SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

ADCO TELMISARTAN 20, tablets
ADCO TELMISARTAN 40, tablets
ADCO TELMISARTAN 80, tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ADCO TELMISARTAN 20: Each tablet contains 20 mg telmisartan.
Contains sugar (mannitol (E 421)): 81,9 mg per tablet.

ADCO TELMISARTAN 40: Each tablet contains 40 mg telmisartan.
Contains sugar (mannitol (E 421)): 163,8 mg per tablet.

ADCO TELMISARTAN 80: Each tablet contains 80 mg telmisartan.
Contains sugar (mannitol (E 421)): 327,7 mg per tablet.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.
ADCO TELMISARTAN 20:
White, round, bevelled tablets with “LC” embossed on one side, 7 mm in diameter.
ADCO TELMISARTAN 40:
White oblong tablets with “LC” embossed on one side, approximately 12,0 x 5,9 mm in size.
ADCO TELMISARTAN 80:
White oblong tablets with “LC” embossed on one side, approximately 16,0 x 8,0 mm in size.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of mild to moderate hypertension, either alone or in combination with hydrochlorothiazide.
Reduction of cardiovascular morbidity and mortality in patients 55 years or older at high risk of cardiovascular disease; the benefit of treatment is evident after at least 6 months of continued treatment.

4.2 Posology and method of administration

Adults

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 ADCO TELMISARTAN can be increased to a maximum of 80 mg once daily. Alternatively, ADCO TELMISARTAN may be used in combination with thiazide-type diuretics such as hydrochlorothiazide 12,5 mg which has been shown to have an additive blood pressure lowering effect with ADCO 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.

Reduction of cardiovascular morbidity and mortality

The recommended dose is 80 mg once daily. It is not known whether doses lower than 80 mg of ADCO TELMISARTAN are effective in reducing cardiovascular morbidity and mortality.
When initiating ADCO TELMISARTAN therapy for the reduction of cardiovascular morbidity and mortality, monitoring of blood pressure is recommended and, if appropriate, adjustment of medications that lower blood pressure may be necessary.
The benefit of treatment is evident only after 6 months of continued treatment.

Special populations

Renal impairment

No dosage adjustment is required for patients with mild to moderate renal impairment. Limited experience is available in patients with severe renal impairment or haemodialysis (see section 4.3).

Hepatic impairment

In patients with mild to moderate hepatic impairment the dosage should not exceed 40 mg once daily.

Elderly

No dosing adjustment is necessary for elderly patients.

Paediatric population

Children and adolescents up to 18 years of age

ADCO TELMISARTAN is not recommended for use in children below 18 years due to a lack of data on safety and efficacy.

Method of administration

For oral use.

4.3 Contraindications

- Hypersensitivity to telmisartan or any of the inactive ingredients of ADCO TELMISARTAN (see section 2 and 6.1).
- A history of angioedema related to previous therapy with angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs): These patients must never again be given these medicines.
- Hereditary or idiopathic angioedema.
- Hypertrophic obstructive cardiomyopathy (HOCM).
- Severe renal function impairment (creatinine clearance less than 30 ml/min).
- Bilateral renal artery stenosis.
- Renal artery stenosis in patients with a single kidney.
- Aortic stenosis.
- Biliary obstructive disorders.
- Severe hepatic impairment.
- Concomitant therapy with potassium sparing diuretics such as spironolactone, triamterene, amiloride (see section 4.5).
- Porphyria.
- Lithium therapy: Concomitant administration with ADCO TELMISARTAN may lead to toxic blood concentrations of lithium (see section 4.5).
- Pregnancy and lactation (see section 4.6).
- The concomitant use of ADCO TELMISARTAN with renin inhibitors, such as aliskiren-containing products is contraindicated (see section 4.4 and 4.5).
- Concomitant use of fluoroquinolones with ACE inhibitors/Angiotensin receptor blockers is contraindicated in patients with moderate to severe renal impairment (Creatinine Clearance ≤ 30ml/min) and in elderly patients.

4.4 Special warnings and precautions for use

ADCO TELMISARTAN should not be initiated during pregnancy.

Should a woman become pregnant while receiving ADCO TELMISARTAN, the treatment should be stopped promptly and switched to a different class of antihypertensive medicine. (see section 4.3 and 4.6).

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 medicines that affect the renin-angiotensin-aldosterone system, such as ADCO TELMISARTAN (see section 4.3).

Renal impairment and kidney transplantation
When ADCO TELMISARTAN 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 ADCO TELMISARTAN in patients with recent kidney transplantation.

