SUMMARY OF PRODUCT CHARACTERISTICS
(As per Annexure C to Module 1 of Guidance for Industry by CDSCO)

1. NAME OF THE MEDICINAL PRODUCT

Kengrexal 50 mg powder for concentrate for solution for injection/infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains cangrelor tetrasodium corresponding to 50 mg cangrelor. After reconstitution 1 mL of concentrate contains 10 mg cangrelor. After dilution 1 mL of solution contains 200 micrograms cangrelor.

Excipient with known effect
Each vial contains 52.2 mg sorbitol.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for concentrate for solution for injection/infusion.
White to off-white lyophilised powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Kengrexal is indicated as an adjunct to percutaneous coronary intervention (PCI) to reduce the risk of periprocedural myocardial infarction (MI), repeat coronary revascularization, and stent thrombosis (ST) in patients who have not been treated with a P2Y12 platelet inhibitor and are not being given a glycoprotein IIb/IIIa inhibitor.

4.2 Posology and method of administration

Kengrexal should be administered by a physician experienced in either acute coronary care or in coronary intervention procedures and is intended for specialised use in an acute and hospital setting.

Posology

The recommended dose of Kengrexal for patients undergoing PCI is a 30 micrograms/kg intravenous bolus followed immediately by 4 micrograms/kg/min intravenous infusion. The bolus and infusion should be initiated prior to the procedure and continued for at least two hours or for the duration of the procedure, whichever is longer. At the discretion of the physician, the infusion may be continued for a total duration of four hours, see section 5.1.

To maintain platelet inhibition after discontinuation of Kengrexal infusion, an oral P2Y12 platelet inhibitor should be administered. Administer one as described below [see Clinical Pharmacology Interaction with other medicinal products, and other forms of interaction, Oral P2Y12 agents (clopidogrel, prasugrel, ticagrelor) (4.5)]:

• Ticagrelor: 180 mg at any time during KENGREXAL infusion or immediately after discontinuation.

• Prasugrel: 60 mg immediately after discontinuation of KENGREXAL. Do not administer prasugrel prior to discontinuation of KENGREXAL.

• Clopidogrel: 600 mg immediately after discontinuation of KENGREXAL. Do not administer clopidogrel prior to discontinuation of KENGREXAL.

Use with other anticoagulant agents
In patients undergoing PCI, standard procedural adjunctive therapy should be implemented (see section 5.1).

Elderly
No dose adjustment is needed in elderly (≥75 years) patients.

Renal impairment
No dose adjustment is needed in patients with mild, moderate or severe renal insufficiency (see sections 4.4 and 5.2).

Hepatic impairment
No dose adjustment is needed (see section 5.2).

Paediatric population
The safety and efficacy of cangrelor in children aged less than 18 years has not been established. No data are available.

Method of administration

Kengrexal is intended for intravenous use, only after reconstitution and dilution.

Kengrexal should be administered via an intravenous line. The bolus volume should be administered rapidly (<1 minute), from the diluted bag via manual intravenous push or pump. Ensure the bolus is completely administered before the start of PCI. Start the infusion immediately after administration of the bolus.

For instructions on reconstitution and dilution of the medicinal product before administration see section 6.6.

4.3 Contraindications

- Active bleeding or increased risk of bleeding, because of impaired haemostasis and/or irreversible coagulation disorders or due to recent major surgery/trauma or uncontrolled severe hypertension.
- Any history of stroke or transient ischaemic attack (TIA).
- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Risk of bleeding

Treatment with Kengrexal may increase the risk of bleeding.

In pivotal studies conducted in patients undergoing PCI, GUSTO (Global Use of Strategies to Open Occluded Arteries), moderate and mild bleeding events were more common in patients treated with cangrelor than in patients treated with clopidogrel, see section 4.8.

Although most bleeding associated with the use of cangrelor occurs at the site of arterial puncture, haemorrhage can occur at any site. Any unexplained fall in blood pressure or haematocrit should lead to the serious consideration of a haemorrhagic event and the cessation of cangrelor administration. Cangrelor should be used with caution in patients with disease states associated with an increased

bleeding risk. Cangrelor should be used with caution in patients taking medicines that may increase the risk of bleeding.

Cangrelor has a half-life of three to six minutes. Platelet function is restored within 60 minutes of stopping infusion.

