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NUFILONG™
Pegfilgrastim

1. DESCRIPTION
1.1 Therapeutic/Pharmacologic Class of Drug
Haematopoietic growth factor
Pharmacotherapeutic group: Cytokines, ATC Code: L03AA13

1.2 Type of Dosage Form
Solution for injection in pre-filled syringe.

1.3 Route of Administration
Subcutaneous injection.

1.4 Sterile/Radioactive Statement
Sterile.

1.5 Qualitative and Quantitative Composition
6 mg of Pegfilgrastim in 0.6 ml (10 mg/ml*) solution for injection.
*Based on protein only. The concentration is 20 mg/ml if the PEG moiety is included.
Pegfilgrastim is composed of filgrastim (recombinant methionyl human G-CSF) with a 20 kDa polyethylene glycol (PEG) molecule covalently bound to the N-terminal methionine residue.
Filgrastim is produced by recombinant DNA technology in E. coli .
Excipients: Sodium **, acetate**, Sorbitol, Polysorbate 20, Water for injections.
**Sodium acetate is formed by titrating glacial acetic acid with sodium hydroxide.

2. CLINICAL PARTICULARS
2.1 Therapeutic Indication(s)
Reduction in the duration of neutropenia and the incidence of febrile neutropenia in patients treated with cytotoxic chemotherapy for malignancy (with the exception of chronic myeloid leukaemia and myelodysplastic syndromes).

2.2 Dosage and Administration
Adults (≥ 18 years): One 6 mg dose (a single pre-filled syringe) of Pegfilgrastim is recommended for each chemotherapy cycle, administered as a subcutaneous injection approximately 24 hours following cytotoxic chemotherapy.
NUFILONG™ therapy should be initiated and supervised by physicians experienced in oncology and/or haematology.

2.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients.

2.4 Warnings and Precautions
2.4.1 General
Limited clinical data suggest a comparable effect on time to recovery of severe neutropenia for Pegfilgrastim to Filgrastim in patients with de novo acute myeloid leukaemia (see section 3.1.2). However, the long-term effects of Pegfilgrastim have not been established in acute myeloid leukaemia; therefore, it should be used with caution in this patient population.
Granulocyte-colony stimulating factor can promote growth of myeloid cells, including malignant 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 Acute Myeloid Leukaemia (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 acute myeloid leukaemia.
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 dosage regimens.

Pulmonary adverse events
Uncommon (≥ 1/1,000 to < 1/100) 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 (see section 2.6).
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 (see section 2.6).

Glomerulonephritis
Glomerulonephritis has been reported in patients receiving Filgrastim and Pegfilgrastim. Generally, events of glomerulonephritis resolved after dose reduction or withdrawal of Filgrastim and Pegfilgrastim. Urinalysis monitoring is recommended.

Capillary leak syndrome
Capillary leak syndrome has been reported after granulocyte-colony stimulating factor administration and is characterised by hypotension, hypoalbuminaemia, oedema and hemoconcentration. 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 (see section 2.6).

Splenomegaly and splenic rupture
Uncommon but generally asymptomatic cases of splenomegaly and uncommon cases of splenic rupture, including some fatal cases, have been reported following administration of Pegfilgrastim (see section 2.6). Therefore, 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.

Thrombocytopenia and anaemia
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 agents which are known to cause severe thrombocytopenia.

Sickle cell anaemia
Sickle cell crises have been associated with the use of Pegfilgrastim in patients with sickle cell trait or sickle cell disease (see section 2.6). Therefore, physicians should use caution when prescribing Pegfilgrastim in patients with sickle cell trait or sickle cell disease, and only after careful evaluation of the potential risk and benefits. Physicians should monitor appropriate clinical parameters and laboratory status and be attentive to the possible association of this medicine with splenic enlargement and vaso-occlusive crisis.

