1. NAME OF THE MEDICINAL PRODUCTS

Wosulin™ R Solution for Injection 100 IU/mL
Wosulin™ N Suspension for Injection 100 IU/mL
Wosulin™ 30/70 Suspension for Injection 100 IU/mL

Wosulin™ is a biosimilar product of Humulin®.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Wosulin™ R

Each mL contains:

Insulin Human	100 IU
m-Cresol	0.25% w/v (as preservative)

Wosulin™ R appears as a 3 mL Cartridge containing a colourless liquid, free from turbidity and foreign matter that is equivalent to 300 international units of regular human insulin (produced in non-pathogenic strain *Escherichia coli* by recombinant DNA technology), adjusted to a pH of 6.9 to 7.8.

Wosulin™ N

Each mL contains:

Insulin Human	100 IU
m-Cresol	0.16% w/v (as preservative)
Phenol	0.065% w/v (as preservative)

Wosulin™ N appears as a 3 mL cartridge containing a sterile suspension of a white precipitate that is equivalent to 300 IU of human insulin (produced in non-pathogenic strain *Escherichia coli* by recombinant DNA technology), in an isotonic phosphate buffer adjusted to a pH of 6.9 to 7.8.

Wosulin™ 30/70

Each mL contains:

Insulin Human (30% Soluble Insulin Injection and 70% Isophane Insulin Injection)	100 IU
m-Cresol	0.16% w/v (as preservative)
Phenol	0.065% w/v (as preservative)

Wosulin™ 30/70 appears as a 3 mL Cartridge containing a white or almost white suspension containing white or almost white precipitate that is equivalent to 300 IU of human insulin (produced in non-pathogenic strain of *Escherichia coli* by recombinant DNA technology), in the proportion of 30% soluble insulin and 70% isophane insulin.

3. PHARMACEUTICAL FORM

Wosulin™ R
A solution for injection in a 3 mL cartridge

Wosulin™ N
A suspension for injection in a 3 mL cartridge.

Wosulin™ 30/70
A suspension for injection in a 3 mL cartridge.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the treatment of patients with diabetes mellitus for whom diet and/or oral agents are not sufficient.

4.2 Posology and Method of Administration

Posology
The dosage should be determined by the physician, according to the requirement of the patient.

Paediatric population
No data are available.

Method of Administration
Wosulin™ R Wosulin™ N and Wosulin™ 30/70 is only suitable for subcutaneous injections from a reusable pen. This formulation should not be administered intravenously.

Subcutaneous administration should be in the upper arms, thighs, buttocks, or abdomen. Use of injection sites should be rotated so that the same site is not used more than approximately once a month.

Care should be taken when injecting any insulin preparations to ensure that a blood vessel has not been entered. After any insulin injection, the injection site should not be massaged. Patients must be educated to use proper injection techniques.

Wosulin™ N may be administered in combination with Wosulin™ R.

Wosulin™ 30/70 formulation is a ready-made defined mixture of soluble and isophane insulin designed to avoid the need for the patient to mix insulin preparations. A patient's treatment regimen should be based on their individual metabolic requirements.

4.3 Contraindications
Hypoglycaemia.

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1, unless used as part of a desensitisation programme.

Under no circumstances should any Wosulin™ formulation other than Wosulin™ R be given intravenously.

4.4 Special Warnings and Precautions for Use
Transferring a patient to another type or brand of insulin should be done under strict medical supervision. Changes in strength, brand (manufacturer), type (soluble, isophane, mixture), species (animal, human, human insulin analogue), and/or method of manufacture (recombinant DNA versus animal-source insulin) may result in the need for a change in dosage.

Some patients taking human insulin may require a change in dosage from that used with animal-source insulins. If an adjustment is needed, it may occur with the first dose or during the first several weeks or months.

A few patients who experienced hypoglycaemic reactions after transfer to human insulin have reported that the early warning symptoms were less pronounced or different from those experienced with their previous animal insulin. Patients whose blood glucose is greatly improved, e.g. by intensified insulin therapy, may lose some or all of the warning symptoms of hypoglycaemia and should be advised accordingly. Other conditions which may make the early warning symptoms of hypoglycaemia different or less pronounced include long duration of diabetes, diabetic nerve disease, or medications such as beta blockers. Uncorrected hypoglycaemic and hyperglycaemic reactions can cause loss of consciousness, coma, or death.

