BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

CORLANOR® (ivabradine)
ENTRESTO™ (sacubitril and valsartan)
VERQUVO™ (vericiguat)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require precertification is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

CORLANOR (ivabradine)

➢ **Criteria for initial therapy:** Corlanor (ivabradine) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Cardiologist.

2. Individual has a confirmed diagnosis of **ONE** of the following:
   a. Adult 18 years of age or older with stable symptomatic heart failure (NYHA class II-IV) (See Definition section)

b. Pediatric individual age of 6 months or older with stable symptomatic heart failure due to dilated cardiomyopathy (NYHA class II-IV or Ross Heart Failure class II-IV (See Definition section))

3. Left ventricular ejection fraction is **ONE** of the following:
   a. ≤ 35% in an **individual 18 years or older**
   b. ≤ 45% in an **individual 6 months to 17 years**

4. Individual is in sinus rhythm with a resting heart rate of **ONE** of the following:
   a. **Individual 18 years or older:** ≥ 70 beats per minute
   b. **Individual 6 months to 17 years:** is elevated for age (See Definition section)

5. **Where clinically indicated, appropriate for age, ethnicity, and condition** individual is using maximally tolerated dose of guideline directed therapy using **ONE** agent in each of the following:
   a. Bisoprolol, carvedilol, or sustained release metoprolol
   b. Angiotensin system inhibitor such as:
      i. Sacubitril-valsartan
      ii. Angiotensin converting enzyme (ACE) inhibitor (such as enalapril, lisinopril, etc.)
      iii. Angiotensin II receptor blocker (ARB) (such as candesartan, losartan, valsartan)
   c. Sodium-glucose cotransporter 2 (SGLT2) inhibitors (such as dapagliflozin, empagliflozin, etc.)
   d. Mineralocorticoid receptor antagonist (MRA, such as spironolactone or eplerenone)
   e. Diuretic agent as needed for fluid overload (such as furosemide, torsemide, etc.)

6. **Where clinically indicated, appropriate for age, ethnicity, and condition**, documented failure (after at least 3 months of use), contraindication per FDA label, intolerance, or not a candidate to maximally tolerated doses, to **one or more** of the following: (See Definitions section for examples)
   a. Hydralazine plus isosorbide dinitrate
   b. Digitalis
   c. Vericiguat

7. There are **NO** FDA-label contraindications, such as:
   a. Acute decompensated heart failure
   b. Blood pressure < 90/50 mmHg or clinically significant hypotension
   c. Sick sinus syndrome, unless has a functioning demand pacemaker
   d. Sinoatrial block, unless has a functioning demand pacemaker
   e. Third degree AV block, unless has a functioning demand pacemaker
   f. Resting heart rate < 60 bpm prior to treatment or clinically significant bradycardia
   g. Severe hepatic impairment (Child-Pugh Class C)
   h. Heart rate that is maintained exclusively by the pacemaker
   i. Simultaneous use of strong CYP3A4 inhibitors (see Definitions section)

8. Individual does not have second degree AV block, unless has a functioning demand pacemaker.

9. Individual does not have a demand pacemaker set to rates ≥ 60 beats per minute.

10. Individual does not have a creatinine clearance below 15 mL/min.

11. There are no significant interacting drugs:
    a. CYP3A4 inhibitor (See Definition section)
    b. CYP3A4 inducer (See Definition section)

Initial approval duration:
- If the individual has **NOT** been seen by a cardiologist within 6 months **AND** the request is for initial **OR** continuation of therapy: 60-day transition of care period to permit ample time to be seen by a cardiologist
- If seen by a cardiologist: 12 months

➢ **Criteria for continuation of coverage (renewal request):** Corlanor (ivabradine) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met (**samples are not considered for continuation of therapy**):

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Cardiologist at least yearly.

