

# MICARDIS®

**Telmisartan**

Tablets

## Composition

Each tablet contains 40 or 80 mg telmisartan.

## Excipients:

Povidone (K25)

Meglumine

Sodium hydroxide

Sorbitol (E420)

Magnesium stearate.

## Pharmacological properties :

### **Pharmacodynamic properties**

Pharmacotherapeutic Group: Angiotensin II Antagonists, plain ATC Code: C09CA07.

### Mechanism of action

Telmisartan is an orally active and specific angiotensin II receptor (type AT1) antagonist. Telmisartan displaces angiotensin II with very high affinity from its binding site at the AT1 receptor subtype, which is responsible for the known actions of angiotensin II. Telmisartan does not exhibit any partial agonist activity at the AT1 receptor. Telmisartan selectively binds the AT1 receptor. The binding is long-lasting. Telmisartan does not show affinity for other receptors, including AT2 and other less characterised AT receptors. The functional role of these receptors is not known, nor is the effect of their possible overstimulation by angiotensin II, whose levels are increased by telmisartan. Plasma aldosterone levels are decreased by telmisartan. Telmisartan does not inhibit human plasma renin or block ion channels. 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.

### Clinical efficacy and safety

Treatment of essential hypertension After the first dose of telmisartan, the antihypertensive activity gradually becomes evident within 3 hours. The maximum reduction in blood pressure is generally attained 4 to 8 weeks after the start of treatment and is sustained during long-term therapy.

The antihypertensive effect persists constantly over 24 hours after dosing and includes the last 4 hours before the next dose as shown by ambulatory blood pressure measurements. This is confirmed by trough to peak ratios consistently above 80 %

seen after doses of 40 and 80 mg of telmisartan in placebo controlled clinical studies. There is an apparent trend to a dose relationship to a time to recovery of baseline systolic blood pressure (SBP). In this respect data concerning diastolic blood pressure (DBP) are inconsistent.

In patients with hypertension telmisartan reduces both systolic and diastolic blood pressure without affecting pulse rate. The contribution of the medicinal product's diuretic and natriuretic effect to its hypotensive activity has still to be defined. The antihypertensive efficacy of telmisartan is comparable to that of agents representative of other classes of antihypertensive medicinal products (demonstrated in clinical trials comparing telmisartan to amlodipine, atenolol, enalapril, hydrochlorothiazide, and lisinopril).

Upon abrupt cessation of treatment with telmisartan, blood pressure gradually returns to pre-treatment values over a period of several days without evidence of rebound hypertension.

The incidence of dry cough was significantly lower in patients treated with telmisartan than in those given angiotensin converting enzyme inhibitors in clinical trials directly comparing the two antihypertensive treatments.

Cardiovascular prevention ONTARGET (ONgoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial) compared the effects of telmisartan, ramipril and the combination of telmisartan and ramipril on cardiovascular outcomes in 25620 patients aged 55 years or older with a history of coronary artery disease, stroke, TIA, peripheral arterial disease, or type 2 diabetes mellitus accompanied by evidence of end-organ damage (e.g. retinopathy, left ventricular hypertrophy, macro- or microalbuminuria), which is a population at risk for cardiovascular events.

Patients were randomized to one of the three following treatment groups: telmisartan 80 mg (n = 8542), ramipril 10 mg (n = 8576), or the combination of telmisartan 80 mg plus ramipril 10 mg (n = 8502), and followed for a mean observation time of 4.5 years.

Telmisartan showed a similar effect to ramipril in reducing the primary composite endpoint of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, or hospitalization for congestive heart failure. The incidence of the primary endpoint was similar in the telmisartan (16.7 %) and ramipril (16.5 %) groups. The hazard ratio for telmisartan vs. ramipril was 1.01 (97.5 % CI 0.93 - 1.10, p (non-inferiority) = 0.0019 at a margin of 1.13). The all-cause mortality rate was 11.6 % and 11.8 % among telmisartan and ramipril treated patients, respectively.