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

Dual blockade of the renin-angiotensin-aldosterone system (RAAS)
There is evidence that the concomitant use of ACE inhibitors, angiotensin II receptor blockers (ARBs) or aliskiren may increase the risk of hypotension, hyperkalaemia and decreases renal function (including acute renal failure). Dual blockade of RAAS through the combined use of ADCO TELMISARTAN and aliskiren is therefore contraindicated (see section 4.3). ADCO TELMISARTAN should not be used concomitantly with renin inhibitors, such as aliskiren (see section 4.3).

Other conditions with stimulation of the renin-angiotensin-aldosterone system (RAAS)
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 other medicines that affect this system, such as telmisartan, as in ADCO TELMISARTAN, has been associated with acute hypotension, uraemia, oliguria, or rarely acute renal failure.

Fluoroquinolones and ACE inhibitors/Angiotensin receptor blockers
Concomitant use of fluoroquinolones and ACE inhibitors/Angiotensin receptor blockers may precipitate acute kidney injury in patients, especially those with moderate to severe renal impairment and elderly patients (see section 4.3). Renal function should be assessed before initiating treatment and monitored during treatment with fluoroquinolones or ACE inhibitors / angiotensin receptor blockers whether used separately and/or concomitantly.

Primary aldosteronism
Patients with primary aldosteronism generally will not respond to antihypertensive medicines

acting through inhibition of the renin-angiotensin system. Therefore, the use of ADCO TELMISARTAN is not recommended.

Aortic and mitral valve stenosis, obstructive hypertrophic cardiomyopathy
ADCO TELMISARTAN is contraindicated in patients suffering from aortic or mitral stenosis, or obstructive hypertrophic cardiomyopathy (see section 4.3).

Hyperkalaemia
The use of medicines that affect the renin-angiotensin-aldosterone system may cause hyperkalaemia. In the elderly, in patients with renal insufficiency and/or heart failure, in diabetic patients, in patients concomitantly treated with other medicines that may increase potassium levels, and/or in patients with intercurrent events, hyperkalaemia may be fatal. Monitoring of serum potassium in patient at risk is recommended.
Concomitant use of ADCO TELMISARTAN with potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium or other medicines that may increase the potassium level (heparin, etc.) may lead to an increase in serum potassium (see section 4.3 and 4.5).

Hepatic impairment
ADCO TELMISARTAN should be used with caution in patients with biliary obstructive disorder or mild to moderate hepatic impairment, because ADCO TELMISARTAN is mostly eliminated in the bile. ADCO TELMISARTAN is contraindicated in patients with severe liver insufficiency (see section 4.3).

Diabetes mellitus
In diabetic patients with an additional cardiovascular risk, i.e. patients with diabetes mellitus and co-existent coronary artery disease (CAD), the risk of fatal myocardial infarction and unexpected cardiovascular death may be increased when treated with blood pressure lowering agents such as ARBs or ACE inhibitors. In patients with diabetes mellitus, CAD may be asymptomatic and therefore undiagnosed. Patients with diabetes mellitus should undergo appropriate diagnostic evaluation, e.g. exercise stress testing, to detect and to treat CAD accordingly before initiating treatment with ADCO TELMISARTAN.

Diabetic patients treated with insulin or antidiabetics
In these patients, hypoglycaemia may occur under telmisartan, as in ADCO TELMISARTAN, treatment. Therefore, in these patients an appropriate blood glucose monitoring should be considered.

Ethnic differences

ADCO TELMISARTAN is 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

Excessive reduction of blood pressure in patients with ischaemic cardiopathy or ischaemic cardiovascular disease could result in a myocardial infarction or stroke.

Excipients

Sodium: This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicines and other forms of interaction

Dual blockade of the RAAS with ARBs, ACE inhibitors, or renin inhibitors, such as aliskiren

Clinical trial data has shown that dual blockade of the renin-angiotensin-aldosterone-system (RAAS) through the combined use of ACE inhibitors, angiotensin II receptor blockers (as contained in ADCO TELMISARTAN) or renin inhibitors, such as aliskiren is associated with a higher frequency of adverse events such as hypotension, hyperkalaemia and decreased renal function (see section 4.3 and 4.4).

Other antihypertensive medicines

The blood pressure lowering effect of other antihypertensive medicines can be increased by concomitant use of ADCO TELMISARTAN. Baclofen and amifostine may potentiate the hypotensive effects of ADCO TELMISARTAN. Furthermore, orthostatic hypotension may be aggravated by alcohol, barbiturates, narcotics or antidepressants.

Digoxin

For digoxin, a 20 % increase in median plasma digoxin trough concentration has been observed. Monitoring of plasma digoxin levels should be considered.

