Bortezomib 1 mg /2.5 mg /3.5 mg powder for solution for injection
Qualitative and quantitative composition: Each vial contains 1 mg (2.5 mg; 3.5 mg) bortezomib (as a mannitol boronic ester). After reconstitution, 1 ml of solution for subcutaneous injection contains 2.5 mg bortezomib (applies only to 2.5 and 3.5 mg); 1 ml of solution for intravenous injection contains 1 mg bortezomib. *Excipients:* Mannitol. **Therapeutic indications:** As monotherapy or in combination with pegylated liposomal doxorubicin or dexamethasone for the treatment of adult patients with progressive multiple myeloma who have received at least one prior therapy and who have already undergone or are unsuitable for haematopoietic stem cell transplantation. In combination with melphalan and prednisone 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, 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, cyclophosphamide, doxorubicin and prednisone for the treatment of adult patients with previously untreated mantle cell lymphoma who are unsuitable for haematopoietic stem cell transplantation. **Posology and method of administration:** For monotherapy, bortezomib is administered via intravenous or subcutaneous injection at the recommended dose of 1.3 mg/m² body surface area twice weekly for two weeks on days 1, 4, 8, and 11 in a 21-day treatment cycle. This 3-week period is considered a treatment cycle. At least 72 hours should elapse between consecutive doses of bortezomib. *Intravenous injection:* Bortezomib reconstituted solution is administered as a 3 – 5-second bolus intravenous injection through a peripheral or central intravenous catheter followed by a flush with sodium chloride 9 mg/ml (0.9 %) solution for injection. *Subcutaneous injection:* Bortezomib 3.5 mg reconstituted solution is administered subcutaneously through the thighs (right or left) or abdomen (right or left). The solution should be injected subcutaneously, at a 45 – 90° angle. Injection sites should be rotated for successive injections. If local injection site reactions occur following bortezomib subcutaneous injection, either a less concentrated Bortezomib solution (Bortezomib 3.5 mg to be reconstituted to 1 mg/ml instead of 2.5 mg/ml) may be administered subcutaneously or a switch to intravenous injection is recommended. **Contraindications:** Hypersensitivity to the active substance, to boron or to any of the excipients, acute diffuse infiltrative pulmonary and pericardial disease. When bortezomib is given in combination with other medicinal products, refer to their SPCs for additional contraindications. **Undesirable effects:** *Infections, infestations:* Herpes zoster (incl disseminated & ophthalmic), pneumonia, herpes simplex, fungal, bacterial, viral infection, sepsis (incl septic shock), bronchopneumonia, Herpes virus infection, meningoencephalitis herpetic, Bacteraemia (incl staphylococcal), hordeolum, influenza, cellulitis, device related infection, skin or ear infection, Staphylococcal infection, tooth infection; meningitis (incl bacterial), Epstein-Barr virus infection, genital herpes, tonsillitis, mastoiditis, post viral fatigue syndrome. *Neoplasm:* Neoplasm malignant, leukaemia plasmacytic, renal cell carcinoma, mass, mycosis fungoides, neoplasm benign. *Blood, lymphatic system:* Thrombocytopenia, neutropenia, anaemia, leukopenia, lymphopenia, pancytopenia, febrile neutropenia, coagulopathy, leukocytosis, lymphadenopathy, haemolytic anaemia; disseminated intravascular coagulation, thrombocytosis, hyperviscosity syndrome, platelet disorder NOS, thrombotic microangiopathy incl. thrombocytopenic purpura, blood disorder NOS, haemorrhagic diathesis, lymphocytic infiltration. *Immune system:* Angioedema, hypersensitivity; anaphylactic shock, amyloidosis, Type III immune complex mediated reaction. *Endocrine:* Cushing's syndrome, hyperthyroidism, inappropriate antidiuretic hormone secretion; hypothyroidism. *Metabolism, nutrition:* Decreased appetite; dehydration, hypokalaemia, hyponatraemia, blood glucose abnormal, hypocalcaemia, enzyme abnormality, tumour lysis syndrome, failure to thrive, hypomagnesaemia, hypophosphataemia, hyperkalaemia, hypercalcaemia, hypernatraemia, uric acid abnormal, diabetes mellitus, fluid retention; hypermagnesaemia, acidosis, electrolyte imbalance, fluid overload, hypochloraemia, hypovolaemia, hyperchloraemia, hyperphosphataemia, metabolic disorder, Vitamin B complex deficiency, Vitamin B12 deficiency, gout, increased appetite, alcohol intolerance. *Psychiatric:* Mood disorders and disturbances, anxiety disorder, sleep disorders and disturbances; mental disorder, hallucination, psychotic disorder, confusion, restlessness; suicidal ideation, adjustment disorder, delirium, libido decreased. *Nervous system:* Neuropathies, peripheral sensory neuropathy, dysaesthesia, neuralgia; motor neuropathy, loss of consciousness (incl syncope), dizziness, dysgeusia, lethargy, headache; tremor, peripheral sensorimotor neuropathy, dyskinesia, cerebellar coordination and balance disturbances, memory loss (excl 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; 