Telmisartan was found to be similarly effective to ramipril in the pre-specified secondary endpoint of cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke [0.99 (97.5 % CI 0.90 - 1.08), p (non-inferiority) = 0.0004], the primary endpoint in the reference study HOPE (The **H**eart **O**utcomes **P**revention **E**valuation Study), which had investigated the effect of ramipril vs. placebo.

TRANSCEND randomized ACE-I intolerant patients with otherwise similar inclusion criteria as ONTARGET to telmisartan 80 mg (n=2954) or placebo (n=2972), both given on top of standard care. The mean duration of follow up was 4 years and 8

months. No statistically significant difference in the incidence of the primary composite endpoint (cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, or hospitalization for congestive heart failure) was found [15.7 % in the telmisartan and 17.0 % in the placebo groups with a hazard ratio of 0.92 (95 % CI 0.81 - 1.05,  $p = 0.22$ )]. There was evidence for a benefit of telmisartan compared to placebo in the pre-specified secondary composite endpoint of cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke [0.87 (95 % CI 0.76 - 1.00,  $p = 0.048$ )]. There was no evidence for benefit on cardiovascular mortality (hazard ratio 1.03, 95 % CI 0.85 - 1.24).

Cough and angioedema were less frequently reported in patients treated with telmisartan than in patients treated with ramipril, whereas hypotension was more frequently reported with telmisartan.

Combining telmisartan with ramipril did not add further benefit over ramipril or telmisartan alone. CV mortality and all cause mortality were numerically higher with the combination. In addition, there was a significantly higher incidence of hyperkalaemia, renal failure, hypotension and syncope in the combination arm. Therefore the use of a combination of telmisartan and ramipril is not recommended in this population.

In the "Prevention Regimen For Effectively avoiding Second Strokes" (PROFESS) trial in patients 50 years and older, who recently experienced stroke, an increased incidence of sepsis was noted for telmisartan compared with placebo, 0.70 % vs. 0.49 % [RR 1.43 (95 % confidence interval 1.00 - 2.06)]; the incidence of fatal sepsis cases was increased for patients taking telmisartan (0.33 %) vs. patients taking placebo (0.16 %) [RR 2.07 (95 % confidence interval 1.14 - 3.76)]. The observed increased occurrence rate of sepsis associated with the use of telmisartan may be either a chance finding or related to a mechanism not currently known.

#### Paediatric population

The safety and efficacy of Micardis in children and adolescents aged below 18 years have not been established.

The blood pressure lowering effects of two doses of telmisartan were assessed in 76 hypertensive, largely overweight patients aged 6 to < 18 years (body weight  $\geq 20$  kg and  $\leq 120$  kg, mean 74.6 kg), after taking telmisartan 1 mg/kg ( $n = 29$  treated) or 2 mg/kg ( $n = 31$  treated) over a four-week treatment period. By inclusion the presence of secondary hypertension was not investigated. In some of the investigated patients the doses used were higher than those recommended in the treatment of hypertension in the adult population, reaching a daily dose comparable to 160 mg, which was tested in adults. After adjustment for age group effects mean SBP changes from baseline (primary objective) were -14.5 (1.7) mm Hg in the telmisartan 2 mg/kg group, -9.7 (1.7) mm Hg in the telmisartan 1 mg/kg group, and -6.0 (2.4) in the placebo group. The adjusted DBP changes from baseline were -8.4 (1.5) mm Hg, -4.5 (1.6) mm Hg and -3.5 (2.1) mm Hg respectively. The change was dose dependent. The safety data from this study in patients aged 6 to < 18 years appeared generally similar to that observed in adults. The safety of long term treatment of telmisartan in children and adolescents was not evaluated. An increase in eosinophils reported in this patient population has not been recorded in adults. Its clinical significance and relevance is

unknown. These clinical data do not allow to make conclusions on the efficacy and safety of telmisartan in hypertensive paediatric population.

## **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 (AUC<sub>0-∞</sub>) 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.