Intracranial haemorrhage

Treatment with Kengrexal may increase the risk of intracranial haemorrhage. In pivotal studies conducted in patients undergoing PCI, there were more intracranial bleeds at 30 days with cangrelor (0.07%) than with clopidogrel (0.02%), of which 4 bleeds with cangrelor and 1 bleed with clopidogrel were fatal. Cangrelor is contraindicated in patients with any history of stroke/TIA, (see sections 4.3 and 4.8).

Cardiac tamponade

Treatment with Kengrexal may increase the risk of cardiac tamponade. In pivotal studies conducted in patients undergoing PCI, there were more cardiac tamponades at 30 days with cangrelor (0.12%) than with clopidogrel (0.02%), (see section 4.8).

Effects on renal function

In pivotal studies conducted in patients undergoing PCI, events of acute renal failure (0.1%), renal failure (0.1%) and increased serum creatinine (0.2%) were reported to occur after administration of cangrelor in clinical trials (see section 4.8). In patients with severe renal impairment (creatinine clearance 15-30 mL/min) a higher rate of worsening in renal function (3.2%) was reported in the cangrelor group compared to clopidogrel (1.4%). In addition, a higher rate of GUSTO moderate bleeding was reported in the cangrelor group (6.7%) compared to clopidogrel (1.4%). Cangrelor should be used with caution in these patients.

Hypersensitivity

Hypersensitivity reactions may occur after treatment with Kengrexal. A higher rate of serious cases of hypersensitivity were recorded with cangrelor (0.05%) than with control (0.007%). These included cases of anaphylactic reactions/shock and angioedema (see section 4.8).

Risk of dyspnoea

Treatment with Kengrexal may increase the risk of dyspnoea. In pivotal studies conducted in patients undergoing PCI dyspnoea (including exertional dyspnoea) occurred more commonly in patients treated with cangrelor (1.3%) than clopidogrel (0.4%). Most dyspnoea events were mild or moderate in severity and the median duration of dyspnoea was two hours in patients receiving cangrelor (see section 4.8).

Fructose intolerance

This medicinal product contains 52.2 mg sorbitol in each vial. Patients with hereditary fructose intolerance (HFI) must not be given this medicine unless strictly necessary.

Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction studies have only been performed in adults.

Oral P2Y12 agents (clopidogrel, prasugrel, ticagrelor)

When clopidogrel is administered during infusion of cangrelor, the expected inhibitory effect of clopidogrel on platelets is not achieved. Administration of 600 mg clopidogrel immediately after the cessation of the cangrelor infusion results in the anticipated full pharmacodynamic effect. No clinically relevant interruption of P2Y12 inhibition was observed in phase III studies when 600 mg clopidogrel was administered immediately after discontinuation of the cangrelor infusion.

Patients can be transitioned from cangrelor to prasugrel when prasugrel is administered immediately following discontinuation of the cangrelor infusion.

A pharmacodynamic interaction study has also been conducted with cangrelor and ticagrelor. No interaction on cangrelor was observed. Patients can be transitioned from cangrelor to ticagrelor without interruption of antiplatelet effect.

Pharmacodynamic effects

Cangrelor exhibits inhibition of activation and aggregation of platelets as shown by aggregometry (light transmission and impedance), point-of care assays, such as the VerifyNow P2Y12 test, VASP-P and flow cytometry.

Following the administration of a 30 micrograms/kg bolus followed by a 4 micrograms/kg/min infusion (the PCI dose), platelet inhibition is observed within two minutes. The pharmacokinetic/pharmacodynamic (PK/PD) effect of cangrelor is maintained consistently for the duration of the infusion.

Irrespective of dose, following cessation of the infusion, cangrelor blood levels decrease rapidly and platelet function returns to normal within one hour.

Acetylsalicylic acid, heparin, nitrogycerin

No pharmacokinetic or pharmacodynamic interaction with cangrelor was observed in an interaction study with aspirin, heparin, or nitroglycerin.

Bivalirudin, low molecular weight heparin, fondaparinux, and GP IIb/IIIa inhibitors

In clinical studies, cangrelor has been co-administered with bivalirudin, low molecular weight heparin, fondaparinux, and GP IIb/IIIa inhibitors (abciximab, eptifibatide, tirofiban) with no apparent effect upon the pharmacokinetics or pharmacodynamics of cangrelor.