The use of dosages which are inadequate or discontinuation of treatment, especially in insulin-dependent diabetics, may lead to hyperglycaemia and diabetic ketoacidosis; conditions which are potentially lethal.

Treatment with human insulin may cause formation of antibodies, but titres of antibodies are lower than those to purified animal insulin.

Insulin requirements may change significantly in diseases of the adrenal, pituitary, or thyroid glands and in the presence of renal or hepatic impairment.

Insulin requirements may be increased during illness or emotional disturbances.

Adjustment of insulin dosage may also be necessary if patients change their level of physical activity or change their usual diet.

Patients must be instructed to perform continuous rotation of the injection site to reduce the risk of developing lipodystrophy and cutaneous amyloidosis. There is a potential risk of delayed insulin absorption and worsened glycaemic control following insulin injections at sites with these reactions. A sudden change in the injection site to an unaffected area has been reported to result in hypoglycaemia. Blood glucose monitoring is recommended after the change in the injection site, and dose adjustment of antidiabetic medications may be considered.

Combination of Human Insulin with Thiazolidinedione

Cases of cardiac failure have been reported when thiazolidinedione was used in combination with insulin, especially in patients with risk factors for development of cardiac heart failure. This should be kept in mind, if treatment with the combination of thiazolidinedione and human insulin is considered. If the combination is used, patients should be observed for signs and symptoms of heart failure, weight gain and oedema. Thiazolidinedione should be discontinued if any deterioration in cardiac symptoms occurs.

4.5 Interactions with Other Medicinal Products and Other Forms of Interaction

A number of medicinal products are known to interact with glucose metabolism and therefore the physician should be consulted when using other medications in addition to human insulin. The physician must therefore take possible interactions into account and should always ask his patients about any medicinal products they take.

Insulin requirements may be increased by substances with hyperglycaemic activity, such as glucocorticoids, thyroid hormones, growth hormone, danazol, $beta_2$-sympathomimetics (such as ritodrine, salbutamol, terbutaline), thiazides.

Insulin requirements may be reduced in the presence of substances with hypoglycaemic activity, such as oral hypoglycaemics (OHA), salicylates (for example, acetylsalicylic acid), certain antidepressants (monoamine oxidase inhibitors), certain angiotensin converting enzyme (ACE) inhibitors (captopril, enalapril), angiotensin II receptor blockers, non-selective beta-blocking agents, and alcohol.

Somatostatin analogues (octreotide, lanreotide) may both decrease or increase insulin dose requirements.

4.6 Fertility, Pregnancy and Lactation

It is essential to maintain good control of the insulin treated (insulin-dependent or gestational diabetes) patient throughout pregnancy. Insulin requirements usually fall during the first trimester and increase during the second and third trimesters. Patients with diabetes should be advised to inform their doctors if they are pregnant or are contemplating pregnancy.

Careful monitoring of glucose control, as well as general health, is essential in pregnant patients with diabetes.

Patients with diabetes who are lactating may require adjustments in insulin dose and/or diet.

4.7 Effects on Ability to Drive and Use Machines

The patient's ability to concentrate and react may be impaired as a result of hypoglycaemia. This may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or operating machinery).

Patients should be advised to take precautions to avoid hypoglycaemia whilst driving, this is particularly important in those who have reduced or absent awareness of the warning signs of hypoglycaemia or have frequent episodes of hypoglycaemia. The advisability of driving should be considered in these circumstances.

4.8 Undesirable Effects

Hypoglycaemia is the most frequent undesirable effect of insulin therapy that a patient with diabetes may suffer. Severe hypoglycaemia may lead to loss of consciousness, and in extreme cases, death. No specific frequency for hypoglycaemia is presented since hypoglycaemia is a result of both the insulin dose and other factors e.g. a patient`s level of diet and exercise.

Local allergy in patients is common (1/100 to < 1/10). Redness, swelling, and itching can occur at the site of insulin injection. This condition usually resolves in a few days to a few weeks. In some instances, local reactions may be related to factors other than insulin, such as irritants in the skin cleansing agent or poor injection technique.

