TEGAR CD

SCHEDULING STATUS S4

1. NAME OF THE MEDICINE

TEGAR CD 40/12.5 mg tablets
TEGAR CD 80/12.5 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

TEGAR CD 40/12.5 mg: Each double-layered tablet contains telmisartan 40 mg and hydrochlorothiazide 12.5 mg
TEGAR CD 80/12.5 mg: Each double-layered tablet contains telmisartan 80 mg and hydrochlorothiazide 12.5 mg
Excipient with known effect: Each tablet contains sugar alcohol (maltitol) 80.00 mg and sugar (lactose monohydrate 49.84 mg) per tablet (see section 4.4).
TEGAR CD 80/12.5 mg contains sugar alcohol (maltitol) 237.70 mg and sugar (lactose monohydrate 49.84 mg) per tablet (see section 4.4).
Essentially 'sodium free'.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

TEGAR CD 40/12.5 mg: Pink, oblong, biconvex film coated tablets with one score line and embossed '40/12.5' on one side and '2' on the other side.
TEGAR CD 80/12.5 mg: Dark pink, oblong, biconvex film coated tablets with one score line and embossed '80/12.5' on one side and '2' on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

TEGAR CD is indicated for the treatment of mild to moderate hypertension in patients whose blood pressure has been stabilised at the same dosage of the individual components given together.

4.2 Posology and method of administration

Posology

Adults

TEGAR CD should be taken once daily, with or without food. Two dosage strengths are available: 40/12.5 mg and 80/12.5 mg. The patient should be stabilised at the relevant dosage of the individual components given together, and then be changed to the appropriate combination tablet. When considering changing the patient's therapy with TEGAR CD it should be borne in mind that treatment needs to be continued for at least 2 weeks, at which time the effect is obtained. When necessary, TEGAR CD may be administered with another antihypertensive medicine.

Special populations

Renal impairment

Due to the hydrochlorothiazide component, TEGAR CD is not recommended for patients with severe renal dysfunction (creatinine clearance < 30 mL/min). Loop diuretics are preferred to thiazides in this population. Experience in patients with mild to moderate renal impairment is modest but it has not suggested adverse renal effects and dose adjustment is not considered necessary. Periodic monitoring of renal function is advised.

Hepatic impairment

In patients with mild Child-Pugh Class A to moderate Child-Pugh Class B hepatic impairment, the dosage should not exceed TEGAR CD 40/12.5 mg once daily. TEGAR CD is not indicated in patients with severe hepatic impairment. Therefore, as TEGAR CD should be used with caution in patients with hepatic impairment.

Elderly

No dosage adjustment is necessary.

Paediatric population

Safety and efficacy in children up to 18 years:
There are no data to date and efficacy of TEGAR CD in children and adolescents up to 18 years.

Method of administration

TEGAR CD tablets are for oral use and administration and should be taken with liquid, with or without food.

4.3 Contraindications

TEGAR CD is contraindicated in:
- patients with hypersensitivity to telmisartan, hydrochlorothiazide or other sulphonamide-derived medicines or to any of the excipients of TEGAR CD (see section 6.1)
- patients with a history of anuria and/or current bowel cold carcinosis and/or squamous cell carcinoma of the skin and lip
- severe renal function impairment (creatinine clearance < 30 mL/min) or anuria
- severe hepatic impairment (see section 4.2 and 4.4)
- refractory hypokalaemia, hypokalaemia, hypercalcaemia and symptomatic hyperuricaemia or gout
- bilateral renal artery stenosis or renal artery stenosis in the presence of a single kidney
- aortic valve stenosis and/or hypertrophic obstructive cardiomyopathy (HOCM) (see section 4.4)
- angioedema on previous exposure to angiotensin receptor blockers (ARBs) or angiotensin-converting enzyme (ACE) inhibitors. Cases of angioedema have been reported with these medicines
- hereditary or idiopathic angioedema
- biliary obstructive disorders
- concomitant therapy with potassium-sparing diuretics such as amiloride, spironolactone, triamterene Addison's disease
- porphyria
- lithium toxicity and history of lithium intolerance (see section 4.5)
- concomitant use of Sacubitril/Valsartan with ACE inhibitors/angiotensin receptor blockers is contraindicated in patients with moderate to severe renal function impairment (creatinine clearance < 30 mL/min) and in elderly patients
- concomitant use with aliskiren-containing medicines
- pregnancy and lactation (see sections 4.4 and 4.6).

4.4 Special warnings and precautions for use

Should a woman become pregnant while taking TEGAR CD, the treatment must be stopped promptly and changed to a different medicine (see section 4.3). If a woman is contemplating pregnancy, a different class of medicine should be used (see section 4.6).

When pregnancy is diagnosed, treatment with TEGAR CD should be stopped immediately and, if appropriate, alternative therapy should be started (see section 4.3).