Leukocytosis
White blood cell (WBC) counts of 100 x 109/l or greater have been observed in less than 1% of patients receiving Pegfilgrastim. No adverse events directly attributable to this degree of leucocytosis have been reported. Such elevation in white blood cells is transient, typically seen 24 to 48 hours after administration and is consistent with the pharmacodynamic effects of this medicine. 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 x 109/l after the expected nadir, this medicine should be discontinued immediately.

Hypersensitivity
Hypersensitivity, including anaphylactic reactions, occurring on initial or subsequent treatment have been reported in patients treated 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
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 with Pegfilgrastim must not be restarted
in this patient at any time.

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
Aortitis has been reported after G-CSF 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 white blood cell count). In most cases aortitis was diagnosed by CT scan and generally resolved after withdrawal of GCSF.

Myelodysplastic syndrome and acute myeloid leukaemia in breast and lung cancer patients

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 patients treated in these settings for signs and symptoms
of MDS/AML.

Other warnings
The safety and efficacy of Pegfilgrastim for the mobilisation of blood progenitor cells in patients or healthy donors have not been adequately evaluated.
The needle cap of the pre-filled syringe contains dry natural rubber (a derivative of latex), which may cause allergic reactions.
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.
NUFILONG™ contains sorbitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.
NUFILONG™ contains less than 1 mmol (23 mg) sodium per 6 mg dose, i.e. essentially 'sodium-free'.
NUFILONG™ is not an interchangeable biosimilar, may not be substituted without prescriber involvement.
In order to improve the traceability of granulocyte-colony stimulating factors (G-CSFs), the trade name of the administered product should be clearly recorded in the patient file.

2.4.2 Ability to Drive and Use Machines
No studies on the effects on the ability to drive and use machines have been performed.

2.4.3 Interactions with other Medicinal Products and other Forms of Interaction
Due to the potential sensitivity of rapidly dividing myeloid cells to cytotoxic chemotherapy, Pegfilgrastim should be administered at least 24 hours after administration of cytotoxic chemotherapy. In clinical trials, Pegfilgrastim has been safely administered 14 days before chemotherapy. Concomitant use of Pegfilgrastim with any chemotherapy agent has not been evaluated in patients. In animal models concomitant administration of Pegfilgrastim and 5-fluorouracil (5-FU) or other antimetabolites has been shown to potentiate myelosuppression.

Possible interactions with other haematopoietic growth factors and cytokines have not been specifically investigated in clinical trials.

The potential for interaction with lithium, which also promotes the release of neutrophils, has not been specifically investigated. There is no evidence that such an interaction would be harmful.

The safety and efficacy of Pegfilgrastim have not been evaluated in patients receiving chemotherapy associated with delayed myelosuppression e.g., nitrosoureas.

Specific interaction or metabolism studies have not been performed, however, clinical trials have not indicated an interaction of Pegfilgrastim with any other medicinal products.

2.5 Use in Special Populations
2.5.1 Pregnancy
There are no data from the use of Pegfilgrastim in pregnant women.

Studies in animals have shown reproductive toxicity (see section 3.3.3). The potential risk to the human embryo or foetus is unknown.
NUFILONG™ should not be used during pregnancy unless clearly necessary.

2.5.2 Nursing Mothers
There is no clinical experience with lactating women, therefore NUFILONG™ should not be administered to women who are breast-feeding.

2.5.3 Pediatric Use
There are insufficient data to recommend the use of NUFILONG™ in children and adolescents under 18 years of age.

