1.3.1 Summary of Product characteristics (SmPC)

1.3.1.1 Name of the medicinal product

International Non– Proprietary Name (INN)	Telmisartan
Trade mark name	**Cortel 40**
Generic Name	Telmisartan Tablets USP

1.3.1.2 ATC and Forensic Classification

Name	ATC Code	Category/Name
Telmisartan	C09CA07	Angiotensin II receptor blockers (ARBs)

1.3.1.3 Qualitative and quantitative composition

Sr. No.	Material Name	Spc.	Function	Theo. qty./ Tab. (mg)
Mixing				
1.	Meglumine	USP	Stabilizer	15.00
2.	Aerosil (Colloidal Silicon Dioxide)	BP	Disintegrant	1.000
3.	Microcrystalline Cellulose	BP	Diluent	122.5
4.	Maize Starch	BP	Disintegrant	94.50
5.	Crospovidone	USP	Disintegrant	8.000
6.	Heavy Magnesium Oxide	BP	Diluent	1.200
7.	MCCP (PH 102)	IH	Diluent	11.80
8.	Sodium Carbonate	BP	Preservative	10.00
Wet Granulation				
9.	$Telmisartan	BP	Active	40.00
10.	Sodium Hydroxide Pellets	BP	Alkaliser	5.000
11.	#Purified Water	BP	Solvent	0.0095 ml
12.	#Isopropyl Alcohol	BP	Solvent	0.080 ml
13.	Tween-80	BP	Surfactant	0.200
Lubrication				
14.	Magnesium Stearate	BP	Lubricant	2.300
15.	Kyron T-314	IH	Disintegrant	20.00
Film Coating				
16.	@Instacoat-IC-S-4017 (Orange)	IH	Colouring Agent	7.000
17.	@#Isopropyl Alcohol	BP	Solvent	0.0667 ml
18.	@#Dichloromethane	BP	Solvent	0.200 gm
Total Weight				**338.5**

Note: $Qty of active materials shall be vary with assay and LOD.
(Assay considered is 100% and LOD 0%).
-Final qty. shall be compensated with Microcrystalline Cellulose Powder.
-#Quantity of these materials will not be calculated in total weight of tablet.
-@Overages of coating materials are added to compensate the loss during coating.
-Average weight of coated tablet after coating should be achieved approximately 2.11%
USP - United States Pharmacopeia
BP - British Pharmacopeia
IH - In-house Specification

1.3.1.4 Pharmaceutical Form

Solid Oral dosage form (Oral Tablet)

Description: Orange coloured, round shaped, biconvex, film coated tables having breakline on one side and other side plain.

1.3.1.5 Clinical particulars

1.3.1.5.1 Therapeutic indications

Hypertension

Treatment of essential hypertension in adults.

Cardiovascular prevention

Reduction of cardiovascular morbidity in adults with: Manifest at herothrombotic cardiovascular disease (history of coronary heart disease, stroke, or peripheral arterial disease) or Type 2 diabetes mellitus with documented target organ damage.

1.3.1.5.2 Posology and method of administration

Treatment of essential hypertension

The usually effective dose is 40 mg once daily. Some patients may already benefit at a daily dose of 20 mg. In cases where the target blood pressure is not achieved, the dose of telmisartan can be increased to a maximum of 80 mg once daily. Alternatively, telmisartan may be used in combination with thiazide-type diuretics such as hydrochlorothiazide, which has been shown to have an additive blood pressure lowering effect with telmisartan.

Cardiovascular prevention

The recommended dose is 80 mg once daily. It is not known whether doses lower than 80 mg of telmisartan are effective in reducing cardiovascular morbidity. When initiating telmisartan therapy forthe reduction of cardiovascular morbidity, close monitoring of blood pressure is recommended, and if appropriate adjustment of medications that lower blood pressure may be necessary.

Method of administration

Telmisartan tablets are for once-daily oral administration and should be taken with liquid, with or without food. Precautions to be taken before handling or administering the medicinal product

Telmisartan should be kept in the sealed strip due to the hygroscopic property of the tablets. Tablets should be taken out of the strip shortly before administration.

1.3.1.5.3 Contraindications

- Hypersensitivity to the active substance orto any of the Excipients.

* Second and third trimesters of pregnancy
* Biliary obstructive disorders
• Severe hepatic impairment. Special warnings and precautions for use.

1.3.1.5.4 Special warnings and precautions for use

Hepatic impairment

Telmisartan is not to be given to patients with cholestasis, biliary obstructive disorders or severe hepatic impairment since telmisartan is mostly eliminated with the bile. Telmisartan should be used only with caution in patients with mild to moderate hepatic impairment.

Renovascular hypertension

There is an increased risk of severe hypotension and renal insufficiency when patients with bilateral renal artery stenosis or stenosis of the artery to a single functioning kidney are treated with medicinal products that affect the renin-angiotensin-aldosterone system.