Systemic allergy, which is very rare (< 1/10,000) but potentially more serious, is a generalised allergy to insulin. It may cause rash over the whole body, shortness of breath, wheezing, reduction in blood pressure, fast pulse, or sweating. Severe cases of generalised allergy may be life-threatening. In the rare event of a severe allergy to Wosulin™, treatment is required immediately. A change of insulin or desensitisation may be required.

Lipodystrophy at the injection site is uncommon (1/1,000 to < 1/100).

Cases of oedema have been reported with insulin therapy, particularly if previous poor metabolic control is improved by intensified insulin therapy.

Skin and Subcutaneous Tissue Disorders

Frequency “not known”: Cutaneous amyloidosis.

Lipodystrophy and cutaneous amyloidosis may occur at the injection site and delay local insulin absorption. Continuous rotation of the injection site within the given injection area may help to reduce or prevent these reactions.

4.9 Overdose

Insulin has no specific overdose definitions, because serum glucose concentrations are a result of complex interactions between insulin levels, glucose availability and other metabolic processes. Hypoglycaemia may occur as a result of an excess of insulin relative to food intake and energy expenditure.

Hypoglycaemia may be associated with listlessness, confusion, palpitations, headache, sweating and vomiting.

Mild hypoglycaemic episodes will respond to oral administration of glucose or sugar products.

Correction of moderately severe hypoglycaemia can be accomplished by intramuscular or subcutaneous administration of glucagon, followed by oral carbohydrate when the patient recovers sufficiently. Patients who fail to respond to glucagon must be given glucose solution intravenously.

If the patient is comatose, glucagon should be administered intramuscularly or subcutaneously. However, glucose solution must be given intravenously, if glucagon is not available or if the patient fails to respond to glucagon. The patient should be given a meal as soon as consciousness is recovered.

Sustained carbohydrate intake and observation may be necessary because hypoglycaemia may occur after apparent clinical recovery.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties:

Pharmacotherapeutic group:

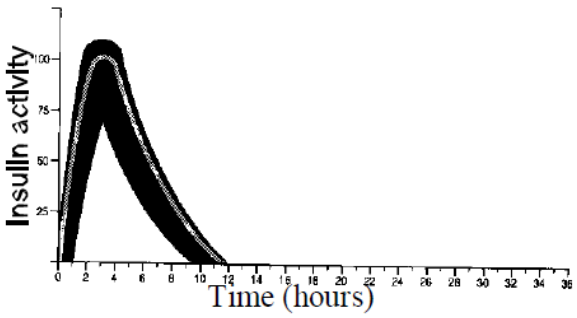
Wosulin™ R, ATC code: A10A B01. Wosulin™ R is a rapidly acting insulin preparation.
Wosulin™ N, ATC code: A10A C01. Wosulin™ N is an intermediate acting insulin preparation.
Wosulin™ 30/70, ATC code: A10A D01. Wosulin™ 30/70 is an intermediate acting insulin preparation.

The prime activity of insulin is the regulation of glucose metabolism.

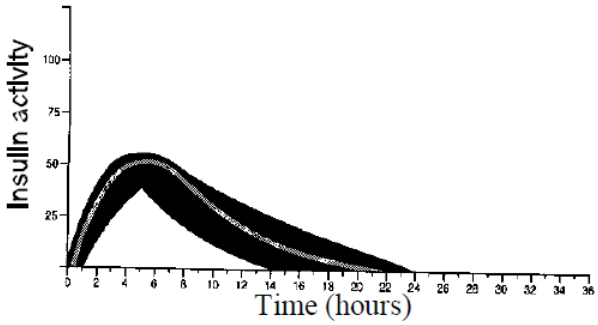
In addition, insulin has several anabolic and anti-catabolic actions on a variety of different tissues. Within muscle tissue this includes increasing glycogen, fatty acid, glycerol and protein synthesis and amino acid uptake, while decreasing glycogenolysis, gluconeogenesis, ketogenesis, lipolysis, protein catabolism and amino acid output.