2.5.4 Geriatric Use
See section 3.2.4 (Pharmacokinetics in Special Populations).

2.5.5 Renal Impairment
See section 3.2.4 (Pharmacokinetics in Special Populations).

2.5.6 Hepatic Impairment
See section 3.2.4 (Pharmacokinetics in Special Populations).

2.6 Undesirable Effects

2.6.1 Clinical Trials
Summary of the safety profile
The most frequently reported adverse reactions were bone pain (very common [≥ 1/10]) and musculoskeletal pain (common). Bone pain was generally of mild to moderate severity, transient and could be controlled in most patients with standard analgesics.
Hypersensitivity-type reactions, including skin rash, urticaria, angioedema, dyspnoea, erythema, flushing, and hypotension occurred on initial or subsequent treatment with Pegfilgrastim (uncommon [≥ 1/1,000 to < 1/100]). Serious allergic reactions, including anaphylaxis can occur in patients receiving Pegfilgrastim (uncommon) (see section 2.4).
Capillary leak syndrome, which can be life-threatening if treatment is delayed, has been reported as uncommon (≥ 1/1,000 to < 1/100) in cancer patients undergoing chemotherapy following administration of granulocyte-colony stimulating factors; see section 2.4 and section "Description of selected adverse reactions" below.
Splenomegaly, generally asymptomatic, is uncommon.
Splenic rupture including some fatal cases is uncommonly reported following administration of Pegfilgrastim (see section 2.4).
Uncommon pulmonary adverse reactions including interstitial pneumonia, pulmonary oedema, pulmonary infiltrates and pulmonary fibrosis have been reported. Uncommonly, cases have resulted in respiratory failure or Acute Respiratory Distress Syndrome (ARDS), which may be fatal (see section 2.4).
Isolated cases of sickle cell crises have been reported in patients with sickle cell trait or sickle cell disease (uncommon in sickle cell patients) (see section 2.4).

Tabulated summary of adverse reactions
The data in the table below describe adverse reactions reported from clinical trials and spontaneous reporting. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

MedDRA system organ class	Adverse Reactions					
	Very common (≥1/10)	Common (≥1/100 to 1/10)	Uncommon (≥1/1000 to1/100)	Rare (≥1/10,000 to 1/1000)	Very Rare (1/10000)	
Blood and lymphatic system disorders		Thrombocytopenia[1] Leukocytosis[2]	Sickle cell crisis [1], Splenomegaly[3] Splenic rupture[4]			
Immune system disorders			Hypersensitivity reactions, Anaphylaxis			
Metabolism and nutrition disorders		Elevations in uric acid				
Nervous system disorders	Headache[5]					
Vascular disorders			Capillary leak syndrome [6]	Aortitis		
Respiratory, thoracic and mediastinal disorders			Acute Respiratory Distress Syndrome [7] Pulmonary adverse reactions (pneumonitis, pulmonary oedema, pulmonary infiltrates and pulmonary fibrosis)			
Gastrointestinal disorders	Nausea[5]					
Neoplasms Benign, malignant and unspecified (incl cysts and polyps)			Myelodysplastic syndrome[8] Acute myeloid leukaemia [8]			
Skin and subcutaneous tissue disorders		Dermatitis contact [5]	Sweet's syndrome (acute fbrile dermatosis)[12]; Cutaneous vasculitis [12]	Stevens-Johnson syndrome		
Musculoskeletal and connective tissue disorders	Bone pain	Musculoskeletal pain(myalgia, arthralgia, pain in extremity, back pain,				

MedDRA system organ class	Adverse Reactions					
	Very common (≥1/10)	Common (≥1/100 to 1/10)	Uncommon (≥1/1000 to1/100)	Rare (≥1/10,000 to 1/1000)	Very Rare (1/10000)	
Musculoskeletal and connective tissue disorders	Bone pain	musculoskeletal pain, neck pain)				
General disorders and administrative site conditions		Injection site pain[5] Non-cardiac chest pain	Injection site reactions[5]			
Investigations			Elevations in lactate dehydrogenase and alkaline phosphatase[9] Glomerulonephritis[1]			
Renal and urinary disorders						

1 See section "Description of selected adverse reactions" below.
2 This adverse reaction was identified through post-marketing surveillance but not observed in randomised, controlled clinical trials in adults. The frequency category was estimated from a statistical calculation based upon 1,576 patients receiving Pegfilgrastim in nine randomised clinical trials.

