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Committee for Human Medicinal Products (CHMP)

Concept paper on the need for revision of the Guideline on clinical investigation of medicinal products in the treatment of hypertension (EMA/CHMP/29947/2013/Rev.4)

Agreed by the Cardiovascular WP	24 September 2026
Adopted by CHMP for release for consultation	5 October 2026
Start of public consultation	19 October 2026
End of consultation (deadline for comments)	31 January 2027

The proposed guideline will replace Guideline on clinical investigation of medicinal products in the treatment of hypertension – (EMA/CHMP/29947/2013/Rev.4).

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Keywords	hypertension, arterial hypertension, blood pressure, high blood pressure
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1. Introduction

Arterial hypertension is the most important modifiable risk factor for all-cause and cardiovascular (CV) morbidity and mortality.^{1,2} The pathophysiology of hypertension (HTN) involves complex interactions between environmental and behavioural factors, genes, hormonal networks, and multiple organ systems (renal, CV, and central nervous system). Most patients have essential HTN, overall, about 10% have secondary HTN with an identifiable cause¹. When insufficiently treated, arterial HTN leads to subclinical organ damage affecting heart, brain, kidneys, eyes, large and medium arteries and microcirculation, and ultimately to CV, cerebrovascular, and renal disease.

The European Society of Cardiology (ESC) 2024 Guidelines continue to define HTN as office systolic blood pressure (BP) of ≥ 140 mmHg or diastolic BP of ≥ 90 mmHg. However, a new BP category called 'Elevated BP' is introduced. Patients with BP values above 130/80 should be treated with antihypertensive drugs if they are at an increased CV risk. Treatment of arterial hypertension could lead to a reduction in CV risk with an estimated about 20% risk reduction associated with a reduction of systolic blood pressure (SBP) by 10 mmHg³. Alongside lifestyle modifications such as reducing salt and increasing potassium intake, increasing physical activities, weight management and diet, reducing alcohol intake and stopping smoking, the main goal of pharmacological treatment is reducing BP to prevent organ damage and CV and renal adverse outcome.

Since the last revision of the Guideline on clinical investigation of medicinal products in the treatment of hypertension (EMA/CHMP/29947/2013/Rev.4), new developments have emerged with focus on specific patient populations like those with rHTN and primary aldosteronism, and new diagnostic and therapeutic options have become available, important enough to be addressed in the scientific guideline. In addition, recommendations with regard to the definition of HTN and treatment targets may be aligned with recent recommendations (ESC Guideline 2024, [1]).

Main antihypertensive drug classes are angiotensin-converting enzyme (ACE) inhibitors (ACE-I), angiotensin receptor blockers (ARB), calcium channel blockers (CCB), diuretics, and beta blockers (BB). Pharmacological treatment recommendations depend on baseline BP and the physical state of a patient. Initial monotherapy is preferred in some instances (patients within the elevated BP category who are at an increased CV risk, patients with moderate to severe frailty, very elderly), but as a general rule it is recommended to initiate therapy with low-dose double combination therapy with ACE-I or ARBs/ CCB/ diuretics, and escalate, if needed to a low dose triple combination therapy out of these classes, and escalate the doses, if needed to the maximally tolerated doses (1).

According to recent recommendations a target SBP of 120–129 mmHg should be pursued on the condition that treatment to this BP target is well tolerated by the patient. More lenient BP targets can be considered in persons with symptomatic orthostatic hypotension, those aged 85 years or over, or those with moderate-to-severe frailty or limited life expectancy. For these selected cases where a target SBP of 120–129 mmHg is not pursued, a BP goal as low as reasonably achievable should be aimed at (1). Some classes of drugs with proven benefit in patients with CV disease have shown BP lowering properties but are not approved for the treatment of HTN. Among these are the angiotensin receptor–neprilysin inhibitors (ARNi) (7), sodium-glucose co-transporter 2 (SGLT2) inhibitors, glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 agonists and non-steroidal mineralocorticoid receptor antagonists (For Review 1,8). Resistant hypertension (rHTN) is not a disease per se. Compared with treated patients who achieve BP control, patients with rHTN have a worse prognosis: risk of myocardial infarction, stroke, end-stage renal disease, and death in these adults may be two- to six-fold higher (1,4). On top of recommended triple therapy, spironolactone, BB, and aprocitan are among the treatment options approved for these patients.

