Supporting Evidence for the Development of a Decision Aid for For Patients with Heart Failure and Reduced Ejection Fraction Who Are Considering Treatment with an Angiotensin Receptor-Neprilysin Inhibitor (ARNI)

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Introduction

The angiotensin receptor-neprilysin inhibitor (ARNI) sacubitril/valsartan, when compared to the angiotensin converting enzyme inhibitor (ACEI) enalapril among patients with heart failure and reduced ejection fraction (HFrEF), has been shown to significantly improve survival (mortality at 27 months, 19.8% enalapril and 17.0% sacubitril/valsartan) and freedom from hospitalization (first hospitalization for worsening HF, 15.6% enalapril, 12.8% sacubitril/valsartan). The medical side-effect profiles of ARNI and ACEI are similar. As such, clinical practice guidelines recommend (level I) use of ARNI in place of ACEI (or an angiotensin receptor blocker [ARB]) in patients with HFrEF. However, sacubitril/valsartan is still a patented medication, and as such, can be relatively expensive for patients. Surveys show that out-of-pocket medication costs are important to patients and factor into medical decision making and ongoing medication adherence.

To this end, we developed a short, easy-to-read ARNI patient decision aid (PtDA). This online ARNI PtDA, developed by the Colorado Program for Patient Centered Decisions (www.patientdecisionaid.org), describes the medications, their risks and benefits, and the potential cost trade-off, all while encouraging patients to consider their values and needs within the context of this information. PtDAs increase patient knowledge and satisfaction while reducing decisional conflict and regret. The primary goal of this PtDA is to help support a healthy shared decision-making process for ACEI, ARB, and ARNI, which in turn promotes long-term use of these agents for patients with HFrEF.

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Development Process

The development of the ARNI PtDA followed the principles as outlined in the Ottawa Decision Support Framework and the International Patient Decision Aid Standards (IPDAS).

Ottawa Decision Support Framework (ODSF)

The Ottawa Decision Support Framework (ODSF) is an evidence-based, practical, mid-range theory for guiding patients making health or social decisions. It uses a three-step process: assess client and practitioner determinants of decisions to identify decision support needs; provide decision support tailored to client needs; and evaluate the decision-making process and outcomes.

SECTION I: SOURCES OF STATISTICS AND INFORMATION PUT FORTH IN THIS DECISION AID

I. Needs Assessment

Pubmed, Web of Science, and the Ottawa Hospital Research Institute (OHRI) complete patient decision aid inventory were scanned for patient decision aids (PtDAs) to assess existing publically available decision support for patients considering switching to an ARNI. Zero publically available PtDAs for medication change to an ARNI were found. The most recent search was conducted in April 2018.

Review of Evidence

The vast majority of data comparing the effect of ACEI versus ARNI on patient outcomes in HFrEF come from the Prospective Comparison of ARNI with ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure Trial (PARADIGM-HF). While there have been other studies examining the effects of the ARNI on patients, they have not applied directly to our targeted patient population (see summary of risks and benefits for more details). We focused on outcomes of primary interest to patients, namely mortality, hospitalizations, quality of life, specific side-effects, and burdens of taking the medications. We also reviewed the literature on the importance of cost in patient decisions surrounding medical choices (see section on cost inclusion in the decision aid for more details). Given the apparent benefit of ARNI on survival with a relatively similar medical side-effect profile, cost is the primary counter-consideration in transitioning patients from ACEI or ARB to ARNI. Currently, no decision aids exist for patients considering ARNI therapy. In addition, very few decision aids address medication costs to patients.

The consolidation of this evidence, and the resulting patient decision aid, can be found at www.patientdecisionaid.org (SupportingEvidence.pdf).

II. Decision Aid Development

Based on our needs assessment, we developed an initial draft of the paper tool which underwent a process of iterative testing to assure accuracy, readability and lack of bias including.

Interviews with Patients and Health Providers

Interviews with patients and clinicians were conducted. Patients were recruited from a large public hospital with a strong heart failure program and interviewed about their experiences with their medications, opinions and comfort levels regarding discussion of medications with their healthcare provider, beliefs about the importance of cost in healthcare, and preferred method of receiving information about healthcare. They were also asked for their opinions of drafts of the PtDA and were encouraged to provide constructive feedback. To see the iterative process, refer

to feedback log. A log of all feedback provided by patients and clinicians was maintained to track the iterative process. It includes the reviewer's name and comments along with reasoning for selecting or declining the suggestions. All selections were agreed to by the study team.

SECTION I: SOURCES OF STATISTICS PUT FORTH IN THIS PATIENT DECISION AID

BENEFIT: MORTALITY

STUDY	YEAR	SUBJECTS (N=)	DURATION	POPULATION	DESIGN	RESULTS		
						INTERVENTION	*CONTROL*	*P-VALUE*
PARADIGM-HF[1]	2014	8,442	27 months (median follow-up)	≥ 18 years of age; NYHA II, III or IV symptoms; EF of ≤ 40%; BNP ≥ 150 pg per mill or NT-proBNP ≥600 pg per mill (if hospitalized in the last 12 months, BNP of ≥ 100 pg per mill or an NT-proBNP of ≥ 400 pg per mill).	Angiotensin-neprilysin inhibitor (LCZ696) vs. ACE inhibitor (enalapril)	17.0% death from any cause	19.8% death from any cause	<0.001

BENEFIT: HOSPITALIZATION

STUDY	YEAR	SUBJECTS (N=)	DURATION	POPULATION	DESIGN	RESULTS		
						INTERVENTION	*CONTROL*	*P-VALUE*
PARADIGM-HF[1]	2014	8,442	27 months (median follow-up)	≥ 18 years of age; NYHA II, III or IV symptoms; EF of ≤ 40%; BNP ≥ 150 pg per mill or NT-proBNP ≥600 pg per mill (if hospitalized in the last 12 months, BNP of ≥ 100 pg per mill or an NT-proBNP of ≥ 400 pg per mill).	Angiotensin-neprilysin inhibitor (LCZ696) vs. ACE inhibitor (enalapril)	12.8% first hospitalization for worsening heart failure	15.6% first hospitalization for worsening heart failure	<0.001

RISK: HYPOTENSION

STUDY	YEAR	SUBJECTS (N=)	DURATION	POPULATION	DESIGN	RESULTS		
						INTERVENTION	*CONTROL*	*P-VALUE*
PARADIGM-HF[1]	2014	8,442	27 months (median follow-up)	≥ 18 years of age; NYHA II, III or IV symptoms; EF of ≤ 40%; BNP ≥ 150 pg per mill or NT-proBNP ≥600 pg per mill (if hospitalized in the last 12 months, BNP of ≥ 100 pg per mill or an NT-proBNP of ≥ 400 pg per mill).	Angiotensin-neprilysin inhibitor (LCZ696) vs. ACE inhibitor (enalapril)	14.0% developed symptomatic hypotension; 2.7% developed symptomatic hypotension with systolic bp <90 mm Hg	9.2% developed symptomatic hypotension; 1.4% developed symptomatic hypotension with systolic bp <90 mm Hg	<0.001

RISK: HYPERKALEMIA

STUDY	YEAR	SUBJECTS (N=)	DURATION	POPULATION	DESIGN	RESULTS		
						INTERVENTION	*CONTROL*	*P-VALUE*
PARADIGM-HF[1]	2014	8,442	27 months (median follow-up)	≥ 18 years of age; NYHA II, III or IV symptoms; EF of ≤ 40%; BNP ≥ 150 pg per mill or NT-proBNP ≥600 pg per mill (if hospitalized in the last 12 months, BNP of ≥ 100 pg per mill or an NT-proBNP of ≥ 400 pg per mill).	Angiotensin-neprilysin inhibitor (LCZ696) vs. ACE inhibitor (enalapril)	16.1% had a serum potassium of >5.5 mmol/liter; 4.3% had a serum potassium of >6.0 mmol/liter.	17.3% had a serum potassium of >5.5 mmol/liter; 5.6% had a serum potassium of >6.0 mmol/liter.	0.15; 0.007