### Linearity/non-linearity

The small reduction in AUC is not expected to cause a reduction in the therapeutic efficacy.

There is no linear relationship between doses and plasma levels. C<sub>max</sub> and to a lesser extent AUC increase disproportionately at doses above 40 mg.

### 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 (V<sub>dss</sub>) is approximately 500 l.

### Biotransformation

Telmisartan is metabolised by conjugation to the glucuronide of the parent compound. No pharmacological activity has been shown for the conjugate.

### Elimination

Telmisartan is characterised by biexponential decay pharmacokinetics with a terminal elimination half-life of >20 hours. The maximum plasma concentration (C<sub>max</sub>) 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 (Cl<sub>tot</sub>) is high (approximately 1,000 ml/min) compared with hepatic blood flow (about 1,500 ml/min).

## **Indications**

### Hypertension

Treatment of essential hypertension in adults.

### Cardiovascular prevention

Reduction of cardiovascular morbidity in adults 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

### Contraindications

- Hypersensitivity to the active substance or to any of the excipients
- Second and third trimesters of pregnancy (see sections Special warnings and precautions and Pregnancy, Lactation and Fertility)
- Biliary obstructive disorders
- Severe hepatic impairment

The concomitant use of telmisartan with aliskiren is contraindicated in patients with diabetes mellitus or renal impairment ( $\text{GFR} < 60 \text{ ml/min/1.73 m}^2$ ) (see sections Dosage and administration, Special warnings and precautions and Interactions).

### Side effects

Summary of the safety profile

Serious adverse drug reactions include anaphylactic reaction and angioedema which may occur rarely ( $\geq 1/10,000$  to  $< 1/1,000$ ), and acute renal failure.

The overall incidence of adverse reactions reported with telmisartan was usually comparable to placebo (41.4 % vs 43.9 %) in controlled trials in patients treated for hypertension. The incidence of adverse reactions was not dose related and showed no correlation with gender, age or race of the patients. The safety profile of telmisartan in patients treated for the reduction of cardiovascular morbidity was consistent with that obtained in hypertensive patients.

The adverse reactions listed below have been accumulated from controlled clinical trials in patients treated for hypertension and from post-marketing reports. The listing also takes into account serious adverse reactions and adverse reactions leading to discontinuation reported in three clinical long-term studies including 21642 patients treated with telmisartan for the reduction of cardiovascular morbidity for up to six years.

### Tabulated summary of adverse reactions

Adverse reactions have been ranked under headings of frequency using the following convention:

Very common ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $< 1/10$ ); uncommon ( $\geq 1/1,000$  to  $< 1/100$ ); rare ( $\geq 1/10,000$  to  $< 1/1,000$ ); very rare ( $< 1/10,000$ ),

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Infections and infestations  
Uncommon: Urinary tract infection including cystitis, upper respiratory tract infection including pharyngitis and sinusitis )  
Rare: Sepsis including fatal outcome1

Blood and the lymphatic system disorders  
Uncommon: Anaemia  
Rare: Eosinophilia, thrombocytopenia,

Immune system disorders  
Rare: Anaphylactic reaction, hypersensitivity

Metabolism and nutrition disorders

Uncommon: Hyperkalaemia  
Rare: Hypoglycaemia (in diabetic patients)

Psychiatric disorders  
Uncommon: Insomnia, depression  
Rare: Anxiety

Nervous system disorders  
Uncommon: Syncope  
Rare: Somnolence

Eye disorders:  
Rare: Visual disturbance

Ear and labyrinth disorders  
Uncommon: Vertigo

Cardiac disorders  
Uncommon: Bradycardia  
Rare: Tachycardia

Vascular disorders  
Uncommon: Hypotension2, orthostatic hypotension

Respiratory, thoracic and mediastinal disorders  
Uncommon: Very rare: Dyspnoea, cough Interstitial lung disease4