1.3.1.5.5 Interaction with other medicinal products and other forms of interaction

As with other medicinal products acting on the renin-angiotensin-aldosterone system, telmisartan may provoke hyperkalaemia. The risk may increase in case of treatment combination with other medicinal products that may also provoke hyperkalaemia (salt substitutes containing potassium, potassium-sparing diuretics, ACE inhibitors, angiotensin II receptor antagonists, non-steroidal anti-inflammatory medicinal products (NSAIDs, including selective COX-2 inhibitors), heparin, immune-suppressive (cyclosporin or tacrolimus), and trimethoprim). The occurrence of hyperkalaemia depends on associated risk factors. The risk is increased in case of the above-mentioned treatment combinations. The risk is particularly high in combination with potassium sparing-diuretics, and when combined with salt substitutes containing potassium. A combination with ACE inhibitors or NSAIDs, for example, presents a lesser risk provided that precautions for use are strictly followed. Concomitant use not recommended

Potassium sparing diuretics or potassium supplements

Angiotensin II receptor antagonists such as telmisartan, attenuate diuretic induced potassium loss. Potassium sparing diuretics e.g. spirinolactone, eplerenone, triamterene, or amiloride, potassium supplements, or potassium-containing salt substitutes may lead to a significant increase in serum potassium. If concomitant use is indicated because of documented hypokalaemia, they should be used with caution and with frequent monitoring of serum potassium.

Lithium

Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with angiotensin converting enzyme inhibitors, and with angiotensin II receptor antagonists, including telmisartan. If use of the combination proves

necessary, careful monitoring of serum lithium levels is recommended. Concomitant use requiring caution

Non-steroidal anti-inflammatory medicinal products

NSAIDs (i.e. acetylsalicylic acid at anti-inflammatory dosage regimens, COX-2 inhibitors and nonselective NSAIDs) may reduce the antihypertensive effect of angiotensin II receptor antagonists. In some patients with compromised renal function (e.g. dehydrated patients or elderly patients with compromised renal function), the co-administration of angiotensin II receptor antagonists and agents that inhibit cyclo-oxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy and periodically thereafter.

Other antihypertensive agents

The blood pressure lowering effect of telmisartan can be increased by concomitant use of other antihypertensive medicinal products. Based on their pharmacological properties it can be expected that the following medicinal products may potentiate the hypotensive effects of all anti-hypertensive including telmisartan: Baclofen, amifostine. Furthermore, orthostatic hypotension may be aggravated by alcohol, barbiturates, narcotics, or antidepressants.

1.3.1.5.6 Pregnancy and lactation

Pregnancy: There are no adequate data from the use of Telmisartan in pregnant women.

Epidemiological evidence regarding the risk of teratogenicity following exposure to ACE inhibitors during the first trimester of pregnancy has not been conclusive: however a small increase in risk cannot be excluded. Whilst there is no controlled epidemiological data on the risk with angiotensin II receptor antagonists, similar risks may exist for this class of drugs. Unless continued angiotensin II receptor antagonist therapy is considered essential, patients planning pregnancy should be changed to alternative antihypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with angiotensin II receptor antagonists should be stopped immediately, and, if appropriate, alternative therapy should be started.

Exposure to angiotensin II receptor antagonist therapy during the second and third trimesters is known to induce human fetotoxicity (decreased renal function, oligohydramnios, skull ossification retardation) and neonatal toxicity (renal failure, hypotension, hyperkalaemia). Should exposure to angiotensin II receptor antagonists have occurred from the second trimester of pregnancy, ultrasound check of renal function and skull is recommended.

Infants whose mothers have taken angiotensin II receptor antagonists should be closely observed for hypotension.

Breast-feeding: Because no information is available regarding the use of Telmisartan during breast-feeding, Telmisartan is not recommended and alternative treatments with better

established safety profiles during breastfeeding are preferable, especially while nursing a newborn or preterm infant.
Fertility In preclinical studies, no effects of Telmisartan on male and female fertility were observed.

1.3.1.5.7 Effects on ability to drive and use machines
When driving vehicles or operating machinery it should be taken into account that dizziness or drowsiness may occasionally occur when taking antihypertensive therapy such as Telmisartan.

1.3.1.5.8 Undesirable effects
Serious adverse drug reactions include anaphylactic reaction and angioedema which may occur rarely (> 1/10,000 to < 1/1,000), and acute renal failure.
Description of selected adverse reactions Sepsis, Hypotension, Hepatic function abnormal/liver disorder, Intestinal lung disease.