2. Individual's condition has responded while on therapy with response defined as **ONE** of the following:
    a. Response in an **individual 6 months of age or older** is defined as:
        i. Achieved and maintains a heart rate (HR) reduction of at least 20%, based on tolerability, without bradycardia or symptoms of bradycardia

    b. Response in an **individual 18 years of age or older** is defined as:
        i. There are no hospitalizations for heart failure in the last 12 months while on therapy
        ii. Achieved and maintains a resting heart rate between 50 and 60 beats per minute (bpm)

3. Individual has been adherent with the medication.

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4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use:
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Atrial fibrillation
        ii. Bradycardia
        iii. Sinus arrest
        iv. Heart block

5. There are no significant interacting drugs such as:
    a. CYP3A4 inhibitor (See Definition section)
    b. CYP3A4 inducer (See Definition section)

Renewal duration: 12 months

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VERQUVO™ (vericiguat)

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

  1. **Off-Label Use of Non-Cancer Medications**

  2. **Off-Label Use of Cancer Medications**

ENTRESTO (sacubitril and valsartan)

- **Criteria for initial therapy:** Entresto (sacubitril and valsartan) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Cardiologist.

  2. Individual has a confirmed diagnosis of **ONE** of the following:
     a. Individual is **18 years of age or older** with chronic heart failure (NYHA class II-IV) with a left ventricular ejection fraction (LVEF) that is below normal
     b. Individual is **1 year of age or older** with symptomatic heart failure (NYHA class II-IV or Ross Heart Failure class II-IV) with systemic left ventricular systolic dysfunction

  3. Left ventricular ejection fraction is **ONE** of the following:
     a. ≤ 40% **or** is ≥ 45% if there is structural heart disease (i.e., left atrial enlargement (LAE), left ventricular hypertrophy (LVH)) in an individual **18 years or older**
     b. ≤ 40% **or** has a fractional shortening of ≤ 20% in an individual **1year to 17 years**

  4. **Where clinically indicated, appropriate for age, ethnicity, and condition** individual is using maximally tolerated dose of guideline directed therapy using **ONE** agent in each of the following:
     a. Bisoprolol, carvedilol, or sustained release metoprolol
     b. Sodium-glucose cotransporter 2 (SGLT2) inhibitors (such as dapagliflozin, empagliflozin, etc.)
     c. Mineralocorticoid receptor antagonist (MRA, such as spironolactone or eplerenone)
     d. Diuretic agent as needed for fluid overload (such as furosemide, torsemide, etc.)

  5. There are **NO** FDA-label contraindications, such as:
     a. History of angioedema to previous ACE inhibitor therapy
     b. History of angioedema to previous ARB therapy
     c. Simultaneous use with ACE inhibitor therapy
     d. Simultaneous use with aliskiren (brand Tekturna or a generic) in patients with diabetes
     e. Use within 36 hours of an ACE inhibitor therapy

  6. Individual does not have severe hepatic impairment (Child-Pugh Class C).

  7. Individual does not have a history of angioedema, history of angioedema from use of ACE inhibitor or ARB, or a history of hereditary angioedema.

Initial approval duration:
- If the individual has **NOT** been seen by a cardiologist within 6 months **AND** the request is for initial **OR** continuation of therapy: 60-day transition of care period to permit ample time to be seen by a cardiologist
- If seen by a cardiologist: 12 months

➢ **Criteria for continuation of coverage (renewal request):** Entresto (sacubitril and valsartan) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met (**samples are not considered for continuation of therapy**):

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Cardiologist at least yearly.

2. Individual's condition responded while on therapy with response defined as **TWO** of the following:
    a. There has been a reduction in hospitalizations for heart failure in the last 12 months while on therapy compared to baseline or compared to previous year
    b. Achieves and maintains a reduction in B-type natriuretic peptide level (BNP) or N-terminal pro-BNP level
    c. There is no evidence of disease progression, defined as **either**:
        i. Worsening signs and symptoms of heart failure that requires intensification of heart failure therapy such as hospitalization with or without an intensive care unit stay
        ii. Worsening NYHA/Ross functional class

3. Individual has been adherent with the medication.

4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use:
    a. Contraindications as listed in the criteria Initial therapy section
    b. Significant adverse effect such as:
        i. Angioedema
        ii. Progressive and/or significant deterioration of kidney function

