointestinal malformation, Ichthyosis, Death (incl. sudden), Multi-organ failure, Injection site haemorrhage, Hernia (incl. hiatus), Impaired healing, Inflammation, Injection site phlebitis, Tenderness, Ulcer, Irritability, Non-cardiac chest pain, Catheter site pain, Sensation of foreign body, Blood gases abnormal, Electrocardiogram abnormalities (incl. QT prolongation), International normalised ratio abnormal, Gastric pH decreased, Platelet aggregation increased, Troponin I increased, Virus identification and serology, Urine analysis abnormal, Transfusion reaction, Fractures, Rigors, Face injury, Joint injury, Burns, Laceration, Procedural pain, Radiation injuries, Macrophage activation, Mantle Cell Lymphoma: very common: Pneumonia, Thrombocytopenia, Febrile neutropenia, Neutropenia, Leukopenia, Anaemia, Lymphopenia, Decreased appetite, Peripheral sensory neuropathy, Dysaesthesia, Neuralgia, Nausea and vomiting symptoms, Diarrhoea, Stomatitis, Constipation, Hair disorder, Pyrexia, Fatigue, Asthenia, common: Sepsis (incl. septic shock), Herpes zoster (incl. disseminated & ophthalmic), Herpes virus infection, Bacterial infections, Upper/lower respiratory tract infection, Fungal infection, Herpes simplex, Hypersensitivity, Hypokalaemia, Blood glucose abnormal, Hyponatraemia, Diabetes mellitus, Fluid retention, Sleep disorders and disturbances, Neuropathies, Motor neuropathy, Loss of consciousness (incl. syncope), Encephalopathy, Peripheral sensorimotor neuropathy, Dizziness, Dysgeusia, Autonomic neuropathy, Vision abnormal, Dysacusis (incl. tinnitus), Cardiac fibrillation (incl. atrial), Arrhythmia, Cardiac failure (incl. left and right ventricular), Myocardial ischaemia, Ventricular dysfunction, Hypertension, Hypotension, Orthostatic hypotension, Dyspnoea, Cough, Hiccups, Gastrointestinal haemorrhage (incl. mucosal), Abdominal distension, Dyspepsia, Oropharyngeal pain, Gastritis, Oral ulceration, Abdominal discomfort, Dysphagia, Gastrointestinal inflammation, Abdominal pain (incl. gastrointestinal and splenic pain), Oral disorder, Hepatotoxicity (incl. liver disorder), Pruritus, Dermatitis, Rash, Muscle spasms, Musculoskeletal pain, Pain in extremity, Urinary tract infection, Oedema (incl. peripheral), Chills, Injection site reaction, Malaise, Hyperbilirubinaemia, Protein analyses abnormal, Weight decreased, increased, uncommon: Hepatitis B, Infection, Bronchopneumonia, Pancytopenia, Anaphylactic reaction, Tumour lysis syndrome, Autonomic nervous system imbalance, Vertigo, Hearing impaired (up to and incl. deafness), Cardiovascular disorder (incl. cardiogenic shock), Acute respiratory distress syndrome, Pulmonary embolism, Pneumonitis, Pulmonary hypertension, Pulmonary oedema (incl. acute), Colitis (incl. clostridium difficile), Hepatic failure. More information available in the summary of product characteristics. Only available on prescription. Last update: August 2021. Marketing Authorisation Holder: EVER Valinject GmbH, Oberburgau 3, 4866 Unterach am Attersee, Austria.