62 The proposed revision aims at amending several aspects of the current guideline to reflect new
63 developments in the diagnostic and therapeutic field.

64 **2. Problem statement**

65 The following points are planned to be addressed in the revised version of the EMA Guideline on clinical
66 investigation of medicinal products in the treatment of hypertension:

67 - 24 h ambulatory BP measurement (24h ABPM)

68 The current version of the guideline states (5.1.3.) “...the clinical trial data on the effects of treatment
69 strategies based solely on out-of-office BP measurements is still scarce. Therefore, the measurement
70 of ABPM is not currently accepted as the sole basis for efficacy in an approval process.” This may be
71 reevaluated. Advantages of 24h ABPM are not restricted to characterizing BP over the whole day and
72 night. Particularly in patients with rHTN, placebo effects are less pronounced with 24 h ABPM. Results
73 in subgroups and dose related efficacy may be more reliably assessed as compared to office BP
74 measurements. Accepting 24h ABPM as primary efficacy endpoint in pivotal trials will be discussed.
75 This implies reference to different BP thresholds and includes a re-evaluation of data on the association
76 between CV outcome and treatment strategies based on 24 h ABPM.

77 - rHTN and primary aldosteronism (PA)

78 rHTN and PA are not specifically discussed in the current version of the guideline. EMA has accepted
79 rHTN as an indication on its own in the past and regulatory experience has been accumulated in this
80 patient population. Furthermore, PA is increasingly be recognised as a reason for secondary HTN. It
81 has been reported in up to 12 % in patients with BP of >180/110 mmHg.⁵ Requirements in clinical
82 development programmes in this patient population may differ, when aiming either at treatment of
83 HTN in patients with PA or at a claim for the treatment of PA going beyond what is expected for
84 essential HTN. It is intended to amend the guideline and reflect experiences and expectations in
85 patients with rHTN and PA.

86 - digital technologies/wearables

87 Digital technologies are increasingly being used by healthy subjects and patients to control
88 physiological parameters such as heart rate, BP, and to monitor physical activities and sleep. Beyond
89 an application as a personal health and lifestyle feature, such devices may be used for diagnostic
90 purposes or treatment modifications. A discussion of the acceptability and validation of such devices in
91 the context of clinical studies in arterial HTN should be included in the guideline.

92 - blood pressure thresholds and targets

93 The current Guideline wording states “In otherwise healthy individuals....values below 140/90 are
94 considered in the normal range.” This definition of normal BP is not entirely in line with recent ESC
95 Guideline recommendations, see section 1. Stricter targets for otherwise healthy individuals may be
96 recommended. On an individual basis more lenient BP goals can be set, e. g. in very old or frail
97 patients.

98 - update of section 5.2

99 Target organ damage: Chest radiography is not part of the diagnostic work-up for diagnosing left
100 ventricular hypertrophy (LVH). It may be considered to add cardiac biomarkers (hs-cTnT or I>99th
101 percentile upper reference limit, NT – proBNP > 125 pg/mL if age < 75 years or > 450 pg/ml if ≥ 75
102 years old ¹).

Renal function endpoints may be reflected as “measured glomerular filtration rate (GFR) or estimated glomerular filtration rate (eGFR)-based endpoints” without being explicit about the method (e. g. consider removing information on “Clearance of para aminohippurate (PAH) clearance”).

3. Discussion (on the problem statement)

An update of the scientific guideline is foreseen.

