

Prescribing Information – Amias® (candesartan cilexetil)

(Refer to Summary of Product Characteristics before prescribing)

Amias® (candesartan cilexetil)

Abbreviated Prescribing Information

Presentation: Tablets containing 4mg, 8mg, 16mg or 32mg candesartan cilexetil. For specific patient populations 2mg. **Indication:** Essential Hypertension; Treatment of patients with heart failure and left ventricle systolic dysfunction (LVEF \leq 40%) as add-on therapy to ACE-inhibitors or when ACE-inhibitors are not tolerated. **Dosage:** In hypertension: Starting and usual maintenance dose is 8mg od with or without food. If necessary, the dose can be increased to 16mg od. If after 4 weeks blood pressure is not sufficiently controlled, the dose may be increased further to 32mg od. No dose adjustment is necessary in the elderly. A starting dose of 4mg is recommended for patients with renal impairment (including haemodialysis) and those at risk of hypotension due to intravascular volume depletion. For patients with mild to moderate hepatic impairment, the recommended starting dose is 2mg. In heart failure: Usual starting dose is 4mg od with or without food. Up-titration to the target dose of 32mg od or the highest tolerated dose is done by doubling the dose at intervals of at least 2 weeks. No dose adjustment is necessary for elderly patients or in patients with intravascular volume depletion, renal impairment or mild to moderate hepatic impairment. Amias can be administered with other heart failure treatment including ACE-inhibitors, beta-blockers, diuretics and digitalis or a combination of these. Safety and efficacy of Amias not established in children. **Contra-indications:** Hypersensitivity to any component of Amias. Pregnancy and lactation. Severe hepatic impairment and/or cholestasis. **Warnings and Precautions:** Monitoring of serum potassium and creatinine levels is recommended during dose titration of Amias in patients with heart failure and regularly in patients taking concomitant ACE-inhibitors and potassium sparing diuretics such as spironolactone. Periodic assessments of renal function is also recommended especially in elderly heart failure patients \geq 75 years and in heart failure patients with impaired renal function. Hypotension may occur during treatment with Amias in heart failure patients. Risk of increased blood urea and serum creatinine in patients with renal artery stenosis. Periodic monitoring of serum potassium and creatinine levels is recommended in patients with renal impairment. Amias should be carefully titrated with thorough monitoring of blood pressure in patients on haemodialysis. Caution should be observed when initiating therapy and correction of hypovolemia should be attempted. Possible hypotension during anaesthesia and surgery. Not recommended in patients with primary hyperaldosteronism. As with other vasodilators, use with caution in patients with aortic and/or mitral valve stenosis or obstructive hypertrophic cardiomyopathy. **Drug Interactions:** No clinically significant interactions identified. Possible interaction with NSAIDs. Anti-hypertensive effect of Amias may be enhanced by other antihypertensives. Careful monitoring of serum lithium levels recommended during concomitant use. Increase in serum potassium may occur with potassium supplements and potassium sparing diuretics. **Side-effects:** In hypertension clinical trials, adverse events were mild and transient with the overall incidence comparable to placebo. Overall incidence showed no association with dose or age. Adverse events in clinical trials include: headache, respiratory infection, back pain and dizziness/vertigo. In heart failure clinical trials (e.g. CHARM), the adverse event profile of Amias was consistent with the pharmacology of the drug and health status of the patients. In the CHARM clinical programme, 21% of the Amias group and 16.1% of the placebo group discontinued treatment due to adverse events. Adverse reactions commonly seen were: hypotension, hyperkalaemia, renal impairment and increases in creatinine, urea and potassium. Postmarketing there have been very rare reports of: nausea, increased liver enzymes, abnormal hepatic function or hepatitis, arthralgia, myalgia, back pain, angioedema, rash, urticaria, pruritus, dizziness, headache, leucopenia, neutropenia, agranulocytosis, hyperkalaemia, hyponatraemia, decreased haemoglobin, increased creatinine and urea, and renal impairment/failure.

Please refer to the summary of product characteristics for details on the full side-effect profile and drug interactions of Amias. Adverse events should be reported. Reporting forms and information can be found at www.yellowcard.gov.uk Adverse events should also be reported to Takeda UK Ltd.