The typical activity profile (glucose utilisation curve) following subcutaneous injection is illustrated below by the heavy line. Variations that a patient may experience in timing and/or intensity of insulin activity are illustrated by the shaded area. Individual variability will depend on factors such as size of dose, site of injection temperature and physical activity of the patient.

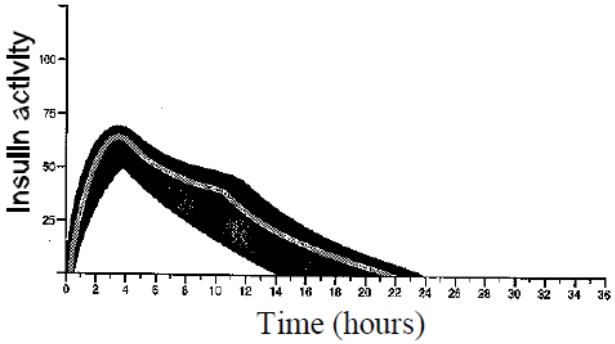
Wosulin™ R



Wosulin™ N



Wosulin™ 30/70



A Study to Compare Pharmacokinetics and Pharmacodynamics of Proposed Biosimilar Product with Reference Medicinal Product (Humulin® R) in Healthy Subjects was Conducted.

A Randomised, Single Centre, Double Blind, Three Treatment, Three-Period, Crossover, Glucose Clamp Study was conducted to test for Bioequivalence between Recombinant Human Insulins, Wockhardt's Regular Insulin Injection Soluble (*E. coli*) with Wockhardt's Regular Insulin Injection Soluble (Yeast) and Bioequivalence between Wockhardt's Regular Insulin Injection Soluble (*E. coli*) with Humulin® R in Healthy Subjects.

The primary objective was to test for bioequivalence (BE) based on the pharmacokinetic (PK) parameters (C_{max} and $AUC_{0\text{-}12h}$) and pharmacodynamics (PD) parameters (AUC-$GIR_{0\text{-}12h}$, and GIR_{max}) between recombinant human insulin formulations. Comparative safety and local tolerability of the three insulin preparations was also assessed. During the clamp procedure, blood was collected over 12 hours at pre-specified intervals for determination of blood glucose, plasma insulin and C-peptide. There was an interval of 5 to 28 days between the treatments. Concentration-time profile of plasma insulin was determined in the time interval of 0 to 12 hours post-dose, and the PK endpoints for Wockhardt's Regular Insulin Injection Soluble (*E. coli*), Wockhardt's Regular Insulin Injection Soluble (Yeast) and Humulin® R derived from the individual profile and used for PK analysis. Glucose infusion rate (GIR) was recorded during the clamp period of 0 to 12 hour post dose, and the PD endpoint for plasma insulin was derived from the individual GIR profile. C-peptide was assessed during the glucose clamp as a measure of endogenous insulin secretion. A total of 60 subjects were included in the study and were randomised into 3 arms to receive single subcutaneous (SC) injections of Wockhardt's Regular Insulin Injection Soluble (*E. coli*)/Test drug (A), Humulin® R/Reference-1 (C) and Wockhardt's Regular Insulin Injection Soluble (Yeast)/Reference-2 (B) as crossover. Plasma data from all 59 subjects with complete data in all the dosing visits were available and utilized for PK and PD analyses. The PD data from one of the subjects was identified as an outlier and was excluded from the PD analysis.

Pharmacokinetic (PK) comparison between Recombinant Human Insulins in healthy subjects

Primary PK Parameters	Formulation N=59	Least Square Means	Test Formulation	
			Wosulin™ R *E.coli*	
			Geometric Mean Ratio	90% CI
C_{max} (ng/mL)	Wosulin R *E. coli* (T) Vs Wosulin R Yeast (R)	2.49 : 2.60	96.02	92.06 to 100.14
	Wosulin R *E. coli* (T) Vs Humulin R® (R)	2.49 : 2.74	90.79	87.06 to 94.69
AUC_{0-12h} (h*ng/mL)	Wosulin R *E. coli* (T) Vs Wosulin R Yeast (R)	14.54 : 14.97	97.27	94.20 to 100.44
	Wosulin R *E. coli* (T) Vs Humulin R® (R)	14.54 : 15.07	96.74	93.69 to 99.89

PK=pharmacokinetics; LS=least squares; C_{max}= maximum observed plasma concentration; AUC_{0-12h}=area under the plasma concentration curve from time 0 to 12 hours.

