

Policies Repository



Policy Title Oral Antihypertensive Agents

Policy Number FS.CLIN.9

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Policy

Angiotensin II receptor blockers (ARBs) are indicated to treat primary hypertension and nephropathy in individuals who have Type 2 diabetes. These agents are also indicated for the treatment of individuals with heart failure and hypertension with left ventricular hypertrophy.

Aliskiren (Tekturna®) and aliskiren HCT (Tekturna HCT®) are indicated for the treatment of hypertension; aliskiren (Tekturna®) and aliskiren HCT (Tekturna HCT®) are one of the first renin inhibitors approved by the US Food and Drug Administration (FDA).

Amlodipine/olmesartan (Azor™) is indicated for the treatment of hypertension, alone or in combination with other antihypertensive medications.

Amlodipine/valsartan (Exforge®) combination therapy is indicated for individuals whose blood pressure is not controlled on monotherapy with a calcium channel blocker or an angiotensin receptor blocker. Amlodipine/valsartan (Exforge®) is a new formulation that combines the generic drug, amlodipine, and Diovan.

Amlodipine/valsartan/hydrochlorothiazide (Exforge HCT®) combination therapy is indicated for individuals whose blood pressure is not controlled on any two of the antihypertensive classes: calcium channel blockers, angiotensin receptor blockers, and diuretics. Amlodipine/valsartan/hydrochlorothiazide (Exforge HCT®) is a new formulation that combines the generic drugs, amlodipine and hydrochlorothiazide, and Diovan for the treatment of hypertension.

The use of ARBs, aliskiren (Tekturna®), aliskiren HCT (Tekturna HCT®), amlodipine/olmesartan (Azor™), and amlodipine/valsartan (Exforge®) / amlodipine/valsartan/hydrochlorothiazide (Exforge HCT®) requires prior authorization (i.e., clinical pharmacy and/or Medical Director review).

Policy Description **Angiotensin II receptor blockers (ARBs)** inhibit the vasoconstricting and aldosterone-

secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT1 receptor in many types of tissues (eg, vascular smooth muscle, adrenal gland). Angiotensin II (formed from angiotensin I) is a potent vasoconstrictor, the primary vasoactive hormone of the renin-angiotensin system, and an important component in the pathophysiology of hypertension. Its effects include: vasoconstriction; stimulation of synthesis and release of aldosterone; cardiac stimulation; and renal re-absorption of sodium.

Aliskiren (Tekturna®) and aliskiren HCT (Tekturna HCT®) are the first drugs in a new class of antihypertensive medications called renin inhibitors. Renin is the enzyme responsible for converting angiotensinogen into angiotensin I. Angiotensin I is then converted into the potent vasoconstrictor angiotensin II by the angiotensin converting enzyme (ACE). The inhibition of renin results in decreased formation of angiotensin I and, ultimately, angiotensin II.

Amlodipine/olmesartan (Azor™) is a combination of amlodipine and olmesartan. Amlodipine is a dihydropyridine calcium channel blocker that inhibits the transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle. The decrease in calcium influx leads to reduced contraction of the vascular smooth muscle and vasodilation, which leads to a decrease in blood pressure. Olmesartan is an angiotensin II receptor blocker. By blocking the angiotensin II receptors, olmesartan decreases the vasoconstricting effects of angiotensin II and decreases blood pressure.

Amlodipine/valsartan (Exforge®) is a combination of amlodipine and valsartan.

Amlodipine/valsartan/hydrochlorothiazide (Exforge HCT®) is a combination of amlodipine, valsartan, and hydrochlorothiazide. Amlodipine is a dihydropyridine calcium channel blocker that inhibits the transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle. The decrease in calcium influx leads to reduced contraction of the vascular smooth muscle and vasodilation, which leads to a decrease in blood pressure. Valsartan is an angiotensin II receptor blocker. By blocking the angiotensin II receptors, olmesartan decreases the vasoconstricting effects of angiotensin II and decreases blood pressure. Hydrochlorothiazide is a thiazide diuretic indicated for the management of hypertension alone or in combination in order to enhance the effectiveness of other antihypertensive drugs.