Description of selected adverse reactions
Uncommon cases of Sweet's syndrome have been reported, although in some cases underlying haematological malignancies may play a role.
Uncommon events of cutaneous vasculitis have been reported in patients treated with Pegfilgrastim. The mechanism of vasculitis in patients receiving Pegfilgrastim is unknown.
Injection site reactions, including injection site erythema (uncommon (≥ 1/1,000 to < 1/100)) as well as injection site pain (common events ≥ 1/100 to < 1/10) have occurred on initial or subsequent treatment with Pegfilgrastim.
Reversible, mild to moderate elevations in uric acid, with no associated clinical effects, were common, reversible, mild to moderate elevations in alkaline phosphatase and lactate dehydrogenase, with no associated clinical effects, were very common in patients receiving Pegfilgrastim following cytotoxic chemotherapy.
Nausea and headaches were very commonly observed in patients receiving chemotherapy.
Uncommon elevations in liver function tests (LFTs) for ALT (alanine aminotransferase) or AST (aspartate aminotransferase), have been observed in patients after receiving Pegfilgrastim following cytotoxic chemotherapy. These elevations are transient and return to baseline.
Common cases of thrombocytopenia have been reported.
Cases of capillary leak syndrome have been reported in the post-marketing setting with granulocyte-colony stimulating factor use. These have generally occurred in patients with advanced malignant diseases, sepsis, taking multiple chemotherapy medications or undergoing apheresis (see section 2.4).
An increased risk of MDS/AML following treatment with Pegfilgrastim in conjunction
with chemotherapy and/or radiotherapy has been observed in an epidemiological study
in breast and lung cancer patients.

Paediatric population
The experience in children is limited. A higher frequency of serious adverse reactions in younger children aged 0-5 years (92%) has been observed compared to older children aged 6-11 and 12-21 years respectively (80% and 67%) and adults. The most common adverse reaction reported was bone pain.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions as per local regulations.

2.7 Overdose
Single doses of 300 µg/kg have been administered subcutaneously to a limited number of healthy volunteers and patients with non-small cell lung cancer without serious adverse effects. The adverse events were similar to those in subjects receiving lower doses of Pegfilgrastim.

3. PHARMACOLOGICAL PROPERTIES AND EFFECTS
3.1 Pharmacodynamic Properties
3.1.1 Mechanism of Action
Human granulocyte-colony stimulating factor (G-CSF) is a glycoprotein, which regulates the production and release of neutrophils from the bone marrow. Pegfilgrastim is a covalent conjugate of recombinant human G-CSF (r-metHuG-CSF) with a single 20 kd polyethylene glycol (PEG) molecule. Pegfilgrastim is a sustained duration form of filgrastim due to decreased renal clearance.
Increase of white blood cell count (leukocytosis) is the predicted consequence of Pegfilgrastim administration. No adverse events directly attributable to leukocytosis have been reported. The increase in white blood cells is transient, and is consistent with the pharmacodynamic effects of Pegfilgrastim.
Pegfilgrastim and Filgrastim have been shown to have identical modes of action, causing a marked increase in peripheral blood neutrophil counts within 24 hours, with minor increases in monocytes and/or lymphocytes. Similarly to filgrastim, neutrophils produced in response to Pegfilgrastim show normal or enhanced function as demonstrated by tests of chemotactic and phagocytic function. As with other haematopoietic growth factors, G-CSF has shown in vitro stimulating properties on human endothelial cells.

