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Entresto for HF

There's a new kid on the block for treating heart failure (HF). Entresto® landed in the ODB Formulary last year. After a slow start, it has gained traction in some of our facilities.

HF occurs when the heart is unable to pump enough blood to satisfy the needs of the organ systems and tissues of the body. There are two categories of HF based on the heart's ejection fraction (EF). EF is the percentage of blood pumped from the left ventricle of the heart with each contraction. HF with a low ejection fraction (< 35 - 40%) is called HF_rEF. The "rEF" stands for reduced EF. Patients with HF_pEF have a "preserved" ejection fraction (>50%). These patients generally have thickened ventricles that hold less blood, so although the percentage pumped seems good, the volume leaving the heart is not.

In HF, the renal blood flow is reduced. The kidneys respond by releasing renin, an enzyme that ultimately leads to the production of Angiotensin II (AT2). AT2 constricts arteries to increase blood pressure and

trigger the release of a hormone called aldosterone, which "instructs" the kidneys to retain sodium and water. AT2 is one of the bad guys in HF, and we reduce it by using ACE inhibitors (e.g. Altace/ramipril and Coversyl) which limit AT2 production or ARBs (e.g. valsartan and candesartan) which block its activity.

Beta blockers are also used in HF. They reduce heart rate and workload. Diuretics eliminate excess fluid from the lungs and extremities. Some residents also have spironolactone added to block the action of aldosterone, reducing sodium and water retention. Unfortunately, potassium may accumulate with this drug. Hyperkalemia can be very dangerous, especially when renal function is poor.

These meds are helpful when EF is low (HF with preserved EF is more challenging) but hospitalizations and death can be unavoidable if the HF advances. The heart tries to "save itself" by producing proteins called Natriuretic Peptides (NP). The NPs cause blood vessels to dilate (lower BP), enhance Na and water loss from the kidney and improve the efficiency of cardiac muscle contraction, among other things. These wonderful NPs have a very short lifespan, however, as they are rapidly degraded by enzymes. Entresto® reduces the activity

of one of these enzymes, neprilysin, so the NPs "hang around" longer and continue to do their good work.

The PARADIGM-HF study looked at 8,442 patients with moderate (class II) to advanced (class IV) HF. It compared the ACEI, enalapril, to Entresto® (sacubitril/valsartan). Entresto® diminished hospitalizations and mortality by about 20%. The Entresto® group had less hyperkalemia, cough and renal impairment than the enalapril group. Angioedema was rare in each group and hypotension was higher with Entresto®.

The milligram content of Entresto® is a bit unusual. The 50mg tablet contains 24.3mg of sacubitril and 25.7mg of the ARB valsartan. It also comes in 100 and 200mg strengths in the same proportions. ODB will only cover Entresto® (LU 497) if an ACEI or ARB has been used for four weeks and response has been suboptimal. For those taking an ACEI, a 36-hour washout is required to reduce the risk of angioedema. The drug is given BID and is quite expensive (\$250/month).

Crushing Eliquis

Eliquis® can now "officially" be crushed and added to apple sauce, apple juice, or suspended in 60ml water for instillation into a G-tube. It joins Xarelto®, as the only new (NOAC) oral anticoagulants that can be crushed.

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