RISK: COUGH

STUDY	YEAR	SUBJECTS (N=)	DURATION	POPULATION	DESIGN	RESULTS		
						INTERVENTION	*CONTROL*	*P-VALUE*
PARADIGM-HF[1]	2014	8,442	27 months (median follow-up)	≥ 18 years of age; NYHA II, III or IV symptoms; EF of ≤ 40%; BNP ≥ 150 pg per mill or NT-proBNP ≥600 pg per mill (if hospitalized in the last 12 months, BNP of ≥ 100 pg per mill or an NT-proBNP of ≥ 400 pg per mill).	Angiotensin-neprilysin inhibitor (LCZ696) vs. ACE inhibitor (enalapril)	11.3% developed a cough	14.3% developed a cough	<0.001

RISK: RENAL IMPAIRMENT

STUDY	YEAR	SUBJECTS (N=)	DURATION	POPULATION	DESIGN	RESULTS		
						INTERVENTION	*CONTROL*	*P-VALUE*
PARADIGM-HF[1]	2014	8,442	27 months (median follow-up)	≥ 18 years of age; NYHA II, III or IV symptoms; EF of ≤ 40%; BNP ≥ 150 pg per mill or NT-proBNP ≥600 pg per mill (if hospitalized in the last 12 months, BNP of ≥ 100 pg per mill or an NT-proBNP of ≥ 400 pg per mill).	Angiotensin-neprilysin inhibitor (LCZ696) vs. ACE inhibitor (enalapril)	0.7% discontinued use due to renal impairment	1.4% discontinued use due to renal impairment	0.002

Risks and Benefits Summary:
Currently, there is only one phase 3 clinical trial in HFrEF for the comparison of sacubitril/valsartan to an ACEI (enalapril), the previous standard of care. While other studies have examine the effects of an ARNI, they have been within the context of hypertension[2], or HFrEF[3], these patient populations are not among the population being targeted by this decision aid. Given the singular nature of the data from the PARADIGM trial, we chose to report the outcomes that were determined to be either key primary outcomes for the study (mortality and hospitalization) as well as the most common side effects (hypotension, hyperkalemia, cough and renal impairment).

COST OF SACUBITRIL/VALSARTAN BY INSURANCE STATUS

Insurance-Related Cost Summary:
We chose to utilize the pharmacy websites, GoodRx and Blink, as the sources for our cost data. These websites offer a comprehensive overview of medication pricing by pharmacy, insurance plan, and location. The reported deductible for uninsured patients fell between $410.00 and $498.00, so we chose to represent a median value for this group. Due to the wide range of potential out-of-pocket costs for those with partial coverage, we chose to simply report that costs may vary widely. Finally, after browsing potential costs for various private plans, we chose a median range of $39.00-$45.00 for those with good coverage.

INSURANCE STATUS	PRICE	SOURCE
Uninsured	~$480.00 month	Goodrx.com; Blinkhealth.com; wellrx.com
Partial Coverage	Cost varies widely	Goodrx.com (co-pay range is reported as anywhere between $17.00-$533.00)
Good Coverage	$39.00-$45.00/month	Goodrx.com

Evidence for the Inclusion of Cost in a Patient Decision Making
Cost is of central importance to this PtDA. The primary benefits of the ARNI derive from improve patient outcomes: it offers patients lower morbidity and mortality. Meanwhile, ARNI has very similar methods of delivery, timing of delivery, and side-effect profiles to ACEI and ARB; the major discernable difference is cost. Furthermore, there is significant evidence that patients are interested in obtaining cost information about their medications[4-6]. In a recent survey asking patients to identify key characteristics of high-value health care, a plurality (45%) chose “My Out-of-Pocket Costs Are Affordable,” whereas only 32% chose “My Health Improves.” Given the chance to select the five most important value characteristics, 90% of patients chose combinations different from any combination chosen by physicians; in general, cost and service were far more important in determining value for patients than for physicians[7]. A study of 110 patient-provider dyads at three large internal general medicine practices found that 63% of patients surveyed were interested in treatment cost information, and wanted to discuss cost with their physician[6]. While the majority of physicians reported being aware of these desires, only 15% of patients and 35% of physicians had ever actually discussed cost[8]. Another study of 5,085 patients from the longitudinal Translating Research Into Action for Diabetes Study found that two-thirds of the patients interviewed were interested in discussing trade-off strategies around their medications: 38% of these patients indicated they’d be interested in discussing lower-cost drugs with a higher chance of adverse effects[4]. However, of the patients who expressed interest in cost trade-offs, only 19% reported actually discussing medication cost with their provider[8]. Access to straight-forward comparative cost information has also been found to help patients make higher-quality healthcare decisions[9]. Taken together, both the desire for cost

information and higher-quality healthcare decisions made by patients with access to comparative cost information suggests that cost is, in fact, a crucial component of most medical shared decision making.

SECTION II: PATIENT AND PROVIDER FEEDBACK LOGS

We iteratively developed this PtDA over a period of 12 months. In order to create a well-rounded PtDA, we approached a number of stakeholders for feedback during this time, including both patients and healthcare providers. Feedback came in the form of in-depth, one-on-one interviews regarding the content of the PtDA, group discussion with a patient advisory panel, feedback from a group of providers in cardiology, and less formal feedback from team members and other trusted peers. Additionally, we received further feedback from Novartis, the commercial owner of the patent to the only available ARNI. This resulted in roughly 15 rounds of revision, each with a distinct iteration of the PtDA. Changes included anything from color scheme to wording around certain terms or concepts. All changes implemented during this period are recorded in chronological order in the patient and provider feedback log below.

Date Rec	Reviewer	Stakeholder Suggestions	Reasoning behind Changes
02/16/17	Internal team or team member	**General Impressions:** • Format: page 1 Intro, page 2 options, page 3 cost, page 4 questions • Use sacubitril/valsartan throughout, not Entresto **Page 2:** • Leave cost issue out of benefits/risks on page 2; needs separate page **Page 3:** • have three patient scenarios, 1 with insurance, one without, one with Medicare part D, describing cost of sacubitril/valsartan for each • At bottom of page, have a prompt to call insurance company and “record what Sacubitril/Valsartan costs you here”	Early development stage of decision aid; internal team members were drafting the first version. All suggested changes were made.
03/04/17	Internal team or team member	**General Impressions:** • Try to consolidate DA to four pages • Shorten first page, shrink hero image and combine content of page 1 &2 Page 2:	Early development stage of decision aid; internal team members were drafting the first version. All suggested changes were made.