The following points are proposed to be addressed in the update:

1. The acceptability of 24h ABPM as a primary endpoint, and description of the place of derived parameters (e.g. "dippers" or night-time BP)

2. The guidance with respect to patient populations of special interest, such as patients with rHTN and PA

3. The acceptability of new technologies such as wearables to assess efficacy and safety parameters in patients with arterial HTN

4. The recommendations as regards target BP and diagnostic work-up in line with updated ESC HTN GDLs 2024.

5. The concept of estimands will be briefly contextualised in the field of HTN trials.

4. Recommendation

The Cardiovascular Working Party (CVSWP) at the EMA recommends revising the Guideline on clinical investigation of medicinal products in the treatment of hypertension – Scientific guideline (EMA/CHMP/29947/2013/Rev.4) considering the issues identified above.

5. Proposed timetable

This Concept Paper is released for 6 months public consultation. It is anticipated that the draft Guideline may be released 18 months after adoption of the Concept Paper by the CHMP. The draft document will then be released for 6 months of external consultation and following the receipt of comments it will be finalised within approximately 12 months.

6. Resource requirements for preparation

The drafting process will involve the co-operation between the Cardiovascular Working Party (CVSWP), and the Scientific Advise Working Party (SAWP) at the EMA.

7. Impact assessment (anticipated)

It is anticipated that the proposed changes and clarifications may contribute to streamline planning of clinical programs in the therapeutic field and may better serve as a reference for the CHMP when assessing such programs and the final data.

8. Interested parties

The following interested groups may provide additional valuable input:

Pharmaceutical Industry,

137 National Competent Authorities.

138 Disease specific patient groups and patient representatives

139 Academia/Learned societies: European Society of Cardiology (ESC), European Society of Hypertension
140 (ESH), European Society of Endocrinology (ESE), European Stroke Organisation (ESO).

141 **9. References to literature, guidelines, etc.**

142 (1) McEvoy, John William et al. "2024 ESC Guidelines for the management of elevated blood pressure
143 and hypertension." *European heart journal* vol. 45,38 (2024): 3912-4018.
144 doi:10.1093/eurheartj/ehae178

145 (2) GBD 2019 Risk Factors Collaborators. "Global burden of 87 risk factors in 204 countries and
146 territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019." *Lancet*
147 (London, England) vol. 396,10258 (2020): 1223-1249. doi:10.1016/S0140-6736(20)30752-2

148 (3) Blood Pressure Lowering Treatment Trialists' Collaboration. "Pharmacological blood pressure lowering
149 for primary and secondary prevention of cardiovascular disease across different levels of blood pressure:
150 an individual participant-level data meta-analysis." *Lancet* (London, England) vol. 397,10285 (2021):
151 1625-1636. doi:10.1016/S0140-6736(21)00590-0.

152 (4) Carey, Robert M et al. "Resistant Hypertension: Detection, Evaluation, and Management: A
153 Scientific Statement From the American Heart Association." *Hypertension* (Dallas, Tex.: 1979) vol.
154 72,5 (2018): e53-e90. doi:10.1161/HYP.0000000000000084

155 (5) Monticone, Silvia et al. "Prevalence and Clinical Manifestations of Primary Aldosteronism
156 Encountered in Primary Care Practice." *Journal of the American College of Cardiology* vol. 69,14
157 (2017): 1811-1820. doi:10.1016/j.jacc.2017.01.052

158 (6) Guideline on clinical investigation of medicinal products in the treatment of hypertension –
159 Scientific guideline (EMA/CHMP/29947/2013/Rev.4); [https://www.ema.europa.eu/en/clinical-](https://www.ema.europa.eu/en/clinical-investigation-medicinal-products-treatment-hypertension-scientific-guideline)
160 [investigation-medicinal-products-treatment-hypertension-scientific-guideline](https://www.ema.europa.eu/en/clinical-investigation-medicinal-products-treatment-hypertension-scientific-guideline)

161 (7) McMurray, John J V et al. "Angiotensin-neprilysin inhibition versus enalapril in heart failure." *The New*
162 *England journal of medicine* vol. 371,11 (2014): 993-1004. doi:10.1056/NEJMoa1409077

163 (8) Yang, Ying et al. "Maximizing blood pressure lowering effects: a review of drug class comparisons
164 and rationale for combination approaches." *Frontiers in cardiovascular medicine* vol. 12 1656818. 26
165 Nov. 2025, doi:10.3389/fcvm.2025.1656818