

MICARDIS® (Telmisartan)

Medical media backgrounder

What is MICARDIS® (telmisartan)?

- ▶ MICARDIS® (telmisartan) is an anti-hypertensive medication, belonging to the class of angiotensin II receptor blockers (ARBs). It is effective and well tolerated, providing powerful 24-hour blood pressure reductions with a once-daily dose.



- ▶ MICARDIS® is widely approved for the treatment of hypertension. MICARDIS® is also available in two fixed-dosed combinations with the thiazide diuretic, hydrochlorothiazide (HCTZ):
 - MICARDISPLUS® 80/12.5 - indicated as second-line therapy for essential hypertension not adequately controlled by MICARDIS® monotherapy (EU and US) or HCTZ monotherapy (US)
 - MICARDISPLUS® 80/25 - recently approved by the European Commission; a therapeutic option for patients not controlled with a combination of an ARB and HCTZ 12.5 mg.

What is the mode of action of ARBs?

- ▶ Like angiotensin converting enzyme inhibitors (ACEIs), ARBs target the renin-angiotensin system (RAS), a system that plays an important role in regulating blood pressure.

- ▶ Angiotensin II, one of the hormones in the RAS system, causes the muscles surrounding blood vessels to contract, increasing blood pressure.¹
- ▶ While ACEIs inhibit the conversion of circulating angiotensin I to angiotensin II, ARBs block the action of angiotensin II at the point of its main receptor, the AT₁ receptor. ARBs therefore achieve a more complete blockade of the AT₁ receptor as some angiotensin II can also be produced in the tissues via ACE-independent pathways.²
- ▶ ARBs selectively block AT₁ receptors, which mediate most of the negative cardiovascular effects of the RAS; they do not affect another receptor subtype, the AT₂ receptors. AT₂ receptors are associated with beneficial cardiovascular effects when bound to angiotensin II.³

What makes MICARDIS® unique?

24-hour blood pressure reductions

- ▶ MICARDIS® provides powerful and consistent blood pressure reductions over a full 24-hour period,⁴⁻⁸ particularly in the risky early morning hours when blood pressure surges^{8,9} and the risk of cardiovascular events is at its highest.^{9,10}
- ▶ MICARDIS® achieves superior blood pressure lowering to the ARBs losartan¹¹ and valsartan¹² and has also been shown to achieve blood pressure lowering at least as efficacious as leading medicines in other classes including enalapril, lisinopril, ramipril, amlodipine and atenolol.¹³⁻¹⁷

Protection against cardiovascular events

- ▶ MICARDIS® is the only ARB shown to provide cardio and vascular protection beyond the effects of blood pressure lowering in a broad range of high-risk cardiovascular patients, reducing the risk of cardiovascular death, heart attack, stroke and hospitalisation for congestive heart failure.¹⁸
- ▶ The ONTARGET® Trial showed that MICARDIS® is at least as protective as the current gold standard ramipril (an ACEI) but significantly better tolerated, leading to higher treatment compliance,¹⁸ which is an important consideration for effective life-long treatment for the prevention of cardiovascular events.
- ▶ The TRANSCEND® Trial shows that MICARDIS® reduces the risk of cardiovascular death, heart attack and stroke compared with placebo in high cardiovascular risk patients already receiving the current best standard of care but who are intolerant to ACEIs¹⁹, referring to the same endpoint as the primary endpoint of the landmark HOPE trial, published in 2000).
- ▶ The pre-specified primary endpoint made up of the composite of cardiovascular death, heart attack, stroke and hospitalisation for congestive heart failure was non-significantly reduced by 8% (p=0.223).¹⁹
 - There was no impact on hospitalisation for congestive heart failure; however, all cardiovascular hospitalisations were significantly reduced with MICARDIS® (p=0.025).¹⁹

Unique pharmacological properties

- ▶ MICARDIS® has pharmacological properties that make it unique amongst ARBs:
- It has a longer duration of action than all other members of the ARB class; it takes 24 hours for half the dose of MICARDIS® to be eliminated from the body compared with 6 to 15 hours for other ARBs.^{7,20}

- It also has a higher lipophilicity and volume of distribution compared to other ARBs which means that it extensively penetrates membranes and is available throughout the body, both in the tissues and extracellular spaces.^{21,22}
- It also has selective AT₁ blockade and reported selective PPAR gamma modulation.^{21,22}

Safety and tolerability

- ▶ Clinical trials have shown MICARDIS® to be as well tolerated as placebo,²³ and an evaluation of safety in studies involving over 6,072 patients confirms this.^{24,25}
- ▶ 96.8% of 19,870 patients rated the tolerability of telmisartan as either good or very good in a post-marketing surveillance study.²⁶
- ▶ The excellent tolerability profile of MICARDIS® is supported by its proven safety and efficacy in more vulnerable patients such as the elderly and those with varying degrees of renal impairment, whether mild/moderate, severe or requiring haemodialysis.²⁴⁻²⁷
- ▶ The tolerability profile of MICARDIS® is also particularly beneficial to young patients who may require treatment with an anti-hypertensive for many years.

MICARDIS® clinical trial programme

- ▶ The MICARDIS® clinical trial programme is one of the most far-reaching research programme ever conducted with an ARB, involving over 50,000 patients.
 - The **ONTARGET® Trial Programme** comprises two parallel studies, ONTARGET® and TRANSCEND®, and is the largest ARB cardiovascular trial undertaken. The landmark ONTARGET® Trial Programme was a cardio and vascular protection trial that investigated the benefits of MICARDIS® and ramipril (an ACEI) alone and in

combination in preventing cardiovascular disease and death. Over 31,000 patients were enrolled in the ONTARGET® / TRANSCEND® trials.^{18,19}

- **PROTECTION™** comprises ten trials evaluating the effect of MICARDIS® in heart and kidney protection and the treatment of hypertension in special scenarios. More than 6,500 patients have been enrolled in PROTECTION.²⁸
- **PRoFESS®** was designed to investigate the role of MICARDIS® on top of standard antiplatelet therapy in the prevention of secondary stroke and was the largest such trial ever conducted, including more than 20,000 patients.²⁹

What is cardio and vascular protection?

- ▶ Cardio and vascular protection means protection of the vascular system, the heart and organs against damage that can cause a cardiovascular event including myocardial infarction (MI), stroke, congestive heart failure (CHF) and renal failure.
- ▶ Providing cardio and vascular protection is an important aim of patient management in cardiovascular disease and benefits patients by reducing cardiovascular morbidity and mortality as a result of preventing cardiovascular events, and can also benefit patients by providing protection of other organs, for example the kidneys.



Notes to editors

Telmisartan (Micardis®/Kinzal®/Pritor®)

- ▶ Telmisartan was discovered and developed by Boehringer Ingelheim. Under the trademarks Micardis® and MicardisPlus® (combination with HCTZ), the company markets telmisartan in 84 countries around the world, including the USA, Japan and European countries. Telmisartan is marketed in

cooperation with Astellas Pharma Inc. in Japan, Bayer HealthCare in Europe and GlaxoSmithKline in selected markets. Bayer HealthCare promotes telmisartan under the brand names Kinzalmono®, Kinzalkomb® (combination with HCTZ), and Pritor® and PritorPlus® in markets across Europe. Pritor® and PritorPlus® are also marketed by GlaxoSmithKline in selected markets.

For further information see:

www.news-ontarget.com, www.micardis.com,
www.ontarget-telmisartan.com,
www.ontarget.cardio.on.ca,
www.profess.com

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