		• Present just all-cause death rate, not hospitalization and cardiac deaths Page 3: • Not sure like three scenarios—maybe get rid of	
03/05/17	Internal team or team member	**General Impressions:** • Put generic names in lower case, brand names in upper case **Page 1:** • Include term “neprilysin inhibitor” in description of how drug works on page 1 **Page 2:** • Change figure showing cardiac mortality & hospitalization outcomes to just all-cause mortality outcomes	Early development stage of decision aid; internal team members were drafting the first version. All suggested changes were made.
03/08/17	Internal team or team member	**Page 1:** • Get rid of “it replaces” on page one, paragraph 2. • Use just one bottle of Entresto in image on page 1 • Like up bullet points for brand names of ACEI and ARB • Incorporate sentence about how these medicines work on page 1 • Change “highest dose” to “current dose” on page 1 • On page two, get rid of “what they do” section; include on page 1 **Page 2:** • Change “felt better and had fewer hospitalizations” to “felt better, lived longer, and had fewer hospitalizations” • Make the three hearts saved in the sacubitril/valsartan	Early development stage of decision aid; internal team members were drafting the first version. All suggested changes were made.

		figure green so can differentiate • Add figure between ACEI and sacubitril/valsartan that shows that red hearts=alive and black hearts=dead • Change highlighted differences in Form of Admin and Risks and Side Effects from yellow to dark red so stands out more **Page 3:** • Pg. 3. Change "Big Difference" to "Big Trade-Off" • Shrink patient figures and move questions from page 4 about cost to page 3 • Switch patient images; while male should be patient C, white female patient B • Simplify patient C insurance explanation • Get rid of last line in third paragraph; self-explanatory **Page 4**: • Page 4: add figure to show cost/benefit trade-off of switching (see-saw a la colon cancer DA)	
03/10/17	Internal team or team member	**Page 3:** • "Less I more" in terms of information on patient C—suggest cutting out super specific information in favor of more general, like: "Patient C has **partial coverage.** Some people have insurance plans which only cover a part of the cost. This can vary widely! It is important to call your insurance company and make sure you can afford this medication before starting.	Early development stage of decision aid; internal team members were drafting the first version. All suggested changes were made.

		• Change trade-offs graphic from see-saw to something else; patients interpret cost/benefit in opposite manner (higher=greater/heavier)	
03/11/17	Internal team or team member	**Page 1:** - Tweak definition of how medicines work on page 1; *"What these drugs do: ACEI and ARB work by relaxing blood vessels so that blood can flow more easily, which makes it easier for your heart to pump blood to your body. Entresto pairs an ARB with a unique neprilysin inhibitor drug, and the combination of these two appears to work even better than ARB or ACEI alone."* **Page 2:** • For page 2 use darker background for lighter fonts to make sure it pops. • Try not to split concepts/words from the end of one line onto the next line. **Page 3:** • Change "big trade off" on page 3 to "main trade off" • Cut out redundant text(patient A: good insurance: patient A has good insurance) above figures on pg. 3 **Page 4**: • Suggest sub different graphics (strongman heart and dollar sign) for see-saw; use size to differentiate trade-off	Early development stage of decision aid; internal team members were drafting the first version. All suggested changes were made.
3/17/20	Internal team or team member	**Page 3:** • Incorporate script for patient to use when they call their insurance company to ask about medicine: "*My doctor is considering switching me to Entresto (*the brand name of	Early development stage of decision aid; internal team members were drafting the first version. All suggested changes were made.

		sacubitril/valsartan*) twice a day. Would you please tell me how much it would cost on my plan for a month of this medicine?"*	
03/19/17	Internal team or team member	**Page 1:** • On page 1, boxes on the left show the medicine class with the generic below; the medicine on the right is the generic with the brand below. Should be consistent. • On page one, make the box larger to include the pill box in the picture with drug names **Page 2:** • On pg 2, under forms of admin, change "orally" to "by mouth" and "pill form" to "pill" for low literacy patients. • Can we change ACEI to ACE? Feels like too many initials. • The graphics on page 2 are a little hard to follow; consider changing to a table that includes 3 columns • Will people understand the "three lives saved" part of the graphic on page 2? Suggest keeping in 83/100 to keep consistent with ACEI **Page 3:** • Like the part about "call your insurance company" on page 3; maybe add "your doctor can also send a prescription to the pharmacy and they can figure out the cost for you" • Some of the language around cost could probably still be shortened and modified.	Accepted and modified; on page 3, have made it two options, option 1 to call insurance company and option 2 to ask your doctor to run a prescription through your pharmacy. Rejected change re: out-of-pocket cost; trying to cut down on text, and felt current text specifying cost could vary widely was sufficient. Also got rid of cost/benefit heart and money sign graphic on page four entirely. Rejected change of ACEI to ACE; two different things, so would not be appropriate to abbreviate. Did, however, remove dash so there are fewer characters. Rejected change to page 2 to turn graphics in to a table; it made the page look too busy and cluttered Rejected getting rid of "three lives saved" on page two; part of decision aid is to highlight the difference in survival between the two medicines Agreed and shortened.

		• On page 3, mention that out-of-pocket cost can change over time. • Remove word “relatively” on page 3 • Cost of Lisinopril gets lost on page 3; need to highlight that **Page 4:** • Do not like graphic of weightlifting heart and money sign as visual representation of cost on page 4; feels like it implies those who can’t afford medicine are going to be weak and are losers. **General Impressions:** • Can we change ACEI to ACE? Feels like too many initials.	Agreed and added. Agreed and removed. Agreed—incorporated information about cost of Lisinopril in to each scenario. Agreed and changed; created a values clarification scale for cost instead. Disagreed—this is how most educational materials and literature abbreviate ACE Inhibitors.
3/20/17	Internal team or team member	**Page 3:** • Incorporate section on page 3 that offers suggestions about ways to lower cost; Entresto Central program, Patient Assistance, ask health care provider if they know of any coupons. • Add dosing information to phone call script on page 3 (60 tablets of 49/51 mg) so patients can specify to insurance agent when asking about how much it will cost them personally.	Agreed and accepted all suggested changes.
3/29/17	Patient	**Page 2:** • Concerned with side effects regarding kidneys; very wary of taking medicine because of that **Page 3:** • Felt page 3 was not particularly helpful; “didn’t tell me how much it’s gonna cost”	Tailored estimates for the cost of Sacubitril/Valsartan is not possible for this DA

		• Confused by "Lisinopril is <$10 per month" on page 3—did not link Lisinopril back to being an ACEI	Changed sentence about cost of Lisinopril on page 3 to " Lisinopril, **an ACEI**, is <$10 per month" to tie back to ACEI
3/29/17	Patient	**Page 2:** • Really liked the box in the middle of page 2 explaining sacubitril. **Page 3:** • Liked inclusion of patient assistance programs information on page 3; "people should know about those" **General Impressions:** • Thought the things were explained in a straightforward manner, could easily understand issues at hand; just felt that "if the medications are doing their job, and you can pay less, you know, it's kinda more the fact that you're gonna lean that way"	No changes were made based off of this interview, as patient did not have any content-related suggestions.
3/29/17	Patient	**General Impressions:** • Expressed opinion that this was not his decision, that he would never use something like this, that it was his doctors' decision as the expert **Page 1:** • Really put-off by "appears to work better" on page 1; felt it sounded like advertising, and why would he switch to something that only "appears" to work **Page 3:** • Confused by cost comparison with Lisinopril on page 3—need to specify Lisinopril is an ACEI • Felt that this decision came down to cost—pointed out it was a spectrum, of people who absolutely cannot afford	Same change as first patient re: ACEI: Changed sentence about cost of Lisinopril on page 3 to "Lisinopril, **an ACEI**, is <$10 per month" to tie back to ACEI Noted that all three patients spent very little time on cost page; focused in on patient scenarios, but skipped over the "call your provider" section. In an attempt to differentiate, separated this two concepts out in to two different pages, with patient scenarios/ways of lowering cost on page 3 and strategies for finding out how much the medicine would cost on page 4. Included a scale of **The cost is way too much for my monthly budget** to " **The cost is easily within my monthly budget"** to help capture what third patient talked about in terms of cost being a sliding scale for most people.