Pharmacodynamic (PD) comparison between Recombinant Human Insulins in healthy subjects

Primary PD Parameters	Formulation N=59	Least Square Means	Test Formulation	
			Wosulin™ R *E.coli*	
			Geometric Mean Ratio	95% CI
GIR_{max} (mg/kg/min)	Wosulin R *E. coli* (T) Vs Wosulin R Yeast (R)	7.21 : 7.85	91.91	83.68 to 100.94
	Wosulin R *E. coli* (T) Vs Humulin R® (R)	7.21 : 7.32	98.54	89.71 to 108.22
$AUC_{GIR,0-12h}$ (h*mg/kg/min)	Wosulin R *E. coli* (T) Vs Wosulin R Yeast (R)	39.58 : 41.67	94.97	85.90 to 105.00
	Wosulin R *E. coli* (T) Vs Humulin R® (R)	39.58 : 38.59	102.55	92.75 to 113.38

PD=pharmacodynamics; GIR=glucose infusion rate; LS=least squares; AUC-GIR_{0-12h} =area under the glucose infusion rate-time curve from time 0 to 12 hours.

The CI 90% for the geometric LS mean ratio for both PK endpoints, C_{max} and AUC_{0-12h} was entirely contained within the bioequivalence interval of 80% to 125%. Bioequivalence was also demonstrated for primary Pharmacodynamic endpoints as CI 95% of the geometric LS mean ratios for AUC-GIR_{0-12h} and GIR_{max} were entirely contained within the bioequivalence interval of 80% to 125%.

Conclusion

Wockhardt's Regular Insulin Injection Soluble (*E. coli*) demonstrated average bioequivalence to Wockhardt's Regular Insulin Injection Soluble (Yeast) and to Humulin® R respectively in all PK and PD endpoints. The AEs experienced by subjects were similar in all three arms. Hence, it can be concluded that all the both formulations were comparably safe and well tolerated when compared to Humulin® R.

A Study to Compare Pharmacokinetics of Proposed Biosimilar Product with Reference Medicinal Product (Humulin® N) in Healthy Subjects was Conducted.

A Randomised, Single Centre, Double Blind, Two Treatment, Two-sequence, Two Period, Crossover Glucose Clamp Study to Test for Bioequivalence between Wockhardt's Wosulin™ N (Brand name used in the Clinical Trial) (100 IU/mL) {Insulin Injection Isophane, r-DNA Origin} and Humulin® N (100 U/mL) {Insulin Injection Isophane (r-DNA Origin)}, in Healthy subjects.

The primary objective is to test for bioequivalence based on the pharmacokinetic parameters (C_{max} and AUC_{0-24h}) of Insulin Injection Isophane, r-DNA origin formulations, Wockhardt's Wosulin N (*E. coli*) and Humulin® N in healthy subjects.

Analysis of the PK parameter showed that the 90% CI of the geometric LS mean ratio for AUC_{0-24h} was entirely contained within the bioequivalence interval of 80% to 125%; similarly, the 90% CI of the geometric LS (least squares) mean ratio for C_{max} was entirely contained within the bioequivalence interval of 80% to 125%. Therefore, Wockhardt's Wosulin™ N and Humulin® N (Eli Lilly) formulations are bioequivalent because the 90 % CI of geometric LS mean ratios for both parameters were entirely contained within the bioequivalence interval.

Results of PK parameters in healthy subjects

PK Parameter	Geometric Least Square Mean		T/R Ratio	90% CI of the ratio
	Wosulin™ N (N=39)	Humulin® N (N=39)		
AUC_{0-24} (h*pmol/L)	1951.49	1802.85	108.24	100.61 to 116.46
C_{max} (pmol/L)	133.13	120.82	110.19	99.76 to 121.71

Note: Out of 50 participated subjects, 43 subjects completed the study & considered for the PD analysis while 39 subjects were considered for PK analysis as four subjects (*i.e.* Subject nos. 13, 34, 43 & 45) were excluded from BE analysis as pre-dose concentrations were found to be greater than 5 % C_{max} of their respective period.