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 antagonists, including telmisartan, as in ADCO TELMISARTAN (see section 4.3).

Potassium-sparing diuretics or potassium supplements

Angiotensin II receptor antagonists such as ADCO TELMISARTAN attenuate diuretic-induced potassium loss. Potassium-sparing diuretics, such as spironolactone, eplerenone, triamterene or amiloride, potassium supplements or potassium-containing salt substitutes may lead to a significant increase in serum potassium (see section 4.3 and 4.4).

Nonsteroidal anti-inflammatory drugs (NSAIDs)
Concomitant treatment with NSAIDs (including aspirin at anti-inflammatory dosage regimens, COX-2 inhibitors and non-selective NSAIDs) may increase the risk for acute renal impairment in patients who are dehydrated. Patients taking NSAIDs concomitantly with ADCO TELMISARTAN should be adequately hydrated and renal function should be monitored.
A reduced effect of antihypertensive medicines like ADCO TELMISARTAN by inhibition of vasodilating prostaglandins has been reported during combined treatment with NSAIDs.

Diuretic medicines (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 treatment with ADCO TELMISARTAN.

Corticosteroids (systemic route)
Concomitant use may cause a reduction of the antihypertensive effect.

Fluoroquinolones and ACE inhibitors/Angiotensin receptor blockers
Concomitant use of fluoroquinolones and ACE inhibitors/Angiotensin receptor blockers may precipitate acute kidney injury. The mechanism of the possible interaction between the different classes of medicines, over and above different mechanisms of kidney damage, is unknown (see section 4.3).

Hyperkalaemia
As with other medicinal products acting on RAAS, telmisartan, as in ADCO TELMISARTAN, may provoke hyperkalaemia (see section 4.4). The risk may increase in case of treatment combination with other medicinal products that may also provoke hyperkalaemia (salt substitutes containing potassium, ACE inhibitors, angiotensin II receptor antagonists, 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 abovementioned treatment combinations. The risk is particularly high 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.
Combination treatment with potassium-sparing diuretics is contraindicated (see section 4.3).

General

Concomitant use of ADCO TELMISARTAN did not result in a clinically significant interaction with warfarin, hydrochlorothiazide, glibenclamide, paracetamol, ibuprofen, simvastatin or amlodipine.

4.6 Fertility, pregnancy and lactation

Pregnancy and lactation

ADCO TELMISARTAN is contraindicated during pregnancy and lactation (safety in pregnancy and lactation has not been established). See section 4.3 and 4.4.

When pregnancy is planned or confirmed ADCO TELMISARTAN should be discontinued.

Medicines affecting the renin-angiotensin system, such as ADCO TELMISARTAN, can cause embryonal toxicity, foetal and neonatal morbidity and mortality when administered to pregnant women.

Women of childbearing age should use adequate contraception.

Since it is not known whether telmisartan is excreted in human milk, ADCO TELMISARTAN is contraindicated during breastfeeding (see section 4.3 and 4.4).

Fertility

No effects of telmisartan, as in ADCO TELMISARTAN, on male and female fertility were observed in reported studies.

4.7 Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed. However, when driving vehicles or operating machinery it must be borne in mind that dizziness or drowsiness may occasionally occur when taking ADCO TELMISARTAN.

4.8 Undesirable effects

Tabulated list of adverse reactions

SYSTEM ORGAN CLASS	**FREQUENCY**	**ADVERSE REACTIONS**
Infections and infestations	Less frequent	Urinary tract infections (including cystitis), upper respiratory tract infections including pharyngitis and sinusitis, sepsis (including fatal outcome)
Blood and lymphatic system disorders	Less frequent	Anaemia, thrombocytopenia, eosinophilia
Immune system disorders	Less frequent	Hypersensitivity, angioedema (with fatal outcome), anaphylactic reaction

Metabolism and nutrition disorders	Less frequent	Hyperkalaemia, hypoglycaemia (in diabetic patients)
Psychiatric disorders	Less frequent	Anxiety, depression, insomnia
Nervous system disorders	Less frequent	Syncope/fainting, somnolence
Eye disorders	Less frequent	Abnormal vision
Ear and labyrinth disorders	Less frequent	Vertigo
Cardiac disorders	Less frequent	Bradycardia, tachycardia
Vascular disorders	Less frequent	Hypotension, orthostatic hypotension
Respiratory, thoracic and mediastinal disorders	Less frequent	Dyspnoea, cough, interstitial lung disease
Gastrointestinal disorders	Less frequent	Abdominal pain, diarrhoea, dyspepsia, flatulence, vomiting, dry mouth, stomach upset, dysgeusia
Hepato-biliary disorders	Less frequent	Abnormal hepatic function, liver disorder
Skin and subcutaneous tissue disorders	Less frequent	Hyperhidrosis, erythema, pruritus, eczema, rash, drug eruption, toxic skin eruption, urticaria
Musculoskeletal and connective tissue disorders	Less frequent	Arthralgia, myalgia, back pain (e.g. sciatica), muscle cramps, pain in extremity, tendon pain (tendinitis-like symptoms)
Renal and urinary disorders	Less frequent	Renal impairment, including acute renal failure
General disorders and administration site conditions	Less frequent	Chest pain, influenza-like illness, asthenia
Investigations	Less frequent	Haemoglobin decreased, blood uric acid increased, blood creatinine increased, hepatic enzymes increased, blood creatine phosphokinase increased