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 NOS, motor dysfunction, nervous system disorder NOS, radiculitis, drooling, hypotonia, Guillain-Barré syndrome, demyelinating polyneuropathy. *Eye:* Eye swelling, vision abnormal, conjunctivitis; eye haemorrhage, eyelid infection, Chalazion, Blepharitis, eye inflammation, diplopia, dry eye, eye irritation, eye pain, lacrimation increased, eye discharge; corneal lesion, exophthalmos, retinitis, scotoma, eye disorder (inc. eyelid) NOS, dacryoadenitis acquired, photophobia, photopsia, optic neuropathy, different degrees of visual impairment (up to blindness). *Ear:* Vertigo, dysacusis (incl tinnitus), hearing impaired (up to and incl deafness), ear discomfort; ear haemorrhage, vestibular neuronitis, ear disorder NOS. *Cardiac:* Cardiac tamponade, cardio-pulmonary arrest, cardiac fibrillation (inc atrial), cardiac failure (incl left and right ventricular), arrhythmia, tachycardia, palpitations, angina pectoris, pericarditis (incl pericardial effusion), cardiomyopathy, ventricular dysfunction, bradycardia; atrial flutter, myocardial infarction, atrioventricular block, cardiovascular disorder (inc cardiogenic shock), torsade de pointes, angina unstable, cardiac valve disorders, coronary artery insufficiency, sinus arrest. *Vascular:* Hypotension, orthostatic hypotension, hypertension; 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); peripheral embolism, lymphoedema, pallor, erythromelalgia, vasodilatation, vein discolouration, venous insufficiency. *Respiratory, thoracic and mediastinal:* Dyspnoea, epistaxis, upper/lower respiratory tract infection, cough;

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; 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. *Gastrointestinal:* Nausea and vomiting symptoms, diarrhoea, constipation; gastrointestinal haemorrhage (incl mucosal), dyspepsia, stomatitis, abdominal distension, oropharyngeal pain, abdominal pain (incl gastrointestinal and splenic pain), oral disorder, flatulence; pancreatitis (incl chronic), haematemesis, lip swelling, gastrointestinal obstruction (incl small intestinal obstruction, ileus), abdominal discomfort, oral ulceration, enteritis, gastritis, gingival bleeding, gastrooesophageal reflux disease, colitis (inc clostridium difficile), colitis ischaemic, gastrointestinal inflammation, dysphagia, irritable bowel syndrome, gastrointestinal disorder NOS, tongue coated, gastrointestinal motility disorder, salivary gland disorder; pancreatitis acute, peritonitis, tongue oedema, ascites, oesophagitis, cheilitis, 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. *Hepatobiliary:* Hepatic enzyme abnormality; hepatotoxicity (incl liver disorder), hepatitis, cholestasis; hepatic failure, hepatomegaly, Budd-Chiari syndrome, cytomegalovirus hepatitis, hepatic haemorrhage, cholelithiasis. *Skin, subcutaneous tissue:* Rash, pruritus, erythema, dry skin; 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; skin reaction, Jessner's lymphocytic infiltration, palmar-plantar erythrodysaesthesia syndrome, haemorrhage subcutaneous, livedo reticularis, skin induration, papule, photosensitivity reaction, seborrhoea, cold sweat, skin disorder NOS, erythrosis, skin ulcer, nail disorder. *Musculoskeletal, connective tissue:* Musculoskeletal pain; muscle spasms, pain in extremity, muscular weakness; muscle twitching, joint swelling, arthritis, joint stiffness, myopathies, sensation of heaviness; rhabdomyolysis, temporomandibular joint syndrome, fistula, joint effusion, pain in jaw, bone disorder, musculoskeletal and connective tissue infections and inflammations, synovial cyst. *Renal, urinary:* Renal impairment; renal failure acute or chronic, urinary tract infection, urinary tract signs and symptoms, haematuria, urinary retention, micturition disorder, proteinuria, azotaemia, oliguria, pollakisuria; bladder irritation. *Reproductive system:* Vaginal haemorrhage, genital pain, erectile dysfunction; testicular disorder, prostatitis, breast disorder female, epididymal tenderness, epididymitis, pelvic pain, vulval ulceration. *Congenital:* Aplasia, gastrointestinal malformation, ichthyosis. *General, administration site:* Pyrexia, fatigue, asthenia; oedema (incl peripheral), chills, pain, malaise; 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; 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. *Investigations:* Weight decreased; hyperbilirubinaemia, protein analyses abnormal, weight increased, blood test abnormal, C-reactive protein increased; 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. *Injury:* Fall, contusion; transfusion reaction, fractures, rigors, face injury, joint injury, burns, laceration, procedural pain, radiation injuries. Macrophage activation. **Legal classification:** POM (prescription only medicine). **Marketing authorisation holder:** medac GmbH Theaterstraße 6; 22880 Wedel, Germany. **Date of revision of text:** 04/2025

Bortezomib has been authorised in Finland, Germany, Italy, Poland, Sweden, United Kingdom (not all strengths are authorized in all countries)