Cytochrome P450 (CYP)

Metabolism of cangrelor is not dependent on CYPs and CYP isoenzymes are not inhibited by therapeutic concentrations of cangrelor or its major metabolites.

Breast cancer resistance protein (BCRP)

In vitro inhibition of BCRP by the metabolite ARC-69712XX at clinically relevant concentrations has been observed. Possible implications for the *in vivo* situation have not been investigated, but caution is advised when cangrelor is to be combined with a BCRP substrate.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of Kengrexal in pregnant women. Studies in animals have shown reproductive toxicity.

Kengrexal produced dose-related foetal growth retardation characterised by increased incidences of incomplete ossification and unossified hind limb metatarsals in rats. In rabbits, Kengrexal was associated with increased incidences of abortion and intrauterine losses, as well as foetal growth retardation at higher doses which may have been secondary to maternal toxicity. Kengrexal did not produce malformations in either the rat or rabbit reproductive studies.
Kengrexal is not recommended during pregnancy.

Breast-feeding

It is unknown whether Kengrexal is excreted in human milk. A risk to the newborns/infants cannot be excluded.

Fertility

No effect on female fertility parameters were observed in animal studies with Kengrexal. Effects on fertility, ability to produce a pregnancy with female partner(s), sperm morphology and sperm motility were observed in the male rat fertility study when Kengrexal was administered at human equivalent doses. These effects were not apparent at lower doses and were reversible following cessation of treatment.

4.7 Effects on ability to drive and use machines

Kengrexal has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most common adverse reactions with cangrelor include mild and moderate bleeding and dyspnoea. Serious adverse reactions associated with cangrelor in patients with coronary artery disease include severe/life threatening bleeding and hypersensitivity.

Tabulated list of adverse reactions

Table 1 depicts adverse reactions that have been identified based upon a pooling of combined data from all CHAMPION studies. Adverse reactions are classified according to frequency and system organ class. Frequency categories are defined according to the following conventions: Very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000).

Table 1: Adverse reactions for cangrelor in CHAMPION pooled studies within 48 hours

System organ class	Common	Uncommon	Rare	Very rare
Infections and infestations				Haematoma infection
Neoplasms benign, malignant and unspecified (includes cysts and polyps)				Skin neoplasm bleeding
Blood and lymphatic system disorders			Anaemia, thrombo-cytopenia	

System organ class	Common	Uncommon	Rare	Very rare
Immune system disorders			Anaphylactic reaction (anaphylactic shock), hypersensitivity	
Nervous system disorders			Haemorrhage intracranial [d] *	
Eye disorders			Eye haemorrhage	
Ear and labyrinth disorders				Ear haemorrhage
Cardiac disorders		Cardiac tamponade (pericardial haemorrhage)		
Vascular disorders	Haematoma <5 cm, haemorrhage	Haemodynamic instability	Wound haemorrhage, vascular pseudoaneurysm	
Respiratory, thoracic and mediastinal disorders	Dyspnoea (dyspnoea exertional)	Epistaxis, haemoptysis	Pulmonary haemorrhage	
Gastrointestinal disorders		Retroperitoneal haemorrhage,* peritoneal haematoma, gastrointestinal haemorrhage [a]		
Skin and subcutaneous tissue disorders	Ecchymosis (petechiae, purpura)	Rash, pruritus, urticaria [f]	Angioedema	
Renal and urinary disorders		Haemorrhage urinary tract, [e] acute renal failure (renal failure)		
Reproductive system and breast disorders			Pelvic haemorrhage	Menorrhagia, penile haemorrhage
General disorders and administration site conditions	Vessel puncture site discharge	Vessel puncture site haematoma [b]		
Investigations	Haematocrit decreased, haemoglobin decreased**	Blood creatinine increased	Platelet count decreased, red blood cell count decreased, international normalised ratio increased [c]	
Injury, poisoning and procedural complications	Haematoma ≥5 cm		Contusion	Periorbital haematoma, subcutaneous haematoma

Multiple related adverse reaction terms have been grouped together in the table and include medical terms as described below:

a. Upper gastrointestinal haemorrhage, mouth haemorrhage, gingival bleeding, oesophageal haemorrhage, duodenal ulcer haemorrhage, haematemesis, lower gastrointestinal haemorrhage, rectal haemorrhage, haemorrhoidal haemorrhage, haematochezia.
b. Application site bleeding, catheter site haemorrhage or haematoma, infusion site haemorrhage or haematoma.
c. Coagulation time abnormal, prothrombin time prolonged.
d. Cerebral haemorrhage, cerebrovascular accident.
e. Haematuria, blood urine present, urethral haemorrhage.
f. Erythema, rash erythematous, rash pruritic.