Neuromuscular hypersensitivity

There is an increased risk of severe hypertension and renal insufficiency where patients with bilateral artery stenosis or renal artery stenosis in a single functioning kidney is treated with medicines that affect the renin-angiotensin-aldosterone system (RAAS) (see section 4.3).

Renal artery stenosis

TEGAR CD may increase serum creatinine and blood urea in patients with bilateral renal artery stenosis or renal artery stenosis in a single functioning kidney. Such changes in renal function may be reversible on withdrawal (see section 4.3).

Renal impairment and kidney transplantation

Patients with renal vascular conditions (diseases – 30 mL/min) should not take TEGAR CD (see section 4.3). Diarrhea, associated with hydrochlorothiazide, an TEGAR CD, may occur in patients with renal impairment. Use periodic monitoring of potassium, creatinine and uric levels in medications in patients with mild to moderate renal impairment.

There is no experience with respect to the administration of TEGAR CD in patients with a recent kidney transplant or severe renal impairment (see section 4.3).

Telmisartan is not removed from blood by hemodialysis.

Intravascular volume depletion

Symptomatic hypotension, particularly after first dose and/or sodium depletion caused by vigorous diuretic therapy, diarrhea, vomiting or dietary salt restriction, hypotension may occur especially after the first dose of TEGAR CD. The use of TEGAR CD is not recommended until this condition has been corrected.
Sodium/chloride depletion accompanied by neurological symptoms (nausea, progressive disorientation, apathy) have been observed with the use of hydrochlorothiazide.

Renal blockade of the renin-angiotensin-aldosterone system

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 renal function (including acute renal failure). Dual blockade of renin-angiotensin-aldosterone system (RAAS) through the combined use of TEGAR CD and other medicines affecting the RAAS is therefore not recommended (see section 4.5). TEGAR CD should be used concomitantly with aliskiren (see section 4.3).
ACE inhibitors and angiotensin II receptor blockers should not be used concomitantly in patients with diabetic nephropathy.

Other conditions which stimulate the renin-angiotensin-aldosterone system

Treatment with medicines that affect the renin-angiotensin-aldosterone system, including TEGAR CD, in patients whose vascular tone and renal function depend on this system is to be expected. Such a response is to be expected in patients with salt and/or volume depletion, congestive heart failure or hepatic cirrhosis. Therefore, it is recommended that these patients be subjected to careful medical supervision and that they should start treatment with a low dose.

Primary aldosteronism

Patients with primary aldosteronism do not normally respond to antihypertensive medicines which act through inhibition of the renin-angiotensin system. Administration of TEGAR CD is therefore not recommended in these patients.

Aortic and mitral valve stenosis or obstructive hypertrophic cardiomyopathy

As with other vasodilators, special care is advised for patients with hypertrophic cardiomyopathy or mitral or aortic valve stenosis (see section 4.3).

Choroidal effusion

Although thiazide-type diuretics and hypokalaemia have not been documented with telmisartan/hydrochlorothiazide in combination, hypokalaemia may occur during treatment with other medicines that affect the renin-angiotensin-aldosterone system, or secondary to other medicines prescribed for treatment and/or renal impairment and diabetes mellitus.
Co-administration of TEGAR CD with potassium supplements, potassium-sparing diuretics, salt substitutes containing potassium, or other medicines which may increase potassium levels (e.g. heparin) should be taken with caution.

Hepatic impairment

Thiazides should be used with caution in patients with progressive liver disease or mild to moderate hepatic impairment, since minor alterations of electrolyte balance and fluid may induce hepatic coma. There is no clinical experience with TEGAR CD in patients with hepatic impairment.

Metabolic and endocrine effects

Treatment with TEGAR CD may impair glucose tolerance, therefore dose adjustment of antidiabetic medicines including insulin may be necessary. Latent diabetes mellitus may occur during TEGAR CD treatment. Increases in serum cholesterol and triglycerides are associated with thiazide diuretic therapy. Thiazides, including hydrochlorothiazide, an TEGAR CD, is potential stimulation effect of parathyroid hormone secretion. Thiazides should undergo appropriate diagnostic evaluation prior initiation of treatment in patients with elevated serum calcium levels. Thiazides should be used to stabilize bone, before initiation of TEGAR CD treatment, before initiating treatment with TEGAR CD.

Choroidal effusion, acute myopia and angle-closure glaucoma

Hydrochlorothiazide, a sulphonamide, can cause an idiosyncratic reaction, resulting in choroidal effusion with visual field defect, acute transient myopia and acute angle-closure glaucoma. Symptoms include acute onset of decreased visual acuity or ocular pain and typically occur within hours to weeks of drug initiation. Untreated acute angle-closure glaucoma can lead to permanent vision loss. The primary treatment is to discontinue hydrochlorothiazide as rapidly as possible. Other risk factors for developing acute angle-closure glaucoma may include a history of sulphonamide or penicillin allergy.