Gastrointestinal disorders

Uncommon: Abdominal pain, diarrhoea, dyspepsia, flatulence, vomiting

Rare: Dry mouth, stomach discomfort,

Hepato-biliary disorders

Rare: Hepatic function abnormal/liver disorder<sup>3</sup>

Skin and subcutaneous tissue disorders

Uncommon: Pruritus, hyperhidrosis, rash

Rare: Angioedema (also with fatal outcome), eczema, erythema, ,

urticaria, drug eruption, toxic skin eruption

Musculoskeletal

and connective tissue disorders Back pain (e.g. sciatica), muscle spasms, myalgia

Uncommon: Arthralgia, pain in extremity, tendon pain (tendinitis like symptoms)

Renal and

urinary disorders Uncommon: Renal impairment including acute renal failure

General disorders and

administration site conditions Uncommon: Chest pain, asthenia (weakness) Influenza-like illness

Investigations

Uncommon: Blood creatinine increased Haemoglobin decreased, Rare: blood uric acid increased, hepatic

enzyme  
increased,  
blood creatine  
phosphokinase  
increased

1,2,3,4: for further descriptions, please see sub-section “*Description of selected adverse reactions*”

### Description of selected adverse reactions

#### Sepsis

In the PROFESS trial, an increased incidence of sepsis was observed with telmisartan compared with placebo. The event may be a chance finding or related to a mechanism currently not known (see also section Pharmacodynamic properties).

#### Hypotension

This adverse reaction was reported as common in patients with controlled blood pressure who were treated with telmisartan for the reduction of cardiovascular morbidity on top of standard care.

#### Hepatic function abnormal / liver disorder

Most cases of hepatic function abnormal / liver disorder from post-marketing experience occurred in Japanese patients. Japanese patients are more likely to experience these adverse reactions.

#### Interstitial lung disease

Cases of interstitial lung disease have been reported from post-marketing experience in temporal association with the intake of telmisartan. However, a causal relationship has not been established.

### **Special warnings and precautions**

#### Pregnancy

Angiotensin II receptor antagonists should not be initiated during pregnancy. 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 (see sections Contraindications and Pregnancy, Lactation and Fertility).

#### Hepatic impairment

Micardis is not to be given to patients with cholestasis, biliary obstructive disorders or severe hepatic impairment (see section Contraindications) since telmisartan is mostly eliminated with the bile. These patients can be expected to have reduced hepatic clearance for telmisartan. Micardis 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.

#### Renal impairment and kidney transplantation

When Micardis is used in patients with impaired renal function, periodic monitoring of potassium and creatinine serum levels is recommended. There is no experience regarding the administration of Micardis in patients with recent kidney transplantation.

#### Intravascular hypovolaemia

Symptomatic hypotension, especially after the first dose of Micardis, may occur in patients who are volume and/or sodium depleted by vigorous diuretic therapy, dietary salt restriction, diarrhoea, or vomiting. Such conditions should be corrected before the administration of Micardis. Volume and/or sodium depletion should be corrected prior to administration of Micardis.

#### Dual blockade of the renin-angiotensin-aldosterone system

The use of telmisartan in combination with aliskiren is contraindicated in patients with diabetes mellitus or renal impairment ( $\text{GFR} < 60 \text{ ml/min/1.73 m}^2$ ) (see section Contraindications).

As a consequence of inhibiting the renin-angiotensin-aldosterone system, hypotension, syncope, hyperkalaemia and changes in renal function (including acute renal failure) have been reported in susceptible individuals, especially if combining medicinal products that affect this system. Dual blockade of the renin-angiotensin-aldosterone system (e.g. by administering telmisartan with other blockers of the renin-angiotensin-aldosterone system) is therefore not recommended. Close monitoring of renal function is advisable if co-administration is considered necessary.

#### Other conditions with stimulation of the renin-angiotensin-aldosterone system

In patients whose vascular tone and renal function depend predominantly on the activity of the renin-angiotensin-aldosterone system (e.g. patients with severe congestive heart failure or underlying renal disease, including renal artery stenosis), treatment with medicinal products that affect this system such as telmisartan has been associated with acute hypotension, hyperazotaemia, oliguria, or rarely acute renal failure (see section Side effects).

