

Direct Healthcare Professional Communication

Amlodipine & Valsartan (Senergy®): Restrictions on Combining Different Classes of Medicines That Act on The Renin-Angiotensin System (RAS)

February, 2026

Dear Healthcare Professional,

MS Pharma in agreement with Saudi Food and Drug authority (SFDA) would like to inform you of this letter is for health care professionals who treat or might treat patients with (Amlodipine/Valsartan).

This communication is being sent to remind you of the restrictions on combining different classes of medicines that act on the renin–angiotensin system (RAS).

It aims to further reinforce awareness among healthcare professionals, considering that this risk is already reflected in the approved SmPC and PIL.

Summary

- Restrictions on combining different classes of medicines that act on the renin-angiotensin system (RAS), a hormone system that controls blood pressure and the volume of fluids in the body.
- These medicines (called RAS-acting agents) belong to three main classes: angiotensin-receptor blockers (ARBs, sometimes known as sartans), angiotensin-converting enzyme inhibitors (ACE-inhibitors) and direct renin inhibitors such as aliskiren. Combination of medicines from any two of these classes is not recommended and, in particular, patients with diabetes-related kidney problems (diabetic nephropathy) should not be given an ARB with an ACE-inhibitor.
- Where combination of these medicines (dual blockade) is considered absolutely necessary, it must be carried out under specialist supervision with close monitoring of kidney function, fluid and salt balance and blood pressure. This would include the licensed use of the ARBs candesartan or valsartan as add-on therapy to ACE-inhibitors in patients with heart failure who require such a combination. The combination of aliskiren with an ARB or ACE-inhibitor is strictly contraindicated in those with kidney impairment or diabetes.
- Studies found that combination of an ARB with an ACE-inhibitor was associated with an increased risk of hyperkalaemia (increased potassium in the blood), kidney damage or low blood pressure compared with using either medicine alone. Furthermore, no significant benefits from dual blockade were seen in patients without heart failure and benefits were thought to outweigh risk only in a selected group of patients with heart failure in whom other treatments were unsuitable.

Further information on the safety concern and the recommendations:

- Amlodipine & Valsartan is used in treatment of essential hypertension.
- Amlodipine & Valsartan is indicated in adults whose blood pressure is not adequately controlled on amlodipine or valsartan monotherapy.

- On the basis of current evidence, dual RAS blockade therapy through the combined use of ACE-inhibitors, ARBs or aliskiren is not recommended in any patient. In particular, ACE-inhibitors and ARBs should not be used concomitantly in patients with diabetic nephropathy, and existing contraindications on the use of aliskiren with either an ARB or an ACE inhibitor in patients with diabetes mellitus or moderate to severe renal impairment (GFR < 60 ml/min/1.73 m²) are confirmed.
- Only when considered clinically essential, the combined use of an ARB and ACE inhibitor must be performed under specialist supervision with close monitoring of renal function, electrolytes and blood pressure.
- Such supervised use would include the licensed use of candesartan or valsartan as add-on therapy to ACE inhibitors in patients with heart failure. However, in patients with chronic heart failure, dual blockade should be limited to those intolerant to mineralocorticoid antagonists and with persistent symptoms despite other optimal therapy.
- These recommendations are based on a detailed review of the available data, including clinical trials, meta-analyses and publications, as well as advice from a group of experts on cardiovascular medicine.
- There is considerable evidence from large clinical trials such as ONTARGET3, ALTITUDE4 and VA NEPHRON-D5 and from meta-analyses such as that of Makani6 (involving over 68,000 patients) demonstrating that dual RAS blockade through the combined use of ACE-inhibitors, ARBs or aliskiren is associated with an increased risk of adverse events, including hypotension, hyperkalaemia and renal failure compared with monotherapy, in particular in patients with diabetic nephropathy. This is of particular concern, as these patients and patients with renal impairment are already prone to developing hyperkalaemia.
- Available efficacy data indicate that such dual blockade does not provide significant benefit in the general patient population, although some selected patient sub-populations may possibly benefit. In patients with heart failure there is some evidence that the addition of a second RAS-acting agent may reduce hospital admissions.
- The existing contraindication on the concomitant use of ACE-inhibitors or ARBs with aliskiren-containing products in patients with diabetes mellitus or renal impairment (GFR < 60 ml/min/1.73 m²), which is based on the ALTITUDE study data, was confirmed in the light of the additional data reviewed.

Call For Reporting:

Report suspected adverse drug reactions associated with Senergy® (Amlodipine & Valsartan) or request additional copies of this DHPC by contacting:

- **Pharmacovigilance Department at MS Pharma:**
- **Email:** pharmacovigilance@mspharma.com
- **Website:** www.mspharma.com
- **Phone No:** + 966112790122 Ext. 6013

- **The National Pharmacovigilance Center (NPC): (Saudi food and drug authority)**
- **Email:** npc.drug@sfd.gov.sa
- **Call Center:** 19999
- **Website:** <https://ade.sfd.gov.sa/>
- **QR Code:** 