5. There are no significant interacting drugs.

Renewal duration: 12 months

➢ Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

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CORLANOR® (ivabradine)
ENTRESTO™ (sacubitril and valsartan)
VERQUVO™ (vericiguat)

VERQUVO (vericiguat)

- **Criteria for initial therapy:** Verquvo (vericiguat) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Cardiologist.
2. Individual is 18 years of age or older.
3. Individual has a confirmed diagnosis of Symptomatic worsening chronic heart failure (New York Heart Association Class II-IV).
4. Left ventricular ejection fraction is less than 45%.
5. Experiences episodes of worsening heart failure defined as **ONE** of the following:
    a. History of previous heart failure hospitalization within the last 6 months
    b. Out-patient intravenous diuretic for heart failure (without hospitalization) within previous 3 months
6. Systolic blood pressure is at least 100 mmHg or has no symptoms of hypotension.
7. **Where clinically indicated, appropriate for age, ethnicity, and condition** individual is using maximally tolerated dose of guideline directed therapy using **ONE** agent in each of the following:
    a. Bisoprolol, carvedilol, or sustained release metoprolol
    b. Angiotensin system inhibitor such as:
        i. Sacubitril-valsartan
        ii. Angiotensin converting enzyme (ACE) inhibitor (such as enalapril, lisinopril, etc.)
        iii. Angiotensin II receptor blocker (ARB) (such as candesartan, losartan, valsartan)
    c. Sodium-glucose cotransporter 2 (SGLT2) inhibitors (such as dapagliflozin, empagliflozin, etc.)
    d. Mineralocorticoid receptor antagonist (MRA, such as spironolactone or eplerenone)
    e. Diuretic agent as needed for fluid overload (such as furosemide, torsemide, etc.)
8. **Where clinically indicated, appropriate for age, ethnicity, and condition**, documented failure (after at least 3 months of use), contraindication per FDA label, intolerance, or not a candidate to maximally tolerated doses, to **one or more** of the following: (See Definitions section for examples)
    a. Hydralazine plus isosorbide dinitrate
    b. Digitalis
    c. Ivabradine
9. The individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
    a. A negative pregnancy test in a woman of childbearing potential
10. There are **NO** FDA-label contraindications, such as:
    a. Concurrent use with other soluble guanylate cyclase stimulators such as Adempas (riociguat)
    b. Woman of childbearing potential who is pregnant

11. Will not be used with phosphodiesterase-5 (PDE-5) inhibitors such as sildenafil, tadalafil, vardenafil.

12. Will not be used in individuals with estimated glomerular filtration rate (eGFR) less than 15 mL/min/1.73m^2 or on dialysis.

13. Will not be used in individuals with severe hepatic impairment (Child-Pugh Class C).

14. There are no significant interacting drugs.

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Verquvo (vericiguat) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met (**samples are not considered for continuation of therapy**):

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Cardiologist.

2. Individual's condition has responded while on therapy with response defined as **THREE** of the following:
    a. There has been a reduction in hospitalizations for heart failure in the last 12 months while on therapy compared to baseline or compared to previous year
    b. There are no out-patient visits for intravenous diuretic for heart failure (without hospitalization)
    c. Achieves and maintains a reduction in B-type natriuretic peptide level (BNP) or N-terminal pro-BNP level
    d. There is no evidence of disease progression, defined as **either**:
        i. Worsening signs and symptoms of heart failure that requires intensification of heart failure therapy such as hospitalization with or without an intensive care unit stay
        ii. Worsening NYHA functional class

3. Individual has been adherent with the medication.

4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Symptomatic hypotension
        ii. Syncope

5. There are no significant interacting drugs.

Renewal duration: 12 months

CORLANOR® (ivabradine)
ENTRESTO™ (sacubitril and valsartan)
VERQUVO™ (vericiguat)

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

  1. **Off-Label Use of Non-Cancer Medications**

  2. **Off-Label Use of Cancer Medications**

Description:

Corlanor (ivabradine) is indicated to reduce the risk of hospitalization for worsening heart failure in adult patients with stable, symptomatic chronic heart failure with reduced left ventricular ejection fraction and it is indicated for the treatment of stable symptomatic heart failure due to dilated cardiomyopathy (DCM) in pediatric patients aged 6 months and older.