Conclusion

In conclusion, a single dose of test formulation Insulin Injection Isophane (Brand name: Wosulin™ N used in the Clinical Trial) was found to be safe and bioequivalent to the reference formulation Insulin Injection Isophane 10 mL 100 units/mL Humulin® N as 90% confidence interval for the geometric least square mean ratios of test to reference formulations, based on ln-transformed PK parameters of C_{max} and $AUC_{0-24h,}$ were within the bioequivalence acceptance range of 80% to 125%. From the adverse event profile and local tolerability of the subjects, it appeared that the test product was equally safe as that of reference product.

A Study to Compare Pharmacokinetics of Proposed Biosimilar Product with Reference Medicinal Product (Humuline® 30/70) in Healthy Subjects was Conducted.

A Randomised, Single Centre, Double Blind, Two Treatment, Two-Period, Crossover Glucose Clamp Study to Test for Bioequivalence between Wockhardt's Wosulin™ 30/70 (100 IU/mL) {Insulin Injection Biphasic Isophane in ration of 70% Human Insulin Isophane Suspension and 30% Human Insulin Injection (r-DNA origin)} and Humuline® 30/70 (100 U/mL) {70% Human Insulin Isophane Suspension and 30% Human Insulin Injection (rDNA origin)} in Healthy Subjects.

The objective is to test for bioequivalence based on the pharmacokinetic parameters (C_{max} and AUC_{0-24h}) of Wockhardt's Wosulin™ 30/70 (100 IU/mL) {Biphasic Isophane Insulin Injection/ 70% Human Insulin Isophane Suspension and 30% Human Insulin Injection (r-DNA origin)} and Humuline® 30/70 (100 U/mL) {70% Human Insulin Isophane Suspension and 30% Human Insulin Injection (rDNA origin)} in healthy subjects.

Analysis of the PK parameter showed that the 90% CI of the geometric LS mean ratio for AUC_{0-24h} was entirely contained within the bioequivalence interval of 80% to 125%; similarly, the 90% CI of the geometric LS (least squares) mean ratio for C_{max} was entirely contained within the bioequivalence interval of 80% to 125%. Therefore, Wockhardt's Wosulin™ 30/70 and Humuline® 30/70 (Eli Lilly) formulations are bioequivalent because the 90 % CI of geometric LS mean ratios for both parameters were entirely contained within the bioequivalence interval.

Results of PK parameters in healthy subjects

PK Parameter	Geometric Least Square Mean		T/R Ratio	90% CI of the ratio
	Wosulin™ 30/70 (N=37)	Humuline® 30/70 (N=37)		
AUC_{0-24} (h*pmol/L)	2550.58	2724.07	93.63	89.65 to 97.79
C_{max} (pmol/L)	244.27	261.10	93.55	86.76 to 100.88

Note: Out of 40 participated subjects, 37 subjects completed the study and considered for the PK-PD analysis as three subjects (i.e. subject nos. 23, 25 and 33) were excluded from BE analysis.

Wosulin™ 30/70 and Humuline® 30/70 are bioequivalent based on the results for the primary PK endpoints. The 90% CI for the geometric LS mean ratio was entirely contained within the bioequivalence interval of 80% to 125% for AUC_{0-24h} and C_{max} - the primary PK end points. These results indicate similar rate and extent of absorption for the two formulations. Based on analysis of AEs, clinical laboratory evaluation, local tolerability test and vital signs

examination it is demonstrated that Wockhardt's Wosulin™ 30/70 is well tolerated and has a comparable safety profile to Humuline® 30/70.

In conclusion, this study demonstrated the PK bioequivalence of Wosulin™ 30/70 and Humuline® 30/70 and both the formulations were comparably safe and well tolerated after administration of 0.4 IU/kg dose in healthy volunteers.

5.2 Pharmacokinetic Properties

The pharmacokinetics of insulin do not reflect the metabolic action of that hormone. Therefore, it is more appropriate to examine glucose utilisation curves (as discussed above) when considering the activity of insulin.