Description of selected adverse reactions

Sepsis

An increased incidence of sepsis has been reported with telmisartan, as in ADCO TELMISARTAN, compared with placebo.

Hypotension

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

Abnormal hepatic function/liver disorder

Most cases of abnormal hepatic function/liver disorder 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 in temporal association with the intake of telmisartan, as in ADCO TELMISARTAN. However, a causal relationship has not been established.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the **"6.04 Adverse Drug Reactions Reporting Form"**, found online under SAHPRA's publications:
https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Symptoms

The most prominent manifestations of telmisartan, as in ADCO TELMISARTAN, overdose were hypotension and tachycardia; bradycardia also occurred.

Treatment

Telmisartan, as in ADCO TELMISARTAN, is not removed by haemodialysis. The patient should be closely monitored, and the treatment should be symptomatic and supportive. Activated charcoal may be useful in the treatment of overdosage. Serum electrolytes and creatinine should be monitored frequently. If symptomatic hypotension occurs, the patient should be placed in a supine position, with salt and volume replacement given quickly.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 7.1.3 Vascular medicines – other hypotensives

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

Telmisartan is a specific angiotensin II receptor (type AT1) antagonist. Telmisartan displaces angiotensin II with 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 at the AT1 receptor. The binding is long-lasting. Telmisartan does not show affinity for other receptors, including AT2 and other less characterised AT receptors. Plasma aldosterone levels are decreased by telmisartan. Telmisartan does not inhibit human plasma renin or block ion channels.

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 weeks after the start of treatment and is sustained during long-term therapy.

The antihypertensive effect persists over 24 hours after dosing. There is an apparent trend to a dose relationship with regard to a time to recovery of baseline systolic blood pressure (SBP). In this respect data concerning diastolic blood pressure (DBP) are inconsistent.

5.2 Pharmacokinetic properties

Telmisartan is well absorbed from the gastrointestinal tract. The mean oral bioavailability is about 50 %. Peak plasma concentrations of telmisartan are reached about 0,5 to 1 hour after an oral dose. Telmisartan is highly bound to plasma proteins (> 99,5 %). Telmisartan is metabolised by conjugation to the glucuronide, which is inactive. The terminal elimination half-life is about 24 hours. It is excreted almost entirely in the faeces via bile, mainly as unchanged compound.

Gender differences:

C_{max} and area under the curve (AUC) were approximately
3- and 2-fold higher, respectively, in females compared to males.

Elderly patients

No difference in the pharmacokinetics of telmisartan was reported between younger and elderly patients.

Patients with renal impairment

Patients with renal insufficiency undergoing dialysis had lower telmisartan plasma concentrations. Telmisartan is highly bound to plasma proteins and cannot be removed by dialysis. The elimination half-life is not changed in these patients.

Patients with hepatic impairment

Absolute bioavailability was increased up to nearly 100 % in patients with hepatic impairment.
The elimination half-life is not changed in these patients.

5.3 Preclinical safety data

No information available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium hydroxide
Povidone (K 25)
Meglumine
Mannitol (E 421)
Magnesium stearate
Crospovidone

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 °C.
Keep the blister strips in the outer carton until required for use.

6.5 Nature and contents of container

ADCO TELMISARTAN tablets are packaged in silver aluminium/aluminium blister packs.
Blister packs of 14, 28, 30, 56, 84, 90, or 98 tablets are available.
Not all pack sizes may be marketed.
The blister strips are packed in a cardboard outer carton.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited
1 New Road
Erand Gardens

Midrand, 1685

Customer Care: 0860 ADCOCK / 232625

8. REGISTRATION NUMBERS

ADCO TELMISARTAN 20: 46/7.1.3/0247

ADCO TELMISARTAN 40: 46/7.1.3/0248

ADCO TELMISARTAN 80: 46/7.1.3/0249

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: 11 June 2018

10. DATE OF REVISION OF THE TEXT

17 April 2023