* Including events with fatal outcome.

** Transfusion was uncommon 101/12,565 (0.8%).

Description of selected adverse reactions

The GUSTO bleeding scale was measured in the CHAMPION (PHOENIX, PLATFORM, and PCI) clinical trials. An analysis of non-coronary artery bypass grafting (CABG)-related bleeding is presented in Table 2.

When administered in the PCI setting, cangrelor was associated with a greater incidence of GUSTO mild bleeding compared with clopidogrel. Further analysis of GUSTO mild bleeding revealed that a large proportion of mild bleeding events were ecchymosis, oozing and <5 cm haematoma. Transfusion and GUSTO severe/life-threatening bleeding rates were similar. In the pooled safety population from the CHAMPION trials, the incidence of fatal bleeding within 30 days of dosing was low and similar in patients who received cangrelor compared to clopidogrel (8 [0.1%] vs. 9 [0.1%]).

No baseline demographic factor altered the relative risk of bleeding with cangrelor.

Table 2: Non-CABG-related bleeding

GUSTO bleeding, n (%)		
CHAMPION pooled	**Cangrelor (N=12,565)**	**Clopidogrel (N=12,542)**
Any GUSTO bleeding	2,196 (17.5)	1,696 (13.5)
Severe/life-threatening	28 (0.2)	23 (0.2)
Moderate	76 (0.6)	56 (0.4)
Mild [a]	2,109 (16.8)	1,627 (13.0)
Mild w/o ecchymosis, oozing and haematoma <5 cm	707 (5.6)	515 (4.1)
Patients with any transfusion	90 (0.7)	70 (0.6)
CHAMPION PHOENIX	**Cangrelor (N=5,529)**	**Clopidogrel (N=5,527)**
Any GUSTO bleeding	178 (3.2)	107 (1.9)
Severe/life-threatening	9 (0.2)	6 (0.1)
Moderate	22 (0.4)	13 (0.2)
Mild [b]	150 (2.7)	88 (1.6)
Mild w/o ecchymosis, oozing and haematoma <5 cm	98 (1.8)	51 (0.9)
Patients with any transfusion	25 (0.5)	16 (0.3)

CABG: Coronary Artery Bypass Graft Surgery; GUSTO: Global Use of Strategies to Open Coronary Arteries; w/o: without

[a] In the CHAMPION pooled analysis, GUSTO Mild was defined as other bleed not requiring blood transfusion or causing haemodynamic compromise.

[b] In CHAMPION PHOENIX, GUSTO Mild was defined as other bleeding requiring intervention but not requiring blood transfusion or causing haemodynamic compromise.

4.9 Overdose

In clinical studies, healthy volunteers received up to two times the proposed daily dose. In clinical trials, the maximum accidental overdose was 10 times (bolus) or 3.5 times the infusion dose normally administered and bleeding was the most frequently observed adverse event.

Bleeding is the most likely pharmacological effect of overdose. If bleeding occurs appropriate supportive measures should be taken, which may include stopping the medicinal product so platelet function can return.

There is no antidote to Kengrexal, however, the pharmacokinetic half-life of Kengrexal is three to six minutes. Platelet function is restored within 60 minutes of stopping the infusion.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Platelet aggregation inhibitors excluding heparin, ATC code: B01AC25.

Mechanism of action

Kengrexal contains cangrelor, a direct P2Y12 platelet receptor antagonist that blocks adenosine diphosphate (ADP)-induced platelet activation and aggregation *in vitro* and *ex vivo*. Cangrelor binds selectively and reversibly to the P2Y12 receptor to prevent further signalling and platelet activation.

Pharmacodynamic effects

Cangrelor exhibits inhibition of activation and aggregation of platelets as shown by aggregometry (light transmission and impedance), point-of care assays, such as the VerifyNow P2Y12test, VASP-P and flow cytometry. Onset of P2Y12 inhibition occurs rapidly upon cangrelor administration.