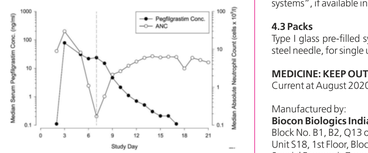
3.1.2 Clinical/Efficacy Studies
Pegfilgrastim was evaluated in three randomized, double-blind, controlled studies. Studies 1 and 2 were active-controlled studies that employed doxorubicin 60 mg/m and docetaxel 75 mg/m administered every 21 days for up to 4 cycles for the treatment of metastatic breast cancer. Study 1 investigated the utility of a fixed dose of Pegfilgrastim. Study 2 employed a weight-adjusted dose. In the absence of growth factor support, similar chemotherapy regimens have been reported to result in a 100% incidence of severe neutropenia (ANC < 0.5 x 10.4) with a mean duration of 5 to 7 days and a 30% to 40% incidence of febrile neutropenia. Based on the correlation between the duration of severe neutropenia and the incidence of febrile neutropenia found in studies with filgrastim, duration of severe neutropenia was chosen as the primary endpoint in both studies, and the efficacy of Pegfilgrastim was demonstrated by establishing comparability to filgrastim-treated patients in the mean days of severe neutropenia.
In Study 1, 157 patients were randomized to receive a single subcutaneous injection of Pegfilgrastim (6 mg) on day 2 of each chemotherapy cycle or daily subcutaneous filgrastim (5 mcg/kg/day) beginning on day 2 of each chemotherapy cycle. In Study 2, 310 patients were randomized to receive a single subcutaneous injection of Pegfilgrastim (100 mcg/kg) on day 2 or daily subcutaneous filgrastim (5 mcg/kg/day) beginning on day 2 of each chemotherapy cycle.
Both studies met the major efficacy outcome measure of demonstrating that the mean days of severe neutropenia of Pegfilgrastim-treated patients did not exceed that of filgrastim-treated patients by more than 1 day in cycle 1 of chemotherapy. The mean days of cycle 1 severe neutropenia in Study 1 were 1.8 days in the Pegfilgrastim arm compared to 1.6 days in the filgrastim arm [difference in means 0.2 (95% CI -0.2, 0.6)] and in Study 2 were 1.7 days in the Pegfilgrastim arm compared to 1.6 days in the filgrastim arm [difference in means 0.1 (95% CI -0.2, 0.4)].
A secondary endpoint in both studies was days of severe neutropenia in cycles 2 through 4 with results similar to those for cycle 1.
Study 3 was a randomized, double-blind, placebo-controlled study that employed docetaxel 100 mg/m2 administered every 21 days for up to 4 cycles for the treatment of metastatic or non-metastatic breast cancer. In this study, 928 patients were randomized to receive a single subcutaneous injection of Pegfilgrastim (6 mg) or placebo on day 2 of each chemotherapy cycle.
Study 3 met the major trial outcome measure of demonstrating that the incidence of febrile neutropenia (defined as temperature ≥ 38.2°C and ANC ≤ 0.5 x 10 /L) was lower for Pegfilgrastim-treated patients as compared to placebo treated patients (1% versus 17%, respectively, $p < 0.001$). The incidence of hospitalizations (1% versus 14%) and IV anti-infective use (2% versus 10%) for the treatment of febrile neutropenia was also lower in the Pegfilgrastim-treated patients compared to the placebo-treated patients.

3.2 Pharmacokinetic Properties
3.2.1 Absorption
After a single subcutaneous dose of Pegfilgrastim, the peak serum concentration of Pegfilgrastim occurs at 16 to 120 hours after dosing.

3.2.2 Distribution
Serum concentrations of Pegfilgrastim are maintained during the period of neutropenia after myelosuppressive chemotherapy.
The distribution of Pegfilgrastim was limited to the plasma compartment.

3.2.3 Elimination
The elimination of Pegfilgrastim is non-linear with respect to dose; serum clearance of Pegfilgrastim decreases with increasing dose. Pegfilgrastim appears to be mainly eliminated by neutrophil-mediated clearance (> 99%), which becomes saturated at higher doses. Consistent with a self-regulating clearance mechanism, the serum concentration of Pegfilgrastim declines rapidly at the onset of neutrophil recovery (see Figure 1).