Ernesto (sacubitril and valsartan) is a combination of the neprilysin inhibitor, sacubitril, and the angiotensin II receptor blocker (ARB), valsartan. In adults, it is indicated to reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure. The benefits are most clearly evident in patients with left ventricular ejection fraction (LVEF) below normal. Ernesto (sacubitril and valsartan) is also indicated for the treatment of symptomatic heart failure with systemic left ventricular systolic dysfunction in pediatric patients aged one year and older. It reduces NT-proBNP and is expected to improve cardiovascular outcomes.

Verquvo (vericiguat) is indicated to reduce the risk of cardiovascular death and heart failure hospitalization following a hospitalization for heart failure or need for outpatient intravenous (IV) diuretics, in adults with symptomatic chronic HF and ejection fraction less than 45%.

Heart failure (HF) is a complex chronic progressive clinical syndrome in which the heart muscle is unable to pump enough blood to meet the body's needs. The diagnosis is made based on a careful history and physical examination. The mortality rate is high, with approximately 50% of patients will die within five years of diagnosis despite the availability of medications with proven mortality benefit.

The New York Heart Association (NYHA) categorizes HF into four classes depending on a patient's functional status, ranging from no limitation in physical activity (Class I), to an inability to carry out any physical activity without discomfort (Class IV). Treatment options for NYHA class II to IV heart failure with reduced ejection fraction include angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor blocker (ARB), angiotensin receptor neprilysin inhibitors (ARNIs), beta-blockers (bisoprolol, carvedilol, or sustained release metoprolol), and mineralocorticoid receptor antagonist (MRA such as eplerenone or spironolactone). Loop diuretics and vasodilators (hydralazine with isosorbide dinitrate) are added depending on symptoms and ethnicity. Digoxin may also be used in certain circumstances.

According to current guidelines, beta-blockers and ACE inhibitors, ARBs, or ARNIs are the cornerstone of the management of HF and have been shown in randomized controlled studies to reduce HF associated morbidity and mortality. Corlanor (ivabradine) has not been evaluated as monotherapy in the treatment of heart failure with reduced ejection fraction (HFrEF) or in the treatment of HF with preserved ejection fraction (HFpEF). Entresto

(sacubitril and valsartan) has not been evaluated for monotherapy for heart failure with reduced ejection fraction, for the treatment of heart failure with preserved ejection fraction, or in the treatment of hypertension.

Signs and symptoms of HF are a result of compensatory mechanisms involved in an effort to restore cardiac output. Neurohumoral adaptations include activation of the renin-angiotensin-aldosterone (RAAS) and the sympathetic adrenergic nervous system, increased release of vasopressin (antidiuretic hormone) and various natriuretic peptides. The net effect of the neurohumoral response is to cause vasoconstriction and to increase blood volume. Over time, these compensatory changes can worsen heart failure. Prolonged HF also leads to a depletion of several endogenous vasoactive peptides are involved in vasodilation, natriuresis, diuresis, and inhibition of pathologic growth and fibrosis.

Vasoactive peptides include atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), C-type natriuretic peptide (CNP), bradykinin, adrenomedullin, substance-P, vasoactive intestinal peptide, and calcitonin gene regulated peptide. Release into the circulation is stimulated by sodium overload, increase in extracellular volume, distension of auricles and ventricles. Their plasma half-life is very short as they are inactivated by neprilysin which degrades these to inactive products. Neprilysin expression is upregulated in heart failure patients. Inhibition of neprilysin increases the levels of vasoactive peptides, countering the neurohurmoral overactivation that contributes to vasoconstriction, sodium retention, and maladaptive remodeling.