Following the administration of a 30 microgram/kg bolus followed by a 4 microgram/kg/min infusion, platelet inhibition is observed within two minutes. The pharmacokinetic/pharmacodynamic (PK/PD) effect of cangrelor is maintained consistently for the duration of the infusion.

Irrespective of dose, following cessation of the infusion, blood levels decrease rapidly and platelet function returns to normal within one hour.

Clinical efficacy and safety

The primary clinical evidence for the efficacy of cangrelor is derived from CHAMPION PHOENIX, a randomised, double-blind study comparing cangrelor (n=5,472) to clopidogrel (n=5,470), both given in combination with aspirin and other standard therapy, including unfractionated heparin (78%), bivalirudin (23%), LMWH (14%) or fondaparinux (2.7%). The median duration of cangrelor infusion was 129 minutes. GP IIb/IIIa inhibitors were permitted for bailout use only and were used in 2.9% of patients. Patients with coronary atherosclerosis were included who required PCI for stable angina (58%), non-ST-segment elevation acute coronary syndrome (NSTE-ACS) (26%), or ST-elevation myocardial infraction (STEMI) (16%).

Data from the CHAMPION pooled population of over 25,000 PCI patients provide additional clinical support for safety.

In CHAMPION PHOENIX, cangrelor significantly reduced (relative risk reduction 22%; absolute risk reduction 1.2%) the primary composite endpoint of all-cause mortality, MI, IDR, and ST compared to clopidogrel at 48 hours (Table 3).

Table 3: Thrombotic events at 48 hours in CHAMPION PHOENIX (mITT population)

		Cangrelor vs. Clopidogrel		
n (%)	**Cangrelor N=5,470**	**Clopidogrel N=5,469**	**OR (95% CI)**	**p-value**
Primary Endpoint Death/MI/IDR/ST [a]	257 (4.7)	322 (5.9)	0.78 (0.66,0.93)	0.005
Key Secondary Endpoint				
Stent thrombosis	46 (0.8)	74 (1.4)	0.62 (0.43, 0.90)	0.010
Death	18 (0.3)	18 (0.3)	1.00 (0.52, 1.92)	>0.999
MI	207 (3.8)	255 (4.7)	0.80 (0.67, 0.97)	0.022
IDR	28 (0.5)	38 (0.7)	0.74 (0.45, 1.20)	0.217

[a] Primary endpoint from logistic regression adjusted for loading dose and patient status. p-values for secondary endpoints based on Chi-squared test.
OR = odds ratio; CI = confidence interval; IDR = ischaemia-driven revascularisation; MI = myocardial infarction; mITT = modified intent-to-treat; ST = stent thrombosis.

Significant reductions in death/MI/IDR/ST and ST observed in the cangrelor group at 48 hours were maintained at 30 days (Table 4).

Table 4: Thrombotic events at 30 days in CHAMPION PHOENIX (mITT population)

		Cangrelor vs. Clopidogrel		
n (%)	**Cangrelor N=5,462**	**Clopidogrel N=5,457**	**OR (95% CI)**	**p-value [a]**
Primary Endpoint Death/MI/IDR/ST	326 (6.0)	380 (7.0)	0.85 (0.73, 0.99)	0.035
Key Secondary Endpoint				
Stent thrombosis	71 (1.3)	104 (1.9)	0.68 (0.50, 0.92)	0.012
Death	60 (1.1)	55 (1.0)	1.09 (0.76, 1.58)	0.643
MI	225 (4.1)	272 (5.0)	0.82 (0.68, 0.98)	0.030
IDR	56 (1.0)	66 (1.2)	0.85 (0.59, 1.21)	0.360

[a] p-values based on Chi-squared test.
OR = odds ratio; CI = confidence interval; IDR = ischaemia-driven revascularisation; MI = myocardial infarction; mITT = modified intent-to-treat; ST = stent thrombosis.

Paediatric Population

Safety and effectiveness in pediatric patients have not been established.

5.2 Pharmacokinetic properties

Absorption

The bioavailability of cangrelor is complete and immediate. Cangrelor is rapidly distributed reaching C_{max} within two minutes after administration of an intravenous bolus followed by infusion. The mean steady state concentration of cangrelor during a constant intravenous infusion of 4 micrograms/kg/min is 488 ng/mL.