Figure 1. Profile of median Pegfilgrastim serum concentration and Absolute Neutrophil Count (ANC) in chemotherapy-treated patients after a single 6 mg injection.



3.2.4 Pharmacokinetics in Special Populations
Due to the neutrophil-mediated clearance mechanism, the pharmacokinetics of Pegfilgrastim is not expected to be affected by renal or hepatic impairment.
Limited data indicate that the pharmacokinetics of Pegfilgrastim in elderly subjects (> 65 years) is similar to that in adults.

3.3 Preclinical Safety
3.3.1 Carcinogenicity
Certain malignant cells have been shown to express granulocyte-colony stimulating factor (G-CSF) receptors. The possibility that Pegfilgrastim can act as a growth factor for any tumour type cannot be excluded.
The carcinogenetic potential of Pegfilgrastim has not been evaluated in long-term animal studies.
In a toxicity study of 6 month duration in rats given once weekly subcutaneous injections of up to 1,000 µg/kg of Pegfilgrastim (approximately 23-fold higher than the recommended human dose), no precancerous or cancerous lesions were noted.

3.3.2 Mutagenicity
Mutagenesis studies have not been conducted.

3.3.3 Teratogenicity
There were no adverse effects observed in offspring from pregnant rats given Pegfilgrastim subcutaneously, but in rabbits Pegfilgrastim has been shown to cause embryo/foetal toxicity (embryo loss) at low subcutaneous doses. In rat studies, it was shown that Pegfilgrastim may cross the placenta. The relevance of these findings for humans is not known.

3.3.4 Other
Preclinical data from conventional studies of repeated dose toxicity revealed the expected pharmacological effects including increases in leukocyte count, myeloid hyperplasia in bone marrow, extramedullary haematopoiesis and splenic enlargement.

4. PHARMACEUTICAL PARTICULARS
4.1 Storage
Store at 2°C – 8°C (in a refrigerator).
NUFILONG™ may be exposed to room temperature (not above 30°C) for a maximum single period of up to 48 hours. NUFILONG™ left at room temperature for more than 48 hours 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 NUFILONG™.
Keep the container in the outer carton, in order to protect from light.
This medicine should not be used after the expiry date (EXP) shown on the pack.

4.2 Special Instructions for Use, Handling and Disposal
NUFILONG™ pre-filled syringe is for single use only.
NUFILONG™ is a sterile but unpreserved solution.
Before administration, NUFILONG™ solution should be inspected for visible particles. Only a solution that is clear and colourless should be injected.
Excessive shaking may aggregate NUFILONG™, rendering it biologically inactive.
Allow the pre-filled syringe to reach room temperature before injecting.
Any unused product or waste material should be disposed of in accordance with local requirements.

Incompatibility
NUFILONG™ is incompatible with sodium chloride solutions.

Disposal of unused/expired medicines
The release of pharmaceuticals in the environment should be minimized. Medicines should not be disposed of via wastewater and disposal through household waste should be avoided. Use established "collection systems", if available in your location.

4.3 Packs
Type I glass pre-filled syringe of 0.6 ml with a stainless steel needle, for single use only

MEDICINE: KEEP OUT OF REACH OF CHILDREN
Current at August 2020

Manufactured by:
Biocon Biologics India Limited,
Block No. B1, B2, Q13 of Q1 and W20 &
Unit S18, 1st Floor, Block B4,
Special Economic Zone,
Plot No. 2, 3, 4 & 5, Phase IV
Bommasandra-Jigani Link Road,
Bommasandra Post, Bengaluru-560099, India

Product Owner:
Biocon Biologics Limited,
16 Great Queen Street, Covent Garden,
London WC2B 5AH, United Kingdom.

Reg No:

Date of Creation generation: November 2021

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Note : Booklet to be sealed with adhesive.