Policy Guideline Inclusion

For new starts* only:

VALSARTAN (DIOVAN/DIOVAN HCT), OLMESARTAN (BENICAR/BENICAR HCT)

Valsartan (Diovan®/Diovan HCT®), olmesartan (Benicar®/Benicar HCT®) are approved when **one** of the following inclusion criterion is met:

- Documentation of a minimum 30-day trial and failure of or intolerance to at least **one** angiotensin converting enzyme (ACE) inhibitor-containing product (eg, enalapril maleate, lisinopril, moexipril HCl, fosinopril sodium, benazepril HCl, captopril, quinapril HCl) or ramipril (Altace) within the past six months
- Diagnosis of Type 2 diabetes with renal insufficiency

For new starts* only:

IRBESARTAN (AVAPRO®/AVALIDE®), CANDESARTAN (ATACAND®/ATACAND HCT®), LOSARTAN (COZAAR®/HYZAAR®), TELMI SARTAN (MICARDIS®/MICARDIS HCT®), EPROSARTAN (TEVETEN®/TEVETEN HCT®)

Irbesartan (Avapro®/Avalide®), candesartan (Atacand®/Atacand HCT®), losartan (Cozaar®/Hyzaar®), telmisartan (Micardis®/Micardis HCT®), eprosartan (Teveten®/Teveten HCT®) are approved when the following inclusion criterion is met:

- Documentation of a minimum 30-day trial and failure of or intolerance to valsartan (Diovan)- **and** olmesartan (Benicar)-containing products [Benicar®/Benicar HCT® and

Diovan®/Diovan HCT® require prior authorization].

In addition, **one** of the following inclusion criteria must also be met in order for treatment with irbesartan (Avapro, Avalide), candesartan (Atacand/Atacand HCT), losartan (Cozaar, Hyzaar), telmisartan (Micardis/Micardis HCT), eprosartan (Teveten/Teveten HCT) to be approved:

- Documentation of a minimum 30-day trial and failure of or intolerance to at least **one** ACE inhibitor-containing product (eg, enalapril maleate, lisinopril, moexipril HCl, fosinopril sodium, benazepril HCl, captopril, quinapril HCl) or ramipril (Altace) within the past six months
- Diagnosis of Type 2 diabetes with renal insufficiency

NOTE: Requests for any of the following angiotensin II receptor blockers (ARBs): irbesartan (Avapro, Avalide), candesartan (Atacand/Atacand HCT), losartan (Cozaar, Hyzaar), telmisartan (Micardis/Micardis HCT), eprosartan (Teveten/Teveten HCT) that have documentation of a minimum 30-day trial and failure of an ACE inhibitor-containing product within the past six months will receive an authorization for both valsartan (Diovan/Diovan HCT) and olmesartan (Benicar/Benicar HCT).

ALISKIREN (TEKTURNA®)/ALISKIREN HCT (TEKTURNA HCT®)

Aliskiren (Tekturna®) and aliskiren HCT (Tekturna HCT®) are approved when **all** of the following inclusion criteria are met:

- Documented diagnosis of hypertension
- Documentation of trial and failure of or contraindication/intolerance/allergy to an ACE inhibitor
- Documentation of trial and failure of or contraindication/intolerance/allergy to Diovan-**or** Benicar-containing products [Benicar®/Benicar HCT® and Diovan®/Diovan HCT® require prior authorization].
- Documentation of trial and failure of or contraindication/intolerance/allergy to an amlodipine- containing product

AMLODIPINE BESYLATE/OLMESARTAN (AZOR™)

Amlodipine besylate/Olmesartan (Azor™) is approved when the following inclusion criterion is met:

- Documentation of a trial and failure of **one** of the following agents:
 - olmesartan/olmesartan HCT (Benicar®/Benicar HCT®) [Benicar®/Benicar HCT® requires prior authorization]
 - an amlodipine-containing product
 - an angiotensin converting enzyme (ACE) inhibitor-containing product

AMLODIPINE BESYLATE/VALSARTAN (EXFORGE®) / AMLODIPINE BESYLATE/VALSARTAN/HYDROCHLOROTHIAZIDE (EXFORGE HCT®)

Amlodipine besylate/valsartan (Exforge®) / amlodipine/valsartan/hydrochlorothiazide (Exforge HCT®) is approved when **all** of the following inclusion criteria are met:

- Documentation of at least a 30-day trial of concurrent therapy of Valsartan/Valsartan

HCT (Diovan®/Diovan HCT®) **and** an amlodipine-containing product [Benicar®/Benicar HCT® and Diovan®/Diovan HCT® require prior authorization].