Distribution

Cangrelor has a volume of distribution of 3.9 L. Cangrelor is 97-98% plasma-protein bound.

Biotransformation

Cangrelor is deactivated rapidly in the plasma by dephosphorylation to form its primary metabolite, a nucleoside. The metabolism of cangrelor is independent of organ function and does not interfere with other drugs metabolised by hepatic enzymes.

Elimination

The half-life of Kengrexal is three to six minutes, independent of dose. Following the intravenous administration of a 2 micrograms/kg/min infusion of [^{3}H] cangrelor to healthy male volunteers, 93% of total radioactivity was recovered. Of the recovered material, 58% was found in urine and the remaining 35% was found in faeces, presumably following biliary excretion. Initial excretion was rapid, such that approximately 50% of the administered radioactivity was recovered in the first 24 hours, and 75% was recovered by 48 hours. Mean clearance was approximately 43.2 L/kg.

Linearity/non-linearity

The pharmacokinetic properties of cangrelor have been evaluated and found to be linear in patients and healthy volunteers.

Pharmacokinetic/pharmacodynamic relationship(s)

Special populations
The pharmacokinetics of cangrelor are not affected by gender, age, or renal or hepatic status. No dose adjustment is needed for these populations.

Weight
Although weight was a significant covariate for PK with higher clearance in heavier patients, the impact of weight on drug exposure is accounted by the use of weight-based dosing.

Paediatric population
Cangrelor has not been evaluated in a paediatric population (see sections 4.2 and 5.1).

5.3 Preclinical safety data

Non-clinical data reveal no relevant safety risk for humans based on studies of safety pharmacology, mutagenicity and clastogenic potential.
The primary adverse effects of Kengrexal in rats and dogs occurred in the upper urinary tract and consisted of injury to renal tubules, renal pelvis, and ureter. Anatomical changes correlated with increased plasma creatinine and urea, and increased albumin and blood cells in urine. Injury to the urinary tract was reversible following cessation of dosing in an investigative study in rats.

Carcinogenicity studies have not been performed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol
Sorbitol
Sodium hydroxide (for pH-adjustment)

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years.

The powder should be reconstituted immediately prior to dilution and use. Do not refrigerate.
From a microbiological point of view, unless the method of reconstitution/dilution precludes the risk of microbiological contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

6.4 Special precautions for storage

Store below 30° C.
For storage conditions after reconstitution and dilution of the medicinal product see section 6.3.

6.5 Nature and contents of container

Powder in 10 mL glass vials (Type 1) closed with a Flurotec coated butyl rubber stopper and sealed with crimped aluminium seal.

Kengrexal is available in packs of 10 vials.

6.6 Special precautions for disposal and other handling

Instructions for preparation

Aseptic procedures should be used for the preparation of Kengrexal.

The vial should be reconsituted immediately prior to dilution and use. Reconstitute each 50 mg/vial by adding 5 mL of sterile water for injection. Swirl gently until all material is dissolved. Avoid vigorous mixing. Allow any foam to settle. Ensure that the contents of the vial are fully dissolved and the reconstituted material is a clear, colourless to pale yellow solution.

Do not use without dilution. Before administration, 5 mL reconstituted solution has to be withdrawn from each vial and must be diluted further with 250 mL sodium chloride 9 mg/mL (0.9%) solution for injection or glucose (5%) solution for injection. Mix the bag thoroughly.

The medicinal product should be inspected visually for particulate matter after reconstitution.

Kengrexal is administered as a weight-based regimen consisting of an initial intravenous bolus followed by an intravenous infusion. The bolus and infusion should be administered from the infusion solution.

This dilution will generate a concentration of 200 micrograms/mL and should be sufficient for at least two hours of dosing as required. Patients 100 kg and over will require a minimum of two bags.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Authorized Indian Agent and Importer:
Paviour Pharmaceuticals Pvt. Ltd.
311-312, Suneja Tower – 1
District Centre, Janakpuri
New Delhi – 110058, India

Owner of the Product Rights:
Chiesi Farmaceutici S.p.A.
Via Palermo, 26/A
43122 Parma
Italy

8. MARKETING AUTHORISATION NUMBER(S)

<to be completed after approval>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<to be completed after approval>

10. DATE OF REVISION OF THE TEXT

<to be completed after approval>