5.3 Preclinical Safety Data

Wosulin™ is human insulin produced by recombinant technology. No serious events have been reported in sub chronic toxicology studies. Human insulin was not mutagenic in a series of *in vitro* and *in vivo* genetic toxicity assays.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Wosulin™ R

Glycerol,
Zinc Oxide,
m-Cresol,
Tri-Sodium Citrate Dihydrate,
Citric Acid Monohydrate,
Sodium Hydroxide (for pH adjustment),
Hydrochloric Acid (for pH adjustment),
Water for Injection (WFI).

Wosulin™ N and Wosulin™ 30/70

Glycerol,
Zinc Oxide,
m-Cresol,
Phenol,
Disodium Hydrogen Phosphate,
Protamine Sulphate,
Sodium Hydroxide (for pH adjustment),
Hydrochloric Acid (for pH adjustment),
Water for Injection (WFI).

6.2 Incompatibilities

Wosulin™ must not be mixed with insulins produced by other manufacturers or with animal insulin preparation.

6.3 Shelf Life
Unopened cartridges
36 months

After first use
28 days

6.4 Special Precautions for Storage
Do not freeze. Do not expose to excessive heat or direct sunlight.

Unopened cartridges
Store in a refrigerator (2°C - 8°C).

After first use
Store below 30°C

6.5 Nature and Contents of Container
Wosulin™ R:
3 mL of solution in a cartridge (type I glass) with a red bromobutyl plunger at the bottom (rubber) and disc seal at the top (rubber).

Available in a box of 1 x 3 mL cartridge and 5 x 3 mL cartridges.

Wosulin™ N and Wosulin™ 30/70:
3 mL of suspension in a cartridge (type I glass) with a red bromobutyl plunger at the bottom (rubber) and disc seal at the top (rubber). The cartridge contains a glass ball (type I glass) to facilitate the resuspension.

Available in a box of 1 x 3 mL cartridge and 5 x 3 mL cartridges.

6.6 Special Precautions for Disposal and Other Handling
Do not reuse needles. Dispose of the needle in a responsible manner. Needles must not be shared. Cartridge can be used until empty, then properly discard. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Instruction for Use and Handling
To prevent the possible transmission of disease, each cartridge must be used by one patient only, even if the needle on the delivery device is changed.

The cartridge is to be used with the reusable pen DELFU Pen Injector, PENOVVA Pen Injector and mypen2 Pen Injector. The reusable pen will be supplied separately.

a) Preparing a dose
Cartridges containing Wosulin™ R should look clear. Do not use if it looks cloudy, thick, slightly coloured, or particles seen in the solution. Cartridges containing Wosulin™ N and Wosulin™ 30/70 should be rolled in the palms of the hand ten times and inverted 180° ten times immediately before use to resuspend the insulin until it appears uniformly cloudy or milky. If not, repeat the above procedure until contents are mixed. Cartridges containing Wosulin™ N and Wosulin™ 30/70 contain a small glass bead to assist mixing. Do not

shake vigorously as this may cause frothing, which may interfere with the correct measurement of the dose.

The cartridge should be examined frequently and should not be used if clumps of material are present or if solid white particles stick to the bottom or wall of the cartridge, giving a frosted appearance.

The cartridges are not designed to allow any other insulin to be mixed in the cartridge. Cartridges are not designed to be refilled.

b) Injecting a dose
Inject the correct dose of insulin, as directed by the doctor or diabetes specialist nurse. Use of the injection sites should be rotated so that the same is not used more than approximately once a month.

7. MANUFACTURER
Wockhardt Limited
E-1/1, Wockhardt Infrastructure Development Limited,
Special Economic Zone (SEZ), E-1, Shendra MIDC Five Star Industrial Area,
Shendra, Chhatrapati Sambhajinagar-431154, Maharashtra State,
India

8. PRODUCT REGISTRATION HOLDER
Pharmaniaga LifeScience Sdn Bhd (198201002939),
Lot 7, Jalan PPU 3,
Taman Perindustrian Puchong Utama,
47100 Puchong, Selangor,
Malaysia

9. DATE OF REVISION
10 February 2026

II/10630 - 228128