- Documentation of non-compliance with valsartan/valsartan HCT (Diovan®/Diovan HCT®) **and** an amlodipine-containing product

***New start** is defined as a member who has not received ARB therapy prior to the submission of the request.

Policy Guideline Exclusion

For new starts* only:

VALSARTAN (DIOVAN®/DIOVAN HCT®), OLMESARTAN (BENICAR®/BENICAR HCT®)

Valsartan (Diovan®/Diovan HCT®), olmesartan (Benicar®/Benicar HCT®) are denied when **any** of the following exclusion criteria are present:

- Use for a diagnosis that is experimental/investigational
- No documentation of a minimum 30-day trial and failure of or intolerance to at least **one** ACE inhibitor-containing product (eg, enalapril maleate, lisinopril, moexipril HCl, fosinopril sodium, benazepril HCl, captopril, quinapril HCl) or ramipril (Altace) within the past six months

For new starts* only:

IRBESARTAN (AVAPRO®/ AVALIDE®), CANDESARTAN (ATACAND®/ATACAND HCT®), LOSARTAN (COZAAR®/ HYZAAR®), TELMISARTAN (MICARDIS®/MICARDIS HCT®), EPROSARTAN (TEVETEN®/TEVETEN HCT®)

Irbesartan (Avapro®, Avalide®), candesartan (Atacand®/Atacand HCT®), losartan (Cozaar®, Hyzaar®), telmisartan (Micardis®/Micardis HCT®), eprosartan (Teveten®/Teveten HCT®) are denied when **any** of the following exclusion criteria are present:

- No documentation of a minimum 30-day trial and failure of or intolerance to valsartan (Diovan)- **and** olmesartan (Benicar)-containing products [Benicar®/Benicar HCT® and Diovan®/Diovan HCT® require prior authorization].
- No documentation of a minimum 30-day trial and failure of or intolerance to at least **one** ACE inhibitor-containing product (eg, enalapril maleate, lisinopril, moexipril HCl, fosinopril sodium, benazepril HCl, captopril, quinapril HCl) or ramipril (Altace) within the past six months
- No documented diagnosis of Type 2 diabetes with renal insufficiency

ALISKIREN (TEKTURNA®)/ALISKIREN HCT (TEKTURNA HCT®)

Aliskiren (Tekturna®) and aliskiren HCT (Tekturna HCT®) are denied when **any** of the following exclusion criteria are present:

- No documented diagnosis of hypertension
- No documentation of trial and failure of or contraindication/intolerance/allergy to an ACE inhibitor
- No documentation of trial and failure of or contraindication/intolerance/allergy to valsartan (Diovan)- **or** olmesartan (Benicar)-containing products [Benicar®/Benicar HCT® requires prior authorization].
- No documentation of trial and failure of or contraindication/intolerance/allergy to an amlodipine-containing product

AMLODIPINE BESYLATE/OLMESARTAN (AZOR™)

Amlodipine besylate/Olmesartan (Azor™) is denied when the following exclusion criterion is present:

- No documentation of a trial and failure of **one** of the following agents:
 - olmesartan/olmesartan HCT (Benicar®/Benicar HCT®) [Benicar®/Benicar HCT® requires prior authorization]
 - an amlodipine-containing product
 - an angiotensin converting enzyme (ACE) inhibitor-containing product

AMLODIPINE BESYLATE/VALSARTAN (EXFORGE®) / AMLODIPINE BESYLATE/VALSARTAN/HYDROCHLOROTHIAZIDE (EXFORGE HCT®)

Amlodipine besylate/Valsartan (Exforge®) / amlodipine/valsartan/hydrochlorothiazide (Exforge HCT®) is denied when **any** of the following exclusion criteria are present:

- No documentation of at least a 30-day trial of concurrent therapy of valsartan/valsartan HCT (Diovan®/Diovan HCT®) **and** an amlodipine-containing product [Diovan®/Diovan HCT® requires prior authorization]
- No documentation of non-compliance with valsartan/valsartan HCT (Diovan®/Diovan HCT®) **and** an amlodipine-containing product

***New start** is defined as a member who has not received ARB therapy prior to the submission of the request.

Policy List of Applicable Drugs

Brand Name	Generic Name
Diovan	Valsartan
Diovan HCT	Valsartan/HCT
Benicar	Olmesartan
Benicar HCT	Olmesartan/HCT
Avapro	Irbesartan
Avalide	Irbesartan/HCT
Atacand	Candesartan
Atacand HCT	Candesartan/HCT
Cozaar	Losartan
Hyzaar	Losartan/HCT
Micardis	Telmisartan
Micardis HCT	Telmisartan/HCT
Teveten	Eprosartan
Teveten HCT	Eprosartan/HCT
Tekturna	Aliskiren
Tekturna HCT	Aliskiren HCT
Azor	Amlodipine besylate/Olmesartan

Exforge	Amlodipine besylate/Valsartan
Exforge HCT	Amlodipine besylate/Valsartan/Hydrochlorothiazide

Dosing and Administration

Refer to the specific manufacturer's prescribing information for administration and dosage details, contraindications, and Black Box warnings.

Policy References

Atacand [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2004. Also available online at: http://www.atacand.com/50693_51024.aspx?mid=18. Accessed September 10, 2008.

