ABBREVIATED PRESCRIBING INFORMATION

Please refer to the Summary of Product Characteristics (SmPC) before prescribing

Pelgraz▼(pegfilgrastim) **6 mg solution for injection in pre-filled syringe or pre-filled injector**

Presentation: Each pre-filled syringe or pre-filled injector contains 6 mg of pegfilgrastim* in 0.6 mL solution for injection. The concentration is 10 mg/mL based on protein only**. *Produced in *Escherichia coli* cells by recombinant DNA technology followed by conjugation with polyethylene glycol (PEG). ** The concentration is 20 mg/mL if the PEG moiety is included. **Indications**: Reduction in the duration of neutropenia and the incidence of febrile neutropenia in adult patients treated with cytotoxic chemotherapy for malignancy (with the exception of chronic myeloid leukaemia and myelodysplastic syndromes). **Dosage and Administration**: Pelgraz therapy should be initiated and supervised by physicians experienced in oncology and/or haematology. **Posology:** One 6 mg dose (a single pre-filled syringe or pre-filled injector) of Pelgraz is recommended for each chemotherapy cycle, given at least 24 hours after cytotoxic chemotherapy. Safety and efficacy of Pelgraz in children and adolescents has not yet been established and no recommendation on a posology can be made. No dose change is recommended in patients with renal impairment, including those with end-stage renal disease. **Method of administration:** Pelgraz is for subcutaneous use. The injections should be given subcutaneously into the thigh, abdomen or upper arm. See SmPC for instructions on handling of the medicinal product before administration. **Contraindications**: Hypersensitivity to pegfilgrastim or any of the excipients in Pelgraz. **Warnings and precautions**: To improve the traceability of biological medicinal products, the trade name of the administered product should be clearly recorded. The long-term effects of pegfilgrastim have not been established in acute myeloid leukaemia (AML); therefore, it should be used with caution in this patient population. G-CSF can promote growth of myeloid cells *in vitro* and similar effects may be seen on some non-myeloid cells *in vitro*. The safety and efficacy of pegfilgrastim have not been investigated in patients with myelodysplastic syndrome, chronic myelogenous leukaemia, and in patients with secondary AML; therefore, it should not be used in such patients. Particular care should be taken to distinguish the diagnosis of blast transformation of chronic myeloid leukaemia from AML. The safety and efficacy of pegfilgrastim administration in *de novo* AML patients aged < 55 years with cytogenetics t(15;17) have not been established. The safety and efficacy of pegfilgrastim have not been investigated in patients receiving high dose chemotherapy. This medicinal product should not be used to increase the dose of cytotoxic chemotherapy beyond established dose regimens. Pulmonary adverse reactions, in particular interstitial pneumonia, have been reported after G-CSF administration. Patients with a recent history of pulmonary infiltrates or pneumonia may be at higher risk. The onset of pulmonary signs such as cough, fever, and dyspnoea in association with radiological signs of pulmonary infiltrates, and deterioration in pulmonary function along with increased neutrophil count may be preliminary signs of acute respiratory distress syndrome (ARDS). In such circumstances pegfilgrastim should be discontinued at the discretion of the physician and the appropriate treatment given. Glomerulonephritis has been reported in patients receiving filgrastim and pegfilgrastim. Generally, glomerulonephritis resolved after dose reduction or withdrawal of filgrastim and pegfilgrastim. Urinalysis monitoring is recommended. Capillary leak syndrome has been reported after G-CSF administration and is characterised by hypotension, hypoalbuminaemia, oedema and haemoconcentration. Patients who develop symptoms of capillary leak syndrome should be closely monitored and receive standard symptomatic treatment, which may include a need for intensive care. Generally asymptomatic cases of splenomegaly and cases of splenic rupture, including some fatal cases, have been reported following administration of pegfilgrastim. Spleen size should be carefully monitored (e.g. clinical examination, ultrasound). A diagnosis of splenic rupture should be considered in patients reporting left upper abdominal pain or shoulder tip pain. Treatment with pegfilgrastim alone does not preclude thrombocytopenia and anaemia because full dose myelosuppressive chemotherapy is maintained on the prescribed schedule. Regular monitoring of platelet count and haematocrit is recommended. Special care should be taken when administering single or combination chemotherapeutic medicinal products which are known to cause severe thrombocytopenia. In the post-marketing observational study setting, pegfilgrastim in conjunction with chemotherapy and/or radiotherapy has been associated with development of myelodysplastic syndrome (MDS) and acute