		the new medication to people for whom it's no problem and everyone in between.	
4/5/17	Internal team or team member	**Page 1:** • Paragraph 2, page 1 is too technical; suggest replacing with "You are likely already taking a heart failure medicine called an ARB or ACEI. Sacubitril/valsartan is similar to those medicines, but can work better to treat heart problems for some people. **Page 4:** • Create a second scale like the one for cost, but with importance of benefits being weighed.	Accepted all changes
4/10/17	Internal team or team member	**Page 1** • bold title, move to top right corner of page • paragraph 2; switch order of ACEI and ARB to keep consistent with rest of page. • paragraph 2; consider adding text bubble spelling out what ACEI and ARB are. • figures: change titles from "What I'm on now" and "What I'm thinking of switching to" to "Where I am" and "Another option" • figure: Make "Where I am" box three columns; ACEI with names, ARB with names, and "newly diagnosed" • figure: get rid of arrow, implies directionality when should be a choice between one or the other. • figure: swap out pill bottles for pictures of pills	Accepted all changes; for page 3, to personalize language, re-wrote opening paragraph to say "Below are three patients that might be like you and their insurance plans"

		• Shorten sentences in “what these medicines do” box (literacy), drop “unique” and “significantly” (unnecessary extra language) • change “switching medicines” to “this new option”—should highlight this is just an option, not a mandate **Page 2:** • change pill bottle figure in “How it is Taken” to pills; reflect the difference (1 pill for ACEI, 2 for entresto) • Change color of hearts in figures at bottom of page—red is more of a “stop” color • make sure all the hearts are the same size • put “after a little over two years” in its own box; separate thought from hospitalizations and mortality rates. **Page 3**: • change “Big” to “Main”; big implies value • can you personalize this page a bit? Relate the scenarios to the reader? Feels impersonal currently • change cost for patient A to range: $3-40 **Page 3**: cost for patient B is incorrect; up to $400 • re-order patient scenarios from none, partial to full; more intuitive • Add line about online programs like goodrx for patient resources and coupons	

		Page 4: • Make “option 1” and “option 2” same size font and underline; less distracting • leave more space for branding at bottom of page	
4/12/17	Physician	**Page 1**: • Grammatical mistake. Should read “you may also hear ACEI referred to as an ACE inhibitor **Page 2**: • The boxes with what’s the same/different are confusing. Is there another way to represent this information so it’s clearer what the differences are? • Make the boxes with the # of people who lived/died for each medicine more obvious—maybe move over the figures instead of under? **Page 3**: • Instead of having ACEI cost represented at the bottom of each scenario, just have it represented once	Agreed and changed. Agreed and changed. Created one box for similarities, and a column for each medicine regarding side effects/dosing instructions unique to that medication. Agreed and changed. Agreed and changed.
4/13/2017	Patient and Family Research Advisory Panel	**Page 1**: • Get rid of intro “If you’re reading this, you may be a good candidate…” sounds too much like marketing gimmick • Confused by what a “neprilysin inhibitor” is—please clarify • Suggest adding a “check one” label and boxes next to medicines in figure on first page **Page 2**: **Page 2**: QOL information should really be emphasized on this page, more than just a few lines in a box; fewer hospitalizations is just as,	Agreed and changed. Included a brief summary of what the ARNI is/does on the first page Did not include; trialed this suggestion, but the page ended up looking too cluttered. Unfortunately the data regarding QOL was not strong enough to include in the DA; therefore we only included QOL info related to hospitalizations.

		if not more, important and lower risk of death • Would like to know ways in which QOL was improved, other than reduced hospitalizations; please clarify • Are there medication interactions between sacubitril/valsartan and other medicines I might be on, like warfarin? Concerned, please clarify **Page 3**: • Swap blue box on page 2 with values clarification on page 4; flows better **Page 4**: Can you check online about your medicines, or do you have to go through your insurance company and call?**Page 4**: Confused by option 2: don't know what "ask your doctor to run a prescription through your pharmacy means". Please change to clearer language—"ask your doctor to call the pharmacy", maybe **General**: • Just shorten to facts list, or have summary on first page of all pros and cons **Overall impressions**: • The language was straight-forward and easy to read, the colors were soothing, the print was a good size; however, some felt like the mere existence of the decision aid felt like propaganda. Panel could not really come up with solution or suggestion for this, other than just making the DA a list of facts about the medicine.	Excellent question; we incorporated a sentence stating that this medication may interact with some medications on the first page Did not include; this suggestion broke up the information in a confusing manner. Excellent question; included a blurb on page 4 about how to get more information about this medication. Did not include; this suggestion would be appropriate for an educational pamphlet, but loses the important qualities of a patient decision aid. Attempted to neutralize the language on the first page to make this patient decision aid sound less like propaganda; got rid of anything along the lines of "if you are reading this, you may be a good candidate…"
4/21/2017	Team of External Physicians	**Page 1:** • The "newly diagnosed with heart problems" box might	P1. #1: did not accept; group consensus is that we want this to be for

		be a little confusing, we thought. Might be easier to understand if it clarified "not yet on medicines for heart failure" or something like that. • We also thought that the details about S-V being an ARB+ neprilysin inhibitor may be difficult to understand. Maybe simplify this further into a combination of ARB and another medication, with the combination working better than an ARB/ACEI • May be worth a single sentence that states ACEI/ARB save lives in HF population may get point across that it is important to take any of these meds in HF. **Page 2:** • Also, if someone just skimmed through the risks and side-effects box and read only the red sentences, it would seem that the side-effects were more on S/V and ACEI/ARB may have fewer side-effects. • The benefit box might be labeled as "benefits" • The labeling in the s/v group is a little challenging in two ways. 1) The white heart says 83, but only 80 are white hearts. 2) The "lives saved" with the green heart may be seen as dramatic. Alternatives could be not to label but rather just to state 3 more patients alive from taking s/v (to address above concern too might just have a separate text box at the	patients who are taking some meds, maybe not just all heart failure meds 2.Accepted and changed 3.Did not incorporate; felt was a little redundant and no patients expressed trouble understanding that these medicines were for heart failure P2. #1: Removed highlighting and condensed risks and side effects to middle box; did not incorporate feedback re: AAs, since this tool should be general and we feel that level of detail should be discussed with the clinician 2 & 3.See above re: reconfiguring risks and side effects format. 4.Did not incorporate; IPDAS requires highlighting of differences between meds. Did change wording to just "lives saved on sacubitril/valsartan" for green hearts

		bottom that says this). Regardless of how you choose to label, it may be worth thinking about adding that doctors don't know who those 3 patients would be. In our early experience, people say "I'd do it if my doctor thought I had a good chance of being one of those 3." So despite totally saying what the numbers "show," they fail the probabilistic reasoning completely. **Page 3:** • It wasn't clear how informative the 3 scenarios would be as discrete scenarios. They don't suggest any particular action, yet they feel like they might be the beginning of an algorithm or decision sequence. "If you are like patient A, it is important to understand whether the benefits are important to you, etc." In other words, the might link up more directly to the values clarification questions you have. • We wondered whether labels like "partial vs complete" or "limited versus full" might be better. **Page 4:** • Regarding the questions, totally trivial, but #1 comes after #2. • The benefits question seems hard to answer in that one might think mortality reduction is important but that the magnitude of the effect of S/V is low. This may be super-picky, but we thought it might	P3, #2. Did not incorporated; Patient B already identified as having partial coverage. Since there is so much nuance between what each kind of coverage can offer, having full coverage vs. partial coverage might not actually guarantee better cost, hence partial vs. good. P4. #2. Accepted and implemented