PREPARED BY:	CHECKED BY:
DATE :	DATE :

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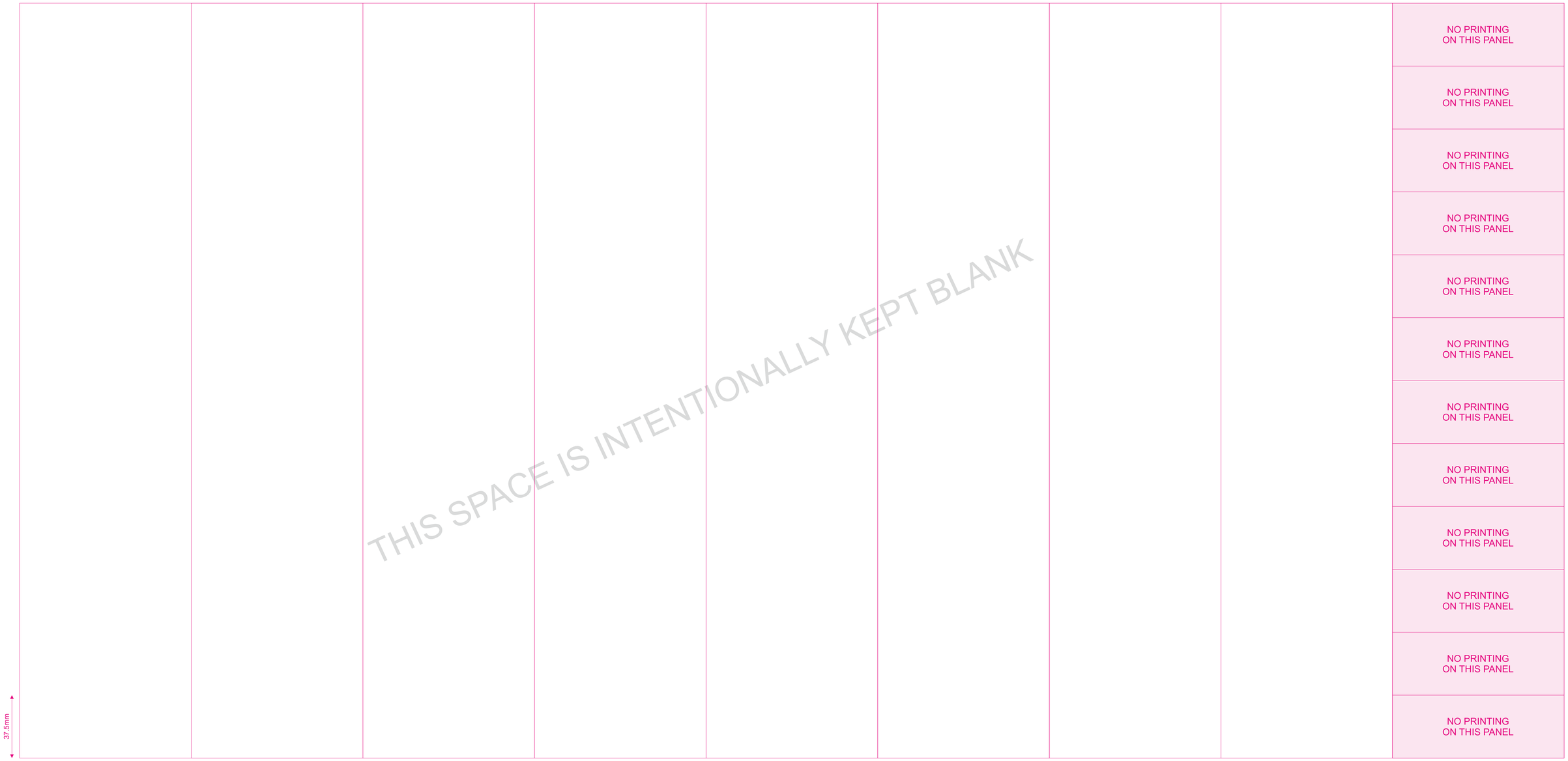

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