Avapro [package insert]. New York, NY: Bristol-Myers Squibb Sanofi-Synthelabo Partnership; 2007. Also available online at: <http://www.avapro.com>. Accessed September 10, 2008.

Azor [prescribing information]. Parsipany, NJ: Daiichi Sankyo; 2007.

Benicar [package insert]. Tokyo, Japan: Daiichi Sankyo Inc.; 2006. Also available online at: http://www.benicar.com/prod_info/index.asp?ref=1001011101. Accessed September 10, 2007.

Chobanian AV, Bakris GL, Black HR, et al. Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hypertension*. 2003;42(6):1206-1252.

Cozaar [package insert]. Whitehouse Station, NJ: Merck; 2005. Also available online at: http://www.cozaar.com/losartan_potassium/cozaar/hcp/index.jsp. Accessed September 10, 2008.

Diovan [package insert]. East Hanover, NJ: Novartis Pharmaceuticals; 2007. Also available online at: <http://www.pharma.us.novartis.com/product/pi/pdf/diovan.pdf>. Accessed September 10, 2008.

Exforge® (amlodipine and valsartan) [prescribing information]. East Hanover, NJ: Novartis Pharmaceutical Corp; 2007.

Exforge HCT® (amlodipine, valsartan, and hydrochlorothiazide) [prescribing information]. East Hanover, NJ: Novartis Pharmaceutical Corp; 2009.

Exforge® (amlodipine and valsartan). In: Drugdex [online through Micromedex Healthcare Series]. Greenwood Village, CO: Thomson Micromedex. Accessed February 14, 2008.

Facts & Comparisons. Amlodipine. [Facts & Comparisons Web site]. Available at: <http://www.factsandcomparisons.com> [via subscription only]. Accessed October 8, 2007.

Facts & Comparisons. Angiotensin II receptor blockers. [Facts & Comparisons Web site]. Available at: <http://www.factsandcomparisons.com/efacts.asp> [via subscription only]. Accessed September 10, 2007.

Facts & Comparisons. Exforge® (amlodipine and valsartan). [Facts & Comparisons Web site]. Available at: <http://www.factsandcomparisons.com> [via subscription only]. Accessed February 14, 2008.

Gradman AH, Schmieder RE, Lins RL, et al. Aliskiren, a novel orally effective renin inhibitor, provides dose- dependent antihypertensive efficacy and placebo-like tolerability in hypertensive patients. *Circulation*. 2005;111(8):1012-1018.

Joint National Committee (JNC). JNC VII guidelines for the treatment of hypertension. [National

Heart, Lung, and Blood Institute (NHLBI) Web site]. Available at: <http://www.nhlbi.nih.gov>. Accessed August 9, 2007.

Micardis [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals; 2006. Also available online at: <http://us.micardis.com/bipi/InformationRequest?page=prescribing&product=micardis>. Accessed September 10, 2008.

Micromedex. Amlodipine. [Micromedex Web site]. Available at: <http://www.micromedex.com> [via subscription only]. Accessed October 8, 2008.

Micromedex. Benicar. [Micromedex Web site]. Available at <http://www.micromedex.com> [via subscription only]. Accessed October 8, 2008.

Micromedex. Tekturna. [Micromedex Web site]. Available at: <http://www.micromedex.com> [via subscription only]. Accessed August 9, 2008.

Oparil S, Yarows SA, Patel S, et al. Efficacy and safety of combined use of aliskiren and valsartan in patients with hypertension: A randomised, double-blind trial. *Lancet*. 2007;370(9583):221-229.

Pool JL, Schmieder RE, Azizi M, et al. Aliskiren, an orally effective renin inhibitor, provides antihypertensive efficacy alone and in combination with valsartan. *Am J Hypertens*. 2007;20(1):11-20.

Stanton A, Jensen C, Nussberger J, O'Brien E. Blood pressure lowering in essential hypertension with an oral renin inhibitor, aliskiren. *Hypertension*. 2003;42(6):1137-1143.

Strasser RH, Puig JG, Farsang C, et al. A comparison of the tolerability of the direct renin inhibitor aliskiren and lisinopril in patients with severe hypertension (Abstract). *J Hum Hypertens*. 2007;21(10):780-787.

Tekturna [package insert]. East Hanover, NJ: Novartis Pharmaceuticals; 2007.

Teveten [package insert]. Cranbury, NJ: Kos Pharmaceuticals; 2005. Also available online at: <http://www.rxabbott.com/pdf/tevetenhct.pdf>. Accessed November 6, 2008.

Villamil A, Chrysant SG, Calhoun D, et al. Renin inhibition with aliskiren provides additive antihypertensive efficacy when used in combination with hydrochlorothiazide. *J Hypertens*. 2007;25(1):217-226.

Policy Link to Related Policies

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