Legal Category: POM. **Packs and Basic NHS Price:** Blister packs, Amias 2mg, £3.39 for 7 tablets (PL 16189/0001); Amias 4mg, £3.68 for 7 tablets and £9.25 for 28 tablets (PL 16189/0002); Amias 8mg, £9.89 for 28 tablets (PL 16189/0003); Amias 16mg, £12.72 for 28 tablets (PL 16189/0004); Amias 32mg, £16.13 for 28 tablets (PL 16189/0007). **PI Date Code:** 01/2010 **PI Approval Code:** TA091232 **Marketing Authorisation Holder:** Takeda UK Ltd., Takeda House, Mercury Park, Wycombe Lane, Wooburn Green, High Wycombe, BUCKS HP10 0HH. **For further information contact the Marketing Authorisation Holder:** Telephone: 01628 537900, Fax: 01628 526615. ®Registered trademark owned by Takeda Pharmaceutical Company Ltd.

References:

1. Meredith PA et al. *J Hum Hypertens* advance online publication, 17 Dec 2009; doi:10.1038/jhh.2009.99.
2. Lacourcière Y et al. *Am J Hypertens* 1999; **12**: 1181-1187.
3. Kjeldsen SE et al. *J Hum Hypertens* 2009 advance online publication; doi:10.1038/jhh.2009.77.
4. Young JB et al. *Circulation* 2004; **110**: 2618-2626.
5. Takeda UK Ltd. Amias (candesartan) Summary of Product Characteristics. June 2007.
6. Merck Sharp & Dohme Ltd. Cozaar (losartan) Summary of Product Characteristics. August 2009.
7. Novartis Pharmaceuticals UK Ltd. Diovan (valsartan) Summary of Product Characteristics. November 2009.

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NEWS AND RESOURCES

Conference update: British Society for Heart Failure 12th Annual Autumn Meeting (26-27 November 2009, London)



Dr Ahmet Fuat

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THE role of B-type natriuretic peptide in helping to diagnose heart failure was one of the key new developments of interest to primary care clinicians at the 12th Annual Autumn Meeting of the British Society for Heart Failure (BSH).

There is now strong evidence for the value of measuring B-type natriuretic peptide (BNP or NP) and N-terminal pro-BNP to help rule out heart failure, allowing more efficient use of echocardiography resources. There has, to date, been limited uptake of BNP testing by primary care trusts (PCTs) but Dr Theresa McDonagh (London), chair of the BSH, said that a recent Health Technology Assessment on use of these peptides in primary care should be a lever to improve availability. She explained that the HTA endorses the role of BNP testing to exclude a diagnosis of heart failure and strongly recommends this over an

ECG, although it suggests that some patients (those with previous myocardial infarction, basal crepitations, and males with ankle oedema) should go straight to echocardiography.

BNP testing is also being investigated as a tool for monitoring heart failure treatment, with therapy being titrated to an NP target. However, the value of this is not yet proven. Dr Fuat reported on trials comparing traditional care with NP-guided therapy, explaining that they have been small with limited follow-up, and have had conflicting results. There is some evidence that efficacy of NP monitoring is reduced in elderly patients, and women were under-represented in the studies, so at present it is unclear how applicable the data are to routine practice.

Heart failure treatment in primary care

Discussing heart failure drug treatment in primary care, Dr Fuat suggested that low use of beta-blockers remains a challenge. We need to get over perceived problems with these drugs. They should be considered for more patients, including patients with chronic obstructive pulmonary disease (COPD) and peripheral vascular disease. Since April 2009, beta-blocker prescribing has been included in the Quality and Outcomes Framework (QOF) heart failure clinical indicators, but there are no data yet on what effect this has had on prescribing.

Primary care prescribing of ACE inhibitors/angiotensin receptor blockers for patients with heart failure is generally high, but few patients are titrated to target doses. Younger males are more likely to get maximal therapy. We all know that for many frail elderly women it can be difficult to get up to high doses, but we should try.

Professor John McMurray (Glasgow) pointed out that the recent HEAAL trial reinforces the message that doses of renin-angiotensin system blockers should be uptitrated in heart failure patients. This trial compared two doses of losartan (50 mg and 150 mg daily) in well-treated patients with symptomatic heart failure and reduced ejection fraction. All-cause death or heart failure hospitalisation (the primary endpoint) was significantly lower with the higher dose, with no significant increase in adverse events.

PCCJ action

Further details about the BSH and future conferences are available on the society's website (www.bsh.org.uk) or from the BSH Secretariat (01865 391836; info@bsh.org.uk).