#### Primary aldosteronism

Patients with primary aldosteronism generally will not respond to antihypertensive medicinal products acting through inhibition of the renin-angiotensin system. Therefore, the use of telmisartan is not recommended.

#### Aortic and mitral valve stenosis, obstructive hypertrophic cardiomyopathy

As with other vasodilators, special caution is indicated in patients suffering from aortic or mitral stenosis, or obstructive hypertrophic cardiomyopathy.

#### Diabetic patients treated with insulin or antidiabetics

In these patients hypoglycaemia may occur under telmisartan treatment. Therefore, in these patients an appropriate blood glucose monitoring should be considered; a dose adjustment of insulin or antidiabetics may be required, when indicated.

#### Hyperkalaemia

The use of medicinal products that affect the renin-angiotensin-aldosterone system may cause hyperkalaemia.

In the elderly, in patients with renal insufficiency, in diabetic patients, in patients concomitantly treated with other medicinal products that may increase potassium levels, and/or in patients with intercurrent events, hyperkalaemia may be fatal.

Before considering the concomitant use of medicinal products that affect the renin-angiotensin-aldosterone system, the benefit risk ratio should be evaluated.

The main risk factors for hyperkalaemia to be considered are:

- Diabetes mellitus, renal impairment, age (>70 years)
- Combination with one or more other medicinal products that affect the renin-angiotensin-aldosterone system and/or potassium supplements. Medicinal products or therapeutic classes of medicinal products that may provoke hyperkalaemia are 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, immunosuppressives (cyclosporin or tacrolimus), and trimethoprim.
- Intercurrent events, in particular dehydration, acute cardiac decompensation, metabolic acidosis, worsening of renal function, sudden worsening of the renal condition (e.g. infectious diseases), cellular lysis (e.g. acute limb ischemia, rhabdomyolysis, extend trauma).

Close monitoring of serum potassium in at risk patients is recommended (see section Interactions).

#### Sorbitol

This medicinal product contains sorbitol (E420). Patients with rare hereditary problems of fructose intolerance should not take Micardis.

#### Ethnic differences

As observed for angiotensin converting enzyme inhibitors, telmisartan and the other angiotensin II receptor antagonists are apparently less effective in lowering blood pressure in black people than in non-blacks, possibly because of higher prevalence of low-renin states in the black hypertensive population.

## Other

As with any antihypertensive agent, excessive reduction of blood pressure in patients with ischaemic cardiopathy or ischaemic cardiovascular disease could result in a myocardial infarction or stroke.

## **Interactions**

*Contraindicated (see section Contraindications)*

### Dual blockade of the renin-angiotensin-aldosterone system (RAAS)

The combination of telmisartan with aliskiren is contraindicated in patients with diabetes mellitus or renal impairment ( $\text{GFR} < 60 \text{ ml/min/1.73 m}^2$ ) and is not recommended in other patients (see sections Contraindications and Special warnings and precautions).

### Digoxin

When telmisartan was co-administered with digoxin, median increases in digoxin peak plasma concentration (49%) and in trough concentration (20%) were observed. When initiating, adjusting, and discontinuing telmisartan, monitor digoxin levels in order to maintain levels within the therapeutic range.

As with other medicinal products acting on the renin-angiotensin-aldosterone system, telmisartan may provoke hyperkalaemia (see section Special warnings and precautions). 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 antiinflammatory medicinal products (NSAIDs, including selective COX-2 inhibitors), heparin, immunosuppressives (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. spironolactone, 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 hypokalemia 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.

In one study the co-administration of telmisartan and ramipril led to an increase of up to 2.5 fold in the AUC<sub>0-24</sub> and C<sub>max</sub> of ramipril and ramiprilat. The clinical relevance of this observation is not known.