Non-melanoma skin cancer

An increased risk of non-melanoma skin cancer (NMSC) (basal cell carcinoma (BCC) and squamous cell carcinoma (SCC)) with increasing cumulative dose of hydrochlorothiazide (HCT) exposure has been observed in two epidemiological studies. Photosensitizing actions of HCT could act as a possible mechanism for NMSC. Patients taking TEGAR CD should be informed of the risk of NMSC and advised to regularly check their skin for any new lesions and promptly report any suspicious skin lesions. Possible preventive measures such as limitation of sun exposure and UV exposure, and use of sun protection should be considered in patients at risk of skin cancer. Suspicious skin lesions should be promptly examined, potentially including histological examinations of biopsies.
TEGAR CD should not be used to treat patients who have had previous and/or current basal cell carcinoma and/or dermatose cell carcinoma of the skin and/or photodermatosis.

Other risks

No with of other prejudice to receptor antagonists, telmisartan (as in TEGAR CD) is apparently less effective in lowering blood pressure in black persons than in non-black patients, possibly because of higher prevalence of low renin states in the black hypertension population.

4.5 Interactions with other medicines and other forms of interaction

This antihypertensive effect of telmisartan, as in TEGAR CD, may increase the hypotensive effects of other medicines used for the treatment of hypertension.
Telmisartan, as TEGAR CD, has no clinically significant interaction with digoxin, hydrochlorothiazide, warfarin, furosemide, glibenclamide, paracetamol, amlodipine and ramipril, when co-administered. Monitoring of plasma digoxin should be considered, since a 20 % increase in median plasma digoxin through concentration has been observed.
Although the clinical relevance is unknown, co-administration of telmisartan (as in TEGAR CD) and ramipril led to an increase of up to 2.5-fold in the AUC0-24 and Cmax of ramipril and ramiprilat during a single dosing study.

Lithium

Orally and reversible increases in serum lithium concentrations have been reported during concomitant use of lithium with ACE inhibitors, ARBs, and thiazide diuretics. Co-administration of lithium with TEGAR CD, including the use of thiazides (as in hydrochlorothiazide, an TEGAR CD), increases the risk of lithium toxicity and the risk of lithium toxicity with TEGAR CD is contraindicated (see section 4.3).

Potassium-sparing and ACE inhibitors/angiotensin receptor blockers

Concomitant use of hydrochlorothiazide 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).

Iodinated contrast products

In the event of dehydration caused by diuretics, there is an increased risk of acute functional renal failure, particularly during use of high doses of iodinated contrast products. Patients should be rehydrated before the iodinated product is required.

Medicines affecting potassium

The potassium-depleting effect of hydrochlorothiazide, an TEGAR CD, could be increased by other medicines which also have potassium-depleting properties (e.g. potassium-containing laxatives, corticosteroids, ACTH, laxatives, carbenoxolone, amphotericin, salicylic acid and derivatives, penicillin G sodium). Monitoring of potassium plasma levels is advised if these medicines are prescribed with TEGAR CD.
Equally, concomitant use of TEGAR CD and ACE inhibitors, potassium-sparing diuretics, potassium supplements or salt substitutes containing potassium, cyclosporin or other medicines that may increase serum potassium levels (e.g. heparin) potassium may lead to increases in serum potassium and should therefore be co-administered cautiously with TEGAR CD, and potassium plasma levels monitored (see section 4.3).

Dual blockade of the RAAS with ACE inhibitors or angiotensin II receptor blockers

Dual blockade of the RAAS through the combination of ACE inhibitors, angiotensin II receptor blockers or aliskiren is associated with a higher frequency of adverse events such as hypotension, hyperkalaemia and decreased renal function (see sections 4.3 and 4.4).

Medicines affected by serum potassium disturbances

Monitoring of serum potassium is recommended when TEGAR CD is administered with medicines affected by serum potassium disturbances (e.g. digitalis glycosides, anti-dysrhythmics and medicines known to induce torsade de pointes, such as:
- class Ia anti-dysrhythmics (e.g. quinidine, hydroquinidine, disopyramide)
- class III anti-dysrhythmics (e.g. amiodarone, sotalol, dofetilide, ibutilide)
- some antipsychotics (e.g. thioridazine, chlorpromazine, levomepromazine, trifluoperazine, cyamemazine, sulpiride, sultopride, amisulpride, tiapride, pimozide, haloperidol, droperidol)
- others (e.g. bepridil, cisapride, diphemanil, erythromycin IV, halofantrine, mizolastine, pentamidine, sparfloxacin, terfenadine, vincamine, IV). Hypokalaemia being a predisposing factor for torsade de pointes, co-administration of TEGAR CD with hydrochlorothiazide and TEGAR CD is contraindicated (see section 4.3).

Hypercalcaemia and carbohydrate metabolism

Concentration use of hypercalcaemia