

Pritor[®]/Kinzalmono[®] and PritorPlus[®]/Kinzalkomb[®]

Product Information

Pharmacodynamic Properties

- Telmisartan, the active component of Pritor[®]/Kinzalmono[®], is a highly selective non-peptide angiotensin II receptor (type AT1) blocker (ARB).
- Telmisartan selectively binds the AT1-receptor with high affinity, causing inhibition of the action of angiotensin II on vascular smooth muscle, which ultimately leads to a reduction in arterial blood pressure. This binding is long-lasting and in man, an 80mg dose of telmisartan almost completely inhibits the angiotensin II-evoked blood pressure increase. This inhibitory effect is maintained over 24 hours and is still measurable for up to 48 hours.
- Telmisartan possesses a unique pharmacological profile which includes:
 - Selective AT1-blockade
 - Slow rate of dissociation from the receptor
 - Highest volume of distribution of ARBs
 - Longest half-life of ARBs: effect maintained over 24 hours with single dose
 - High lipophilicity
 - High level of tissue penetration
 - Unique Selective PPAR- γ Modulations (SPPARM) that translate into a favorable glycaemic and lipid metabolism effect
- PritorPlus[®]/Kinzalkomb[®] is a combination of the angiotensin II receptor antagonist telmisartan and a thiazide diuretic, hydrochlorothiazide

(HCTZ). This combination has an additive antihypertensive effect and reduces blood pressure to a greater degree than either component drug alone.

- HCTZ affects the renal tubular mechanisms of electrolyte reabsorption, directly increasing excretion of sodium and chloride in approximately equivalent amounts.
- The diuretic action of HCTZ reduces plasma volume, increases plasma renin activity and increases aldosterone secretion, thereby increasing urinary potassium and bicarbonate excretion.
- PritorPlus[®]/ Kinzalkomb[®] once daily produces effective and smooth reductions in blood pressure across the 24-hour therapeutic dose range.

Pharmacokinetic Properties

- Telmisartan T_{max} is 0.5 to 1 hour after dosing. Food slightly reduces bioavailability of telmisartan, with an AUC reduction of about 6% with a 40mg tablet, and 19% with a 160mg dose. At 40mg and 160mg, the bioavailability was 42% and 58%, respectively.
- Telmisartan is largely bound to plasma protein (> 99.5 %).
- Telmisartan terminal half-life ($t_{1/2}$) is approximately 24 hr and total plasma clearance is greater than 800ml/min. After IV or oral administration, more than 97% is eliminated unchanged in faeces via biliary excretion.
- Concomitant administration of HCTZ and telmisartan does not appear to affect the pharmacokinetics of either drug in healthy subjects.

- Following oral administration of PritorPlus[®]/Kinzalkomb[®], peak concentrations of HCTZ are reached in approximately 1 to 3 hours after dosing. Based on cumulative renal excretion of HCTZ, the absolute bioavailability was about 60%.
- HCTZ is 68% protein-bound and its apparent volume of distribution is 0.83 to 1.14l/kg. HCTZ is not metabolised in man and is excreted almost entirely as unchanged drug in urine. About 60% of the oral dose is eliminated as unchanged drug within 48 hours. Renal clearance is about 250–300ml/min. The terminal elimination half-life of HCTZ is 10–15 hours.

Indication

- Pritor[®]/Kinzalmono[®] is indicated for the treatment of essential hypertension.
- PritorPlus[®]/Kinzalkomb[®] is indicated for patients whose blood pressure is not adequately controlled by Pritor[®]/Kinzalmono[®] alone or with HCTZ (hydrochlorothiazide) in their separate components.

Dosage

- Pritor[®]/Kinzalmono[®] may be used alone as monotherapy. It is available as tablets for oral administration, containing 20mg, 40mg and 80mg of telmisartan.

- In most patients with mild or moderate hypertension, maximum blood pressure reduction is achieved with 40mg or 80mg once daily.
- PritorPlus[®]/Kinzalkomb[®] is available as tablets for oral administration, containing 40mg/12.5mg or 80mg/12.5mg of telmisartan and HCTZ, respectively. In addition, 80mg/25mg of telmisartan and HCTZ, respectively, is foreseen to be launched in selected European countries throughout 2008-2009.
- In patients whose blood pressure is not adequately controlled on Pritor[®]/Kinzalmono[®], the fixed-dose combination of telmisartan and HCTZ, PritorPlus[®]/Kinzalkomb[®], may be used. HCTZ has been shown to have an additive blood pressure lowering effect when co-administered with telmisartan.

Contraindications

- Hypersensitivity to any of the active substances or to any of the excipients of the products
- Second and third trimesters of pregnancy and lactation
- Biliary obstructive disorders
- Severe hepatic impairment
- Additional Contraindications for PritorPlus[®]/Kinzalkomb[®]:
 - Hypersensitivity to other sulphonamide-derived substances
 - Cholestasis
 - Severe renal impairment (creatinine clearance < 30ml/min)
 - Refractory hypokalaemia
 - Hypercalcaemia

Adverse Effects

- Back pain (e.g. sciatica), chest pain, influenza-like illness, symptoms of infection (e.g. urinary tract infection including cystitis), visual disturbance, hyperhidrosis, vertigo, abdominal pain, diarrhoea, dyspepsia, dry mouth, flatulence, stomach discomfort, arthralgia, muscle spasms or pain in extremity, myalgia, tendonitis, anxiety, upper respiratory tract infection including pharyngitis and sinusitis, eczema, erythema, pruritus, syncope, insomnia, depression, vomiting, hypotension (including orthostatic hypotension), bradycardia, tachycardia, abnormal hepatic function, liver disorder, renal impairment including acute renal failure, hyperkalaemia, dyspnoea, anaemia, eosinophilia, thrombocytopenia, asthenia and lack of efficacy. Isolated cases of angioneurotic oedema, urticaria and other related events.
- Additional Adverse Effects for PritorPlus[®]/Kinzalkomb[®]:
 - Erectile dysfunction, pain, hypersensitivity, dizziness, gastritis, hypercholesterolaemia, hypokalaemia, inadequate control of diabetes mellitus hyperuricaemia, osteoarthritis, bronchitis.
- Laboratory findings (Pritor[®]/Kinzalmono[®]):
 - Haemoglobin decrease or blood uric acid increase. In addition, cases with increased blood creatininephosphokinase have been reported.

Use in Pregnancy and Lactation

- The use of Pritor[®]/Kinzalmono[®], PritorPlus[®]/Kinzalkomb[®] is not recommended during the first trimester of pregnancy.
- The use of Pritor[®]/Kinzalmono[®], PritorPlus[®]/Kinzalkomb[®] is contraindicated during the second and third trimester of pregnancy.
- A switch to a suitable alternative treatment should be carried out in advance of a planned pregnancy, if possible.
- If pregnancy is diagnosed, Pritor[®]/ Kinzalmono[®], PritorPlus[®]/Kinzalkomb[®] should be discontinued.
- Pritor[®]/Kinzalmono[®], PritorPlus[®]/Kinzalkomb[®] is contraindicated during lactation.