



Therapy fact sheet

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

General Information

- The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) approved a new indication for Pritor[®]/Kinzalmono[®] in November 2009:
 - The new indication of telmisartan includes the reduction of cardiovascular (CV) morbidity in patients with manifest atherothrombotic cardiovascular disease (history of coronary heart disease, stroke or peripheral arterial disease) or type 2 diabetes mellitus with documented target organ damage.
 - The decision is based on a review of the data submitted, including the landmark ONTARGET[®] trial results.
 - Therefore Pritor[®]/Kinzalmono[®], as the only treatment of its class with this indication, is setting a new standard in hypertension and CVD management.
- The landmark ONTARGET[®] trial demonstrated that Pritor[®]/Kinzalmono[®] provides a high level of cardiovascular prevention with a better efficacy/tolerability ratio than the current gold standard ACE-inhibitor ramipril in a broad range of CV risk patients, making it the first ARB to ever do so.^{1,2}
- ONTARGET[®] showed that Pritor[®]/Kinzalmono[®] has superior tolerability to ramipril and is associated with higher treatment compliance, even in a patient population selected to tolerate ACE inhibitors.
- Pritor[®]/Kinzalmono[®] (telmisartan) has demonstrated strong reduction of both systolic and diastolic blood pressure, maintained over 24 hours.³
- Pritor[®]/Kinzalmono[®] demonstrated broad renoprotective benefits.⁴
- In addition, Pritor[®]/Kinzalmono[®] has been shown to have favorable metabolic effects (improved glycemic and lipid profile) due to its unique Selective PPAR-γ Modulation (SPPARM).^{5,6,7,8,9,10}

Pharmacodynamic Properties

- Pritor[®]/Kinzalmono[®] (telmisartan) is an angiotensin receptor blocker (ARB) with a unique dual mechanism of action offering comprehensive blood pressure control due to its unique pharmacological profile.
- This unique pharmacological profile includes:
 - Selective AT1-blockade
 - Slow rate of dissociation from the receptor
 - Highest volume of distribution of ARBs
 - High lipophilicity
 - High level of tissue penetration



- Unique Selective PPAR-g Modulation (SPPARM) that may translate into a favorable glycemic and lipid metabolism effect.
- Telmisartan selectively binds the AT1-receptor with high affinity, causing inhibition of the action of angiotensin 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-evoked blood pressure increase. This inhibitory effect is maintained over 24 hours and is still measurable for up to 48 hours.
- PritorPlus[®]/Kinzalkomb[®] is a combination of the angiotensin 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.
- For patients whose blood pressure fails to reach target levels with monotherapy, the combination of telmisartan and HCTZ tends to improve blood pressure control better than an increased dose of monotherapy.
- 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 hours 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 metabolized 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 hypertension¹¹
 - Cardiovascular prevention: reduction of cardiovascular morbidity in patients with¹¹
 - Manifest atherothrombotic cardiovascular disease (history of coronary heart disease, stroke or peripheral arterial disease) or
 - Type 2 diabetes mellitus with documented target organ damage

Dosage

- Pritor[®]/Kinzalmono[®] may be used alone as monotherapy. It is available as tablets for oral administration, containing 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 is being launched in selected European countries through 2008-2010.
- 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 hypokalemia
 - Hypercalcemia



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.

The sponsor of the PROTECTION[®] and ONTARGET[®] trial program is Boehringer Ingelheim, the co-funders in selected countries are Bayer Schering Pharma and GlaxoSmithKline.

Bayer Schering Pharma promotes telmisartan under the brand names Pritor[®] / Kinzalmono[®], and PritorPlus[®] / Kinzalkomb[®] (in combination with HCTZ) in markets across Europe.

Telmisartan was discovered and developed by Boehringer Ingelheim. The company markets telmisartan in 84 countries around the world, including the United States, Japan and European countries, under the trademarks Micardis[®] and MicardisPlus[®] (in combination with HCTZ).

References

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