		be important if the idea is to use these answers as a way to begin a conversation with a provider or to make a decision. • Related to the above, we thought it might be worth stating explicitly that answering these questions may help you to think through with your provider whether this medicine is a good one for you. **Page 5:** • Same comment as the last one about saying very explicitly that answering these questions might help you think through with your provider • We weren't sure how useful these very general questions might be. Would be interested in whether you have data on how people use them. #1, for example, seems really vague. #3 also seems tough in this respect • As we mentioned on the phone, at least the 8 or 10 people we've pre-tested our interview guide with have had a very hard time coming up with answers to questions like #5. Moreover, some come up with answers that may lead them to make bad decisions. For example, one lady said a medicine should cut her mortality risk in half for her to be willing to make a change. This tool has no contextualization of medical benefits for HF, so people	3&4.Changed heading to read "Ask yourself and discuss with your doctor" P5. #1: Added "..and bring your answers to your doctor" 4.Did not incorporate; already instructed patient to discuss with doctor earlier on

		may answer that question in a way that reinforces a totally unrealistic belief and makes the decision feel like a more considered one than it really is. Of course, some people may feel that way, but often that isn't the case. • .We thought it might be important to have a last sentence telling patients what to do with this information they have now. Could let them know to talk with their physician for further discussion etc.	the page, so felt a second line saying the same thing would be redundant.
4/25/2017	Internal team or team member	**General Impressions:** • RE: different possible color schemes: blue seems a little more soothing for a relatively cognitive decision. I don't care too much about the Emory question. I'm fine with either New Dx or Not Yet On Medications. I emailed Robert Page about the warfarin/interaction question. **Page2 :** • I'm on the fence about hospitalization and QoL. The survival stat is dominant. What about doing a KCCQ QoL line 0-100 like we did in the LVAD decision aid? (So add QoL and leave out hosp). • Did not like hearts; suggest change to people **Page 3**: • "Patient A has no *medication coverage*". He's an old dude, so he probably has Medicare	Accepted and incorporated; DA was color coded in blues After group discussion, left as "newly diagnosed with heart problems" Dr. Page confirmed that it is appropriate to take warfarin with entresto, so left box with statement confirming that on page 1. Did not accept; upon further investigation, QOL change in study was not large enough to display in a visually significant manner, so left out. Also did not incorporate visual for hospitalization; instead, created distinct call-out box from figure with a bullet point about benefits not displayed statistically, such as felt better, lived longer, and had fewer hospitalizations Accepted and changed; made partial busts of people, since 100 full people too up too much room. Accepted and changed to "no coverage", "partial coverage" and "good coverage" for continuity

		Part A at a minimum, so not "no insurance".	
5/01/17	Internal team or team member	**Page 2**: • Entresto is always taken twice a day by mouth; so remove "usually" from that section • Move "lower blood pressure" to the top of side effects box, since it is the most common for all three meds • Change "a two year study" to just "a study" since it already says "after two years" in that same graphic	Accepted all changes and implemented
5/31/17	ACC reviewer panel	**General Impressions:** • Appears too much like a commercial and not an information package. • Feels like the questions are asking people to decide if money is more important to them vs. survival. Not really fair questions. Like asking how much is a longer life worth to you? • So in summary, I don't like much or anything about this in its present form. And not something I would be comfortable endorsing. **Page 1** • OK to take other meds and lists only warfarin. Why not just say you are prob. on many other meds which you should continue? • At the end of the box on the top right, in the Sacubitril/valsartan note, it should say shown to be better in some pts. **Page 2**	Agree. We removed all mention of the brand name of the medicine (Entresto) and changed the title to "Should I be on an Angiotensin Receptor-Neprylisin Inhibitor (ARNI)?" in order to shift the focus to the class of drug, as opposed to the brand of drug. We also hope this will allow for easier modification to the DA should future ARNIs come on to the market. To mitigate this, we took out all of the questions about cost--leaving only a space for patients to write down any questions they might have for their doctor or health care provider--and kept only the values -clarification excercises on page 4. Agree and changed. Agree and changed.

		• There needs to be a statement that although these differences appear small they are significant. **Page 3** • Do we really think people can chose from 1-10 the importance of this drug? I know most internists couldn't do this. I also feel the second 1-10 scale is irrelevant and almost again like asking people to choose living or not. **Page 4** • don't ask doctors to call pharmacies. Docs have enough to do. Most patients can do this if they have insurance.	Disagree--we've added the statistic about reduced hospitalization to this page; however, we are already struggling with a built-in bias that comes from comparing one drug from one manufacturer to several drugs from several manufacturers, and do not want to appear too biased. We feel it is best to allow the information to speak for itself. This is our values clarification exercise; values clarification exercises are an IPDAS requirement for DAs. Furthermore, this approach has been shown to be efficacious in previous decision aids. Agree. Took out "ask your doctor to" and option 2 reads as simply "Call your pharmacy".
5/31/17	ACC reviewer panel	**General Impressions:** • I also have multiple concerns also, although we all appreciate the challenge of putting these complex concepts into a patient-friendly format. I do not know if there has been unrestricted sponsorship of this endeavor, but the question will certainly arise as to if/how Novartis has been involved. • Regarding the depiction of data, I would suggest that we agree on the specifics of information to be provided, and ehn the current attractive lay-out can be adapted to provide more aspects of the decision. • The graphic depiction of survival impact is impactful , but there MUST be mention	This is an unrestricted grant. Agree, in part. We have added a blurb to the bottom of page 2 that discusses the reduction of hospitalizations for patients on sacubitril/valsartan vs. an ACEI. However, in terms of QOL measures, the increase of QOL, while statistically significant, was not visually significant in this study. Prior research has found that presenting information on changes in KCCQ are not visually meaningful to patients unless there is a point change of 4 or more; in this study, the difference was 1.64.

		of non-survival endpoints, such as decreases in hospitalization and possible better maintenance of quality of life; although current data does not show improved QOL, it did show less worsening than on placebo. . Many patients may not be swayed by survival itself, but hospitalizations and QOL would be very important..	Thank you--agree and changed.
		Page 1: • Sacubitril is misspelled the second time it appears	Not necessarily--we have yet to hear this question from patients. Also, the mechanisms of how, exactly, the combination works is highly complex and not yet completely understood.
		• Won't patients want to know why the combination works better than either ARB or ACEI alone?	
		• Is there some reason that the panel on the left says "can work better to treat heart problems" rather than to say "to treat heart failure"? If this tool is designed in anticipation that there will be broader indications, then the other data about benefits would have to be revised anyway.	Our prior work shows that patients don't like the term "heart failure" or don't fully understand it, and that "heart problems" is a less emotionally charged equivalent.
		• "Where I am" section: The "take all these medicines without other medicines" box should be moved because it is not entirely clear from its location that it does not mean that ACEI and ARNI could be taken together. It should be noted that ACEI/ARB WILL BE STOPPED. This is probably one of the most crucial instructions regarding ARNI initiation.	Agree. However, instead of adding instructions, we changed the boxes on the first page to one box with three columns, with the caption "Everyone with your heart problems should be on one of these 3 medicines" with ACEIs in the first column, ARBs in the second column, and ARNIs in the third column. This also helps mitigate some of the issues around the DA feeling like a commercial.