myeloid leukaemia (AML) in breast and lung cancer patients. Monitor breast and lung cancer patients for signs and symptoms of MDS/AML.
Sickle cell crises have been associated with the use of pegfilgrastim in patients with sickle cell trait or sickle cell disease. Therefore, use caution when prescribing pegfilgrastim in patients with sickle cell trait or sickle cell disease, monitor appropriate clinical parameters and laboratory status and be attentive to the possible association of this medicinal product with splenic enlargement and vaso-occlusive crisis. White blood cell (WBC) counts of 100×10^9/L or greater have been observed in less than 1% of patients receiving pegfilgrastim. No adverse reactions directly attributable to this degree of leukocytosis have been reported. Such elevation in WBCs is transient, typically seen 24 to 48 hours after administration and is consistent with the pharmacodynamic effects of this medicinal product. Consistent with the clinical effects and the potential for leukocytosis, a WBC count should be performed at regular intervals during therapy. If leukocyte counts exceed 50×10^9/L after the expected nadir, this medicinal product should be discontinued immediately. Hypersensitivity, including anaphylactic reactions, have been reported with pegfilgrastim. Permanently discontinue pegfilgrastim in patients with clinically significant hypersensitivity. Do not administer pegfilgrastim to patients with a history of hypersensitivity to pegfilgrastim or filgrastim. If a serious allergic reaction occurs, appropriate therapy should be administered, with close patient follow-up over several days. Stevens-Johnson syndrome (SJS), which can be life-threatening or fatal, has been reported rarely in association with pegfilgrastim treatment. If the patient has developed SJS with the use of pegfilgrastim, treatment must not be restarted at any time. As with all therapeutic proteins, there is a potential for immunogenicity. Rates of generation of antibodies against pegfilgrastim is generally low. Binding antibodies do occur as expected with all biologics; however, they have not been associated with neutralising activity at present. Aortitis has been reported after filgrastim or pegfilgrastim administration in healthy subjects and in cancer patients. The symptoms experienced included fever, abdominal pain, malaise, back pain and increased inflammatory markers (e.g. C-reactive protein and WBC count). In most cases aortitis was diagnosed by CT scan and generally resolved after withdrawal of filgrastim or pegfilgrastim. The safety and efficacy of Pelgraz for the mobilisation of blood progenitor cells in patients or healthy donors has not been adequately evaluated. Increased haematopoietic activity of the bone marrow in response to growth factor therapy has been associated with transient positive bone-imaging findings. This should be considered when interpreting bone-imaging results. The needle cover of the pre-filled syringe contains dry natural rubber (a derivative of latex), which may cause allergic reactions. The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account. This medicinal product contains less than 1 mmol sodium (23 mg) per 6 mg dose, that is to say essentially 'sodium-free'. **Pregnancy and Lactation**: Pegfilgrastim is not recommended during pregnancy and in women of childbearing potential not using contraception. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from pegfilgrastim therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. **Adverse Events include: Adverse events which could be considered serious include: Common:** Thrombocytopenia. **Uncommon:** Myelodysplastic syndrome, acute myeloid leukaemia, sickle cell anaemia with crisis, capillary leak syndrome, glomerulonephritis, hypersensitivity reactions, Anaphylaxis, splenic rupture, Sweet's syndrome (acute febrile neutrophilic dermatosis), pulmonary adverse reactions including interstitial pneumonia, pulmonary oedema and pulmonary fibrosis have been reported, cutaneous vasculitis, elevations in lactate dehydrogenase. Uncommonly cases have resulted in respiratory failure or ARDS which may be fatal. **Rare:** Aortitis, pulmonary haemorrhage, Stevens-Johnson syndrome. **Other Very Common adverse events:** Headache, nausea, bone pain. **Other Common adverse events:** Leukocytosis, musculoskeletal pain (myalgia, arthralgia, pain in extremity, back pain, musculoskeletal pain, neck pain), injection site pain, non-cardiac chest pain. See SmPC for details of other adverse events. **Shelf Life:** 3 years. Store in a refrigerator (2°C – 8°C). Pelgraz may be exposed to room temperature (not above 25°C ± 2°C) for a maximum single period of up to 15 days. Pelgraz left at room temperature for more than 15 days should be discarded. Do not freeze. Accidental exposure to freezing temperatures for a single period of less than 24 hours does not adversely affect the stability of Pelgraz. Keep the container in the outer carton in order to protect from light. **Pack Size:** One pre-filled syringe or pre-filled syringe injector with one alcohol swab, in a blistered packaging. **Marketing Authorisation Numbers: Pre-filled syringe:** EU/1/18/1313/001,

Pre-filled injector: EU/1/18/1313/002. **Marketing Authorisation Holder (MAH):** Accord Healthcare S.L.U, World Trade Center, Moll de Barcelona, s/n, Edifici Est, 6a planta, Barcelona, 08039 Spain. **Legal Category:** POM. Full prescribing information including the SmPC is available on request from Accord Healthcare Ireland Ltd, Euro House, Little Island, Co. Cork, Tel: 021-4619040 or www.accord-healthcare.ie/products. **Adverse reactions can be reported to Medical Information at Accord Healthcare Ltd. via E-mail:** medinfo@accord-healthcare.com **or Tel:** +44(0)1271385257.
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