#### Diuretics (thiazide or loop diuretics)

Prior treatment with high dose diuretics such as furosemide (loop diuretic) and hydrochlorothiazide (thiazide diuretic) may result in volume depletion and in a risk of hypotension when initiating therapy with telmisartan.

*To be taken into account with concomitant use*

#### 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 antihypertensives including telmisartan: Baclofen, amifostine. Furthermore, orthostatic hypotension may be aggravated by alcohol, barbiturates, narcotics or antidepressants.

Corticosteroids (systemic route) Reduction of the antihypertensive effect.

### **Pregnancy, Lactation and Fertility**

## Pregnancy

The use of angiotensin II receptor antagonists is not recommended during the first trimester of pregnancy (see section Special warnings and precautions). The use of angiotensin II receptor antagonists is contraindicated during the second and third trimesters of pregnancy (see sections Contraindications and Special warnings and precautions).

There are no adequate data from the use of Micardis in pregnant women. Studies in animals have shown reproductive toxicity.

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 (see sections Contraindications and Special warnings and precautions).

## Lactation

Because no information is available regarding the use of Micardis during breast-feeding, Micardis is not recommended and alternative treatments with better established safety profiles during breast-feeding are preferable, especially while nursing a newborn or preterm infant.

## Fertility

In preclinical studies, no effects of Micardis on male and female fertility were observed.

## **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 Micardis.

## **Dosage and administration**

### Posology

### 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. When considering raising the dose, it must be borne in mind that the maximum antihypertensive effect is generally attained four to eight weeks after the start of treatment (see section Pharmacodynamic properties).

### 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 for the reduction of cardiovascular morbidity, close monitoring of blood pressure is recommended, and if appropriate adjustment of medications that lower blood pressure may be necessary.

### *Special populations*

#### Patients with renal impairment

Limited experience is available in patients with severe renal impairment or haemodialysis. A lower starting dose of 20 mg is recommended in these patients (see section Special warnings and precautions). No posology adjustment is required for patients with mild to moderate renal impairment.

Concomitant use of telmisartan with aliskiren is contraindicated in patients with renal impairment (GFR < 60 ml/min/1.73 m<sup>2</sup>) (see section Contraindications).

#### Patients with hepatic impairment

Micardis is contraindicated in patients with severe hepatic impairment (see section Contraindications).

In patients with mild to moderate hepatic impairment, the posology should not exceed 40 mg once daily (see section Special warnings and precautions).

#### Elderly patients

No dose adjustment is necessary for elderly patients.

### ***Paediatric population***

The safety and efficacy of Micardis in children and adolescents aged below 18 years have not been established.

Currently available data are described in section Pharmacodynamic properties and Pharmacokinetic properties but no recommendation on a posology can be made.

### 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 blister due to the hygroscopic property of the tablets. Tablets should be taken out of the blister shortly before administration.

### **Overdose**

There is limited information available with regard to overdose in humans.

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.

### **Storage instructions**

Store in the original package in order to protect from moisture.

Store below 30 C

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

### **Availability**

Tablets of 40 and 80 mg

Aluminium/aluminium blisters (PA/Al/PVC/Al or PA/PA/Al/PVC/Al). One blister contains 7 or 10 tablets.

Pack sizes: Blister with 14, 28, 56, 84, or 98 tablets or perforated unit dose blisters with 28, 30 or 90 tablets; multipacks containing 360 (4 packs of 90) tablets

Not all pack sizes may be marketed.

**Date of package insert:** (SPC) May 2013

**Manufactured by  
Boehringer Ingelheim Pharma GmbH & Co.  
KG  
for Boehringer Ingelheim International  
GmbH  
Ingelheim am Rhein,  
Germany**

**This is a medicament**

Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.

Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament

The doctors and the pharmacist are experts in medicine, its benefits and risks.

Do not by yourself interrupt the period of treatment prescribed for you.

Do not repeat the same prescription without consulting your doctor.

**Keep medicament out of reach of children!**

Council of Arab Health Ministers - Union of Arab Pharmacists