1.3.1.5.9 Overdose
Symptoms: The most prominent manifestations of telmisartan overdose were hypotension and tachycardia; bradycardia dizziness, increase in serum creatinine, and acute renal failure have also been reported.
Treatment: Telmisartan is not removed by haemodialysis. The patient should be closely monitored, and the treatment should be symptomatic and supportive. Management depends on the time since ingestion and the severity of the symptoms. Suggested measures include induction of emesis and / or gastric lavage. Activated charcoal may be useful in the treatment of overdosage. Serum electrolytes and creatinine should be monitored frequently. If hypotension occurs, the patient should be placed in a supine position, with salt and volume replacement given quickly.

1.3.1.6 Pharmacological properties
1.3.1.6.1 Pharmacodynamic properties
Telmisartan is an orally active and specific angiotensin II receptor (type AT 1) antagonist. Telmisartan displaces angiotensin II with very high affinity from its binding site at the AT 1 receptor subtype, which is responsible for the known actions of angiotensin II. Telmisartan does not exhibit any partial agonist activity at the AT 1 receptor. Telmisartan selectively binds the AT 1 receptor. The binding is long-lasting. Telmisartan does not show affinity for other receptors, including AT2 and other less characterised AT receptors. Telmisartan does not inhibit angiotensin converting enzyme (kininase II), the enzyme which also degrades bradykinin. Therefore it is not expected to potentiate bradykinin mediated adverse effects. In human, an 80 mg dose of telmisartan almost completely inhibits the angiotensin II evoked blood pressure increase. The inhibitory effect is maintained over 24 hours and still measurable up to 48 hours.

1.3.1.6.2 Pharmacokinetic properties

Absorption: Absorption of Telmisartan is rapid although the amount absorbed varies. The mean absolute bioavailability for Telmisartan is about 50 %. When Telmisartan is taken with food, the reduction in the area under the plasma concentration-time curve (AUC0-°°) of Telmisartan varies from approximately 6 % (40 mg dose) to approximately 19 % (160 mg dose). By 3 hours after administration, plasma concentrations are similar whether Telmisartan is taken fasting or with food.

Distribution: Telmisartan is largely bound to plasma protein (>99.5 %), mainly albumin and alpha-1 acid glycoprotein. The mean steady state apparent volume of distribution (Vdss) is approximately 5001.

Biotransformation: Telmisartan is metabolised by conjugation to the glucuronide of the parent compound. No pharmacological activity has been shown forthe conjugate. Elimination: Telmisartan is characterised by biexponential decay pharmacokinetics with a terminal elimination half-life of >20 hours.The maximum plasma concentration (Cmax) and, to a smaller extent, the area under the plasma concentration-time curve (AUC), increase disproportionately with dose. There is no evidence of clinically relevant accumulation of telmisartan taken at the recommended dose. Plasma concentrations were higher in females than in males, without relevant influence on efficacy.

After oral (and intravenous) administration, Telmisartan is nearly exclusively excreted with the faeces, mainly as unchanged compound. Cumulative urinary excretion is < 1 % of dose. Total plasma clearance (Cltot) is high (approximately 1,000 ml/min) compared with hepatic blood flow (about 1,500 ml/min).

1.3.1.6.3 Preclinical safety data

In preclinical safety studies, doses producing exposure comparable to that in the clinical therapeutic range caused reduced red cell parameters (erythrocytes, haemoglobin, haematocrit), changes in renal haemodynamics (increased blood urea nitrogen and creatinine), as well as increased serum potassium in normotensive animals. In dogs, renal tubular dilation and atrophy were observed. Gastric mucosal injury (erosion, ulcers or inflammation) also was noted in rats and dogs. These pharmacologically-mediated undesirable effects, known from preclinical studies with both angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists, were prevented by oral sodium chloride solution supplementation.

In both species, increased plasma renin activity and hypertrophy/hyperplasia of the renal juxtaglomerular cells were observed. These changes, also a class effect of angiotensin converting enzyme inhibitors and other angiotensin II receptor antagonists, do not appear to have clinical significance.

No clear evidence of a teratogenic effect was observed, however at toxic dose levels of telmisartan an effect on the postnatal development of the offsprings such as lower body weight and delayed eye opening was observed.

There was no evidence of mutagenicity and relevant clastogenic activity in in vitro studies and no evidence of carcinogenicity in rats and mice.

1.3.1.7 Pharmaceutical particulars

1.3.1.7.1 Incompatibilities

None reported.

1.3.1.7.2 Shelf life

36 Months

1.3.1.7.3 Special precautions for storage

Store below 30°C.
Protect from light and moisture.

1.3.1.7.4 Nature and contents of container

10 Tablets packed in Alu-Alu blister pack and such 3 blister is to be packed in carton along with insert.

1.3.1.7.5 Special precautions for disposal

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

1.3.1.8 Registrant

Pacmai International Limited

1.3.1.9 Registration Number(s)

B4-4385

1.3.1.10 Date of initial or renewed registration

26th March 2015

1.3.1.11 Date of revision of the text