		Page 2: • I would mention that it may be necessary to decrease other medications after the ARNI starts, because it may be more potent. • It should also be mentioned that it is often started at a low dose that is then increased over time. **Page 4** • I agree with Dr. Wasserman that it is not appropriate to tell patients to tell their doctors to call pharmacies to ask about cost. • I would suggest that the patient be referred to a website for help with payment, I am sure there is one created by Novartis. It is not our position to tell patients to ask for coupons or financial assistance. **Page 5** • I do not think that this selection of questions is going to be very helpful to guide decision-making about this medication. The way they are phrased, I think that patients are most likely to decide to continue with current medication. I also think that there will be considerable discomfort from both doctor and physician focusing on the cost-effectiveness issue in these general terms.	Disagree--we have mentioned some of the side effects of the ARNI, such as lowered blood pressure, that are a result of its potency, however we do not want to go in to too great of detail in this DA, as it is not meant to replace discussion in clinic appointments, merely act as an aid or a conversation starter. See our above reply to Dr. Wasserman. Agree--we chose to shorten the questions to just a section for the patient to record any questions they may have for their health care provider or doctor, as we already have a values clarification exercise on page 4 that serves the same purpose as the questions.
5/31/17	ACC reviewer panel	**General Impressions:** • I will defer to the Heart Failure specialists here. Specifically acknowledge their comments that it sounds like an ad. It sounds like an ad because the alternatives are to take the Rx or not and the Rx is produced by one	Thank you. We agree that this is a difficult question to tackle appropriately given the current paramenters--however, to mitigate some of the more "commercial" aspects of this DA, we have shifted the focus from Entresto/Sacubitril Valsartan to ARNIs.

		company. Thus, this is not the best question to ask in an SDM approach. Nevertheless, the tool is written appropriately to answer the question.	
5/31/17	ACC reviewer panel	**General Impressions:** • Leading with "Sacubitril/valsartan (Entresto)" makes the decision aid seem too commercial. Perhaps it is better to lead with "Am I on optimal medical therapy for heart failure--A medication decision aid"	Agree. However, the decision is not for the medicines in general, but whether to switch from an old medication (ACEI or ARB) to a new one (sacubitirl/valsartan), so re-wrote title to place focus on the the class of medicine sacubitiril/valsartan belongs in, vs. the medicine itself. New title reads "Should I be on an Angiotensin Receptor-Neprylisin Inhibitor (ARNI)? A medication decison aid for patients with heart failure and reduced ejection fraction".
		Page 1: • On the left side towards the top, would consider changing ". . . to treat heart problems for some people." to be ". . . to treat a type of heart failure." or ". . . to treat heart failure resulting from reduced pumping function."	Agree and changed.
		• On the left side at the bottom, would consider changing "Most people in your situation fall into 1 of these 3 categories below" to "People with heart failure and reduced pumping function fall into 1 of the 3 categories below:"	Disagree--we don't want the DA to become too clinical. However, mention of the type of heart failure these medications are meant to help has been included in the title of the DA.
		• For the 1st of the 3 categories listed in #3 above, I would change "Newly diagnosed with heart problems" to "Newly diagnosed"	N/A; got rid of the "newly diagnosed" column altogether.

		Page 4: • Would change "Option 2" to read "Option 2. Check with your pharmacy." • In the box at the bottom of the page, it may be worthwhile adding a 2nd sentence to the first listed item that reads: "You are not likely eligible for a coupon if you have Medicare or Medicaid." • In the box at the bottom of the page, it may be worthwhile changing the 4th sentence to read, "You may be eligible for financial support to help cover the cost of sacubitril/valsartan through the manufacturer" then include website link.	Agree and changed. Agree and changed; added a sentence at the bottom of the box reading "Note: Some insurances, like Medicare, may not allow coupons." Agree and changed.
6/6/17	ACC review panel	**Page 1**: • Sacubitril is misspelled the second time it appears • The PARADIGM HF trial compared sacubitirl/valsartan to an ACEI--suggest get rid of "ARB or" in definition box for sacubitril/valsartan • Re: the boxes with medication on page 1: "Do something to indicate these are examples of ACEI and ARB, since the list is not inclusive. Also, put the names in alphabetical order" • Re: box on page 1 with statement about taking medicines with warfarin: "I think this statement implies	Agreed and changed Agreed and changed Re-worked this box so it is clearer that these are medication types with the generic names below, and added caption "everyone with your type of heart problems should be on one of these three medicines". Added a sentence after each type of medicine to clarify the names before were examples of medicines patients can be on (eg, "An ACEI, such as:"). Also changed to alphabetical order. Agree and changed--medicines were all put in to one box (see comment above) and this statement was moved under the medication box and re-written to say "all of these medicines can be taken

		that it is OK to take sacubitril/valsartan w/ ACEI and/or ARB, which is not the case."	with other medicines" so that it is clear other hf medications can still be taken regardless of whether the patient is on ACEI, ARB or ARNI Agree and changed
		• Change "the pros and cons" to "some potential pros and cons"	Agree and changed
		Page 2 • Change "what are the possible burdens or risks" to "what are some of the possible burdens or risks"	
		• Change "a pill" to "dose" in "how is it taken" boxes	Disagree--we want this DA to be patient-friendly and pill is more low-literacy
		• Change "what are the possible benefits" to "what are some possible benefits"	Agreed and changed
		• Add " and side effects" to "what are some possible benefits of each"	Disagree: side effects are mentioned in the above section, under "All 3 medication types an cause"
		• "RE: graphical presentation of mortality at bottom of page 2: ""It looks like this graphic was based on the all-cause death data. • Consider making a graphic using the CV death data. • Consider making a graphic including the hospitalizations for heart failure. • Consider making a graphic for symptomatic low blood pressure.	Disagree. We chose not to include figures on CV data because the key takeaway is the difference in how many patients died on one medication vs. another, regardless of cause. We agree that some information is needed on hospitalizations--to this end, we added a statement under the graphic with the difference in hospitalization rates. Changes in blood pressure were neither primary nor secondary outcomes in the PARADIGM study, so we did not feel it would be appropriate to represent them graphically, as this is the only current data source for sacubitril/valsartan.
		• Suggest take out "ARB" from "After two years on ACEI or	Agree and changed.

		ARB" as PARADIGM study was only for ACEI	Agree and changed.
		Page 3 • RE: first sentence of page 3: "Consider using this ... Because sacubitril/valsartan is a new medication, it is not available as a generic product. It can be more …"	Disagree. We have taken out the "as your doctor" part, but we do not believe that telling patients that it's ok to ask their pharmacist what their medication might cost them is likely to be problematic. We are distinctly not telling them to run a prescriptions, merely ask their pharmacist for an idea of cost.
		Page 4 • RE: Option 2: "Please don't propose this option. The pharmacist would have to run a prescription through to find out the cost. The insurance company may block the prescription with prior auth paperwork."	Agreed. Deleted pharmacist. Also added a note at the bottom of this box that some insurance programs, such as Medicare, may not allow coupons.
		• blue box with suggestions for ways to decrease the price of sacubitril/valsartan: "Delete "or pharmacist". The coupons are given to healthcare providers (physicians, PA, NP, pharmacists) who work in clinics. Also, patients on Medicaid and Medicare can't use coupons."	Agree. We changed this section somewhat to make it a little clearer; there are now two suggestions, one to ask providers for coupons or about Patient Assistance Programs, and one to look at online resources, such as goodrx.com or the manufacturers of sacubitiril/valsartan, for coupons.
		• "RE: blue box with suggestions for ways to decrease the price of sacubitril/valsartan: ""The Entresto(TM) Central program is a patient assistance program. I think it is best not to mention the specific program. • If you decide to leave in the statement about the Entresto Central program, then use	

		lower case for sacubitril/valsartan." **Page 5:** • Suggest changing "questions or concerns I have for my doctor or nurse" to "questions or concerns I have for my healthcare provider"	Agree and changed.
6/15/2017	Patient	**Page 1:** • Patient was confused by Agiotensin Receptor Neprilysin Inhibitor (ARNI) in title—did not like title and thought it should be better explained **General Impression:** • Patient thought the decision aid was fairly straightforward and well explained; did not think it was biased. However, did not really understand what an ACEI was until got to cost page, where there is a sentence that directly equates Lisinopril and ACEI. Once explained that Lisinopril is an ACEI, patient understood the decision aid a little more clearly. **Page 3:** • Patient did not think cost should be so emphasized; however, felt that the most important thing was the medicine, and admitted that patient had a good insurance plan. **Page 2:** • Patient wanted a line that mentioned that this medicine would improve your lifestyle	Disagree—we explain what an ARNI is lower on the page. Once this was explained to participant, participant felt a little better about the title This was a theme we saw with several patients, so we added the most common generic name in next to ACEI and ARB wherever they appear, so that patients have a touchpoint. Used Lisinopril and Losartan. Disagree—this decision is almost entirely about cost. For patients who can afford it, they may feel it is less important, but for patients who cannot, this may be very important information. Somewhat agree—have added a bolded statement on the bottom of page 2 about decreasing hospitalizations on medicine, but cannot necessarily say that sacubitril/valsartan will markedly preserve patients “lifestyle” would not be true
6/15/17	Patient	**General impression:** • Patient felt the DA was helpful, and was very	

		concerned about the cost of the new medication. Patient did not feel the information was overwhelming. Was slightly concerned about the side effects, but seemed concerned about side effects of medications and treatments in general.	No changes based off of this interview, aside from the Lisinopril change mentioned above
6/15/17	Patient	**General impression:** • patient was really impressed by how many more people lived than died. • Patient was concerned about the possibility of being dizzy—wanted more information on that. • Patient did not think decision tool seemed biased; thought it would be very helpful when making a decision around sacubitiril/valsartan. Patient didn't think DA felt like a commercial at all.	Made no changes based off of this interview; patients individual risk of becoming dizzy should be discussed with their provider. This tool is meant to provide general information, not tailored information.
6/20/17	Pharmacist	**Page 3:** • Should change Option 2; worried that could be problematic for pharmacists. Suggest instead "Option 2: Your health care provider can initiate a plan to switch you to ARNI and write a prescription, but before you finalize that plan you can see what the cost is"	Agree and changed to "Your healthcare provider can begin a plan to switch you to ARNI and write a prescription. You'll be able to see the cost before you finalize the plan, and decide whether you'd like to move forward."
6/20/17	Internal team or team member	**Page 1:** • Alter title so that it is clearly differentiated from text of DA and doesn't get lost • Bold ACEI, ARB and ARNI above pill graphics **Page 2:** • change "ACEI (lisinopril)/ARB(losartan) vs. ARNI" to "ACEI (lisinopril) or	Agreed with all and changed

		ARB (losartan) vs. ARNI (sacubitiril/valsartan)" **Pages 3 & 4:** • swap the scales and the cost reduction box so cost reduction box is on page 3 and scales are on page 4	
7/20/17	ACC reviewer	**Page 1:** • I would change the green text in the left upper corner to read "A medication decision aid for some patients with heart failure" • On the left side, I would insert "an" before "ACEI" to read ". . . for some time treated with an ACEI (like Lisinopril) . . ." • On the left side, I would change the 2nd sentence to read "In either case, your care provider may be considering whether to have you on an ARNI." • On the right side in the blue text box, move the "." to be outside the quotation mark = "ACE inhibitor". • On the right side in the blue text box, change "What ACEI and ARB do:" to "What an ACEI and ARB do:". I'm inserting an "an". • On the right side in the blue text box, under "What an ACEI and ARB do:", there is an extra space between "that" and "blood", as well as, "to" and "the" at the end that needs to be removed. • On the right side in the blue text box, under "ARNI:", there is an extra space between "ARB" and "and". • On the right side in the blue text box, under "ARNI:", please insert an "an" before "ACEI."	We disagree--this is not a decision aid for all heart failure medications, but rather a decision aid specific to sacubitiril/valsartan. Agreed and changed: 2-13 Agreed and changed: added sentence at the end of Option 2 reading " if you feel the cost is too high, you may leave the prescription unfilled; however, it's important you then get in touch with your healthcare provider and work together to find a plan that will work better or you."

		• In the long blue box, would change "problems" to "problem" and remove the extra space between "type" and "s" to read "types" • "Ramipril" is misspelled. **Page 2:** I would change "Cough is common with ACE I" to "Cough can occur with an ACEI". Common to me implies that occurs more frequently than not. This is not the case. Also, please insert "an" before "ACEI" • Please change the text to read "A study comparing an ACEI to an ARNI found that:" **Page 3:** • Please remove the extra space between "provider" and "or" in the lower text box. **Page 4:** • Under Option 2, please insert "the" before "ARNI" to read ". . . switch you to the ARNI". I would also add something like "If the cost is too high, you can decline the prescription and work on an alternative plan with your healthcare provider."	
7/20/2017	ACC reviewer	**General Impressions:** • I think the guidelines and the data would suggest most should be on an ARNI, and the cost part is secondary. So it might be best to say something like: ARNIs are a newer drug which may benefit you more than the traditional ACEI, and may reduce hospitalization and deaths due to HF. However, these drugs may	Disagree. We believe our current iteration already addresses the fact that ARNIs are more expensive and that they have some benefit for patients over ACEI (please see call out box on page 1, as well as pages 3 & 4 for reference). However, we respectfully disagree that cost is secondary. We believe this decision aid is about what is valuable to the patient--it's a balance of health benefits vs. out-of-pocket cost. During our discussions with patients regarding this decision aid,

		cost you more and are are some things to consider/use as resources to help keep costs in line (or something like that). From a patient point of view, I would imagine most would say “I’m worth the cost of not dying” so I think that concept needs to be paramount i.e. Talk to your doctor to ensure this is the right drug for you. Since it is new, it is often more expensive, but your insurance and the manufacturer can work to help with the costs in many cases. If you choose not to take it, the alternatives are much cheaper.	we have heard both arguments--that there is no price that can possibly match increasing a patients' life-span, and that if the patient feels they can't afford it, that's it--they can't afford it. Furthermore, Self-Determination Theory argues that allowing patients to make the choice for themselves might improve engagement in adherence; conversely, overly directive language can undermine that.
7/20/2017	ACC reviewer	**General Impressions:** • I agree that this is much much better. I remain concerned that a person would have a hard time with any increase in cost feeling that what looks like a small difference would be worth it. Who thinks they would be one of the 3 extra deaths? Is there some comparison to other beneficial drugs that could be made?	In order to address these concerns about whether patients will recognize the significance of the impacts of Entresto, we have added a call-out box on the bottom of page 2 from the Entresto-side of the figure that states: "compared to other medicines, this is actually a pretty big benefit".
7/20/2017	ACC reviewer	**General Impressions:** • I like it much better and feel that it is more balanced than the initial one that focused on finances. I still think, however, that we need to get in some indication that quality of life may improve, because I am finding that patients often describe better activity tolerance. Although the PARADIGM trial just showed that QOL declined less with ARNI compared to ACEI, but there must be some other smaller experiences showing	Disagree. In the future, we may have data that supports this improved QOL…however, we unfortunately only have the data from PARADIGM currently, which does not suppor t a particularly robust change in QOL. Thus, we do not feel we can currently include a meaningful measure of QOL.

		some benefit for functional capacity or QOL. If so, this could probably be depicted with a line graph with an arrow.	
7/21/2017	ACC reviewer	**Page 1:** • Use lower case for all generic names (captopril, enalapril, lisinopril, etc.) • Use ARNI, not ARNIs, since there is only 1 product in this class of medications. This may require restructuring some of the sentences to match the singular tense, ARNI. • Rephrase the text on page 1 - bottom of the page to: "An ARNI cannot be taken within 36 hours of an ACEI. Other drug interactions are relatively rare. Tell your healthcare provider and pharmacist all the medications that you take, including over-the-counter medications, vitamins, and natural remedies." **Page 2:** • Consider rephrasting the text on the first line of page 2 … Compare ACEI (like lisinopril) or ARB (like losartan) to ARNI (sacubitril/valsartan). • Consider changing the graphic and wording for an ACEI OR ARB on page 2. Consider showing both a round tablet and a capule with the word "or" in between. Consider changing the wording to "Usually a tablet or capsule 1, 2, or 3 times a day." • Consider changing the graphic and wording for an ARNI on page 2. Consider showing an unscored oblong	Agree and changed. Agree and changed. All mention of ARNIs has been changed to the singular tense. Agree and changed. Agree and changed. Partially agree—we have changed the text to “A pill taken by mouth, usually once, twice, or three times a day”. However, we do not want to overload or confuse patients with too many graphics or terms that essentially mean the same thing. Disagree—see above re: graphics and terms.

		tablet instead of the capsule. Consider changing the wording to "A tablet 2 times a day."	
		Page 3:	Agree and changed.
		• Rephrase the text at the top of page 3. Consider … Because an ARNI is a newer medication, it is not available as a generic. This means an ARNI can be much more expensive than an ACEI or ARB.	Agree and changed to “For comparison: Lisinopril (an ACEI) costs less than $10 per month”.
		• Use words, not <, in the text in the box below the pictures on page 3. Many patients do not understand math symbols. Consider … "For comparison, an ACEI (like lisinopril) costs less than $10 per month."	
		• Rephrase the text in box at the bottom of page 3. Consider … Ask your healthcare provider and pharmacist if they know of any available discounts (coupons, patient assistant programs) for the ARNI.	Agree and changed.
		Page 4:	
		• Rephrase the last part of the text in Option 1 on page 4. Consider ... "My healthcare provider is considering prescribing the ARNI, sacubitril/valsartan, for me. Please tell me how much I will have to pay each month for this medicine (sacubitril/valsartan 49/51 mg tablets, 60 tablets per month)."	Agree and changed.
		• Consider omitting option 2 on page 4. The only way the pharmacists can get the price is to fill a prescription and then cancel it. The process may be blocked, if the insurance company requires a prior authorization. The best	Disagree—we discussed this with our heart failure pharmacist and he felt the wording was appropriate.

		way to get the cost information is to call the insurance company. • Consider rephrasing the text in the blue box on page 4. "Ask yourself these questions. 1. How important are the benefits of an ARNI to me? How easily will the cost of an ARNI fit within my monthly budget? Mark your answers on the lines below and discuss your answers with your healthcare provider." • Consider rephrasing the text for the scales on page 4 to make the text more specific for ARNI therapy. Consider … The benefits of an ARNI are not all that important to me. The benefits of an ARNI are really important to me. The cost of an ARNI is way too much for my monthly budget. The cost of an ARNI is easily within my monthly budget. • Consider rephrasing the text in the last sentence on page 4. Consider … Write down the questions and concerns you want to discuss with your healthcare provider concerning an ARNI.	Agree and changed. Agree and changed. Agree and changed.
8/22/2017	ACC team feedback	**General Impressions:** • Please change all mention of “healthcare provider” or doctor to “clinician”. This will standardize the way health professionals are discussed in the DAs.	Accepted and changed.

11/7/2018	Sponsor Feedback	Overall keep this document as an objective description of an ARNI	Thank you for your feedback. We respectfully disagree with this

		without constant reference or comparison to other medications	comment. The International Patient Decision Aid Standards (IPDAS) Collaboration stipulates that one of the criteria for a document to be considered a patient decision aid (PtDA) is that the document explicitly discuss the available options. In this case, the decision is between taking an ARNI versus an ACEI or ARB (versus not taking drug at all). What you have suggested is that we make an informational document for ARNI, which was not the intent.
11/7/2018	Sponsor Feedback	Please remind me of the objective of this piece and how it will be delivered or distributed to patients. The reason I ask is I think overall, while this piece is informative, it is not written at consumer-friendly way. This will be appreciated by proactive seekers but not the strugglers. Let's keep in mind that these patients are overwhelmed and information shared with them should be in bite size, easily understood and written in a way they will understand it. Giving them so much information might overwhelmed them even more and they may not retain anything and take the proper action. If this will explained by an HCP to them, with a few adjustments in copy, it will work better.	Thank you for your feedback. The objective of this document is to function as a patient decision aid (PtDA) for patients considering an ARNI. PtDAs explicitly define reasonable options, the relevant pros and cons of those options, and exercises to help patients clarify what their personal values are and how these treatment options might work with or against them. More information on the objectives and criteria for PtDAs can be found at: http://ipdas.ohri.ca/using.html. We believe we have followed a writing style that is typical of PtDAs. We are not sure what a “consumer-friendly” document would look like; we can say that our intent is not to provide a commercial for ARNI. PtDAs can be of variable length. The goal is to provide enough information to address the basic PtDA criteria and meet the informational needs of the patient, but no more. We went through a rigorous, iterative process of development that included feedback from patients and providers (and now industry). The current length was endorsed by the patients and providers as the right length. PtDAs, including this one, are not intended to be standalone documents; they are intended to facilitate a conversation with their healthcare

			provider. In regards to patient understanding or patients being overwhelmed, there is a Cochrane review of over 115 randomized trails demonstrating that well-designed documents such as this indeed help patients on many outcomes related to involvement, empowerment, and decision quality.
11/7/2018	Sponsor Feedback	*(IN REGARDS TO FIRST PARAGRAPH):* Patients think of a weak heart as a pre-cursor to heart failure. We shouldn't say if you've been diagnosed with a weak heart. Perhaps say, You may have been told that you have a weak heart and that you've been diagnosed with heart failure.... I sitll like using weak heart with heart failure because it is what they hear from their doctors.	Agree and changed.
11/7/2018	Sponsor Feedback	*(IN REGARDS TO FIRST PARAGRAPH):* Sacubitril/valsartan is indicated to reduce the risk of cardiovascular death and hospitalization for heart failure (HF) in patients with chronic heart failure (CHF) in the New York Heart Association functional*1 class II-III and IV and reduced ejection fraction. Valsartan blocks the effects of a body chemical. It reduces blood vessel tightening and the building up of sodium and fluid. Sacubitril blocks the activity of an enzyme called neprilysin. When neprilysin is active, it breaks down helpful peptides. Sacubitril inhibits neprilysin so the peptide levels can go up. These peptides help relax blood vessels and release sodium and fluids in the body.	Please refer to the comment above about writing this document in “bite size, easily understood” way. The suggested language seems in contradiction to this prior concern. We ran the language provided through a readability calculator and it came out on Gunning-Fog as 12th grade level. We aim for 6-8th grade level. While we agree that patients should be well-informed regarding how their medications work. However, during the iterative development process, both patients and providers requested a simplification of the mechanistic descriptions of the drugs. The remaining mechanistic information about ARNI (which includes some of the suggested language) is included in the description of the ARNI in the callout box on page 1, with revisions as detailed below.
11/7/2018	Sponsor Feedback	*(IN REGARDS TO FIRST PARAGRAPH):* *1:Add description of the classes	Descriptions of the classes are included in the callout box on the right side of the page.

11/7/2018	Sponsor Feedback	Add the guideline recommendation--Reference to the Guidelines is missing	Agreed and changed. We have added a sentence at the end of the first paragraph that reads, “For some patients with heart failure, clinical guidelines recommend that an ARNI replace an ACEI or ARB if the ARNI is tolerated.”
11/7/2018	Sponsor Feedback	*(IN REGARDS TO CALL-OUT BOX):* Since we described how an ACE and ARB work, we need to explain how the combination works (ARNI) works 2 different ways. --ARB relaxes blood vessels so blood can flow more easily and the neprilisyin inhibitor has a synergistic effect to help the heart pump blood to the body etc	We agree and have edited this description to read: *ARNI: A combination of an ARB and a neprilysin inhibitor drug. The ARB relaxes