Assays for BNP (B-type natriuretic peptide) and NTproBNP (N-terminal pro-B-type natriuretic peptide), are both natriuretic peptide biomarkers, have been used increasingly to establish the presence and severity of heart failure. A substantial evidence base exists that supports the use of natriuretic peptide biomarkers to assist in the diagnosis or exclusion of heart failure as a cause of symptoms. Current clinical practice guidelines give a Class I recommendation to measure BNP or NT-proBNP to support a clinical diagnosis of heart failure, to assess disease severity, or to establish prognosis.

Angiotensin II that interacts with its AT-1 receptor causes vasoconstriction, sodium and water retention, and fibrosis/hypertrophy. Use of an ARB prevents these actions of angiotensin II.

Corlanor (ivabradine) is a hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blocker. The HCN channel is responsible for the cardiac pacemaker inward funny (I_f) current, which regulates heart rate. The current is activated during the resting potential stage and accelerates diastolic depolarization of the sinus node. In clinical electrophysiology studies, the cardiac effects were most pronounced in the sinoatrial (SA) node, but prolongation of the AH interval has occurred on the surface ECG, as has PR interval prolongation. Ivabradine reduces the spontaneous pacemaker activity of the cardiac sinus node by selectively inhibiting I_f current, resulting in a reduction in heart rate with no effect on ventricular repolarization and no effects on myocardial contractility.

Corlanor (ivabradine) causes a dose-dependent reduction in heart rate. The size of the effect is dependent on the baseline heart rate (i.e., greater heart rate reduction occurs in subjects with higher baseline heart rate). It does not have negative inotropic effects. Ivabradine increases the uncorrected QT interval with heart rate slowing but does not cause rate-corrected prolongation of QT.

Ivabradine can also inhibit the retinal current I_h. I_h is involved in limiting retinal responses to bright light stimuli. Under triggering circumstances (e.g., rapid changes in luminosity), partial inhibition of I_h by ivabradine may cause luminous phenomena experienced by patients. Luminous phenomena (phosphenes) are described as a transient enhanced brightness in a limited area of visual field.

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Sacubitril is a prodrug that is converted to its active metabolite which inhibits neutral endopeptidase (neprilysin). Valsartan inhibits the effects of angiotensin II by selectively blocking at the angiotensin (AT)-1 receptor and it inhibits angiotensin II-dependent aldosterone release.

Verquvo (vericiguat) is a stimulator of soluble guanylate cyclase (sGC), an important enzyme in the nitric oxide (NO) signaling pathway. When NO binds to sGC, the enzyme catalyzes the synthesis of intracellular cyclic guanosine monophosphate (cGMP), a second messenger that plays a role in the regulation of vascular tone, cardiac contractility, and cardiac remodeling. Heart failure is associated with impaired synthesis of NO and decreased activity of sGC, which may contribute to myocardial and vascular dysfunction. By directly stimulating sGC, independently of and synergistically with NO, vericiguat augments levels of intracellular cGMP, leading to smooth muscle relaxation and vasodilation.

Definitions:

Strong inhibitors of Cytochrome P450 3A4: (list is not all inclusive)
- Azole antifungals: itraconazole, ketoconazole
- Macrolide antibiotics: clarithromycin, telithromycin
- HIV protease inhibitors: nelfinavir
- Nefazodone

Moderate inhibitors of Cytochrome P450 3A4: (list is not all inclusive)
- Calcium channel blockers: diltiazem, verapamil
- Grapefruit juice

Inducers of Cytochrome P450 3A4: (list is not all inclusive)
- St. John's wort
- Rifampin
- Barbiturates
- Phenytoin

New York Heart Association (NYHA)/Ross Heart Failure Classification:

	Adult – NYHA Heart Failure	Infant and Children – Ross Heart Failure
Class I	No symptoms and no limitation in ordinary physical activity, e.g., shortness of breath when walking, climbing stairs etc.	No limitations or symptoms
Class II	Mild symptoms mild dyspnea and/or angina, fatigue, palpitations, and slight limitation during ordinary activity or moderate exercising but not during rest	Infant: mild tachypnea or diaphoresis with feeding; older child: mild to moderate dyspnea on exertion; no growth failure
Class III	Marked limitation in activity due to symptoms, even during less-than-ordinary activity, e.g., walking short distances (20-100 m) or minimal exertion that interfere with normal daily activity, comfortable only at rest	Infant: marked tachycardia or diaphoresis with feeding, prolonged feeding times; older child: marked dyspnea on exertion; growth failure from CHF
Class IV	Severe limitations, unable to carry out any physical activity because experiences symptoms even while at rest that worsen with any exertion, mostly bedbound patients	Symptomatic at rest with tachypnea, retractions, grunting, or diaphoresis

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American College of Cardiology (ACC)/American Heart Association (AHA) Stages of HF:

Stage A: At high risk for HF	No symptoms, structural heart disease, or cardiac biomarkers of stretch injury
Stage B: Pre-HF	No symptoms or signs but has evidence of 1 of the following: Structural heart disease Increased filling pressures Other risk factors – increased BNP or persistently elevated cardiac troponins
Stage C: Symptomatic HF	Structural heart disease with prior or current symptoms of HF
Stage D: Advanced HF	Marked HF symptoms that interfere with daily life and with recurrent hospitalizations despite attempts to optimize guideline directed therapy

Normal Resting Heart Rate and Bradycardia for age:

Age	Normal
0-1 months	70-190 beats per minute
1-11 months	80-160 beats per minute
1-2 years	80-130 beats per minute
3-4 years	80-120 beats per minute
5-6 years	75-115 beats per minute
7-9 years old	70-110 beats per minute
10 years and older	60-100 beats per minute
Well trained athletes	40-60 beats per minute

Fractional Shortening:

The reduction of the length of the end-diastolic diameter that occurs by the end of systole. Using the M-Mode the parameters left ventricular end-systolic diameter (LVESD) and the left ventricular end-diastolic diameter (LVEDD) are derived. Using the formula: (LVEDD - LVESD / LVEDD) x 100, the percentage of size differences of the left ventricle as a factor of how well the left ventricle is contracting is calculated. Like the ejection fraction, this is a measure of the heart's muscular contractility. If the diameter fails to shorten by at least 28%, the efficiency of the heart in ejecting blood is impaired. Normal range is 26–45%, Mild is 20–25%, Moderate is 15–19%, and Severe is < 15%. Using 2D measurement, the normal fractional shortening is > 18%.

Other medications used in Heart Failure:

Angiotensin Converting Enzyme (ACE) Inhibitors: Benazepril Captopril Enalapril Fosinopril Lisinopril Moexipril Perindopril Quinapril Ramipril Trandopril	Angiotensin II Receptor Antagonists (ARB): Candesartan Losartan Valsartan	Mineralocorticoid receptor antagonist (MRA): Eplerenone Spironolactone	Loop Diuretics: Bumetanide Ethacrynic acid Furosemide Torsemide
Angiotensin Receptor-Neprilysin Inhibitor (ARNI): Sacubitril-valsartan	Vasodilator + Nitrate: Hydralazine + Isosorbide dinitrate	Soluble guanylate cyclase inhibitor: Vericiguat	Sodium-glucose cotransporter 2 (SGLT2) inhibitors: Canagliflozin Dapagliflozin Empagliflozin

Resources:

Corlanor (ivabradine) product information, revised by Amgen, Inc. 08-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed June 08, 2022.

Entresto (secubitril and valsartan) product information, revised by Novartis Pharmaceuticals Corporation 02-2021, at DailyMed http://dailymed.nlm.nih.gov. Accessed June 08, 2022.

Verquvo (vericiguat) product information, revised by Merck Sharp and Dohme Corp. 05-2022, at DailyMed http://dailymed.nlm.nih.gov. Accessed June 08, 2022.

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Singh RK, Singh TP. Heart failure in children: Management. In: UpToDate, Triedman JK, Armsby C (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated June 05, 2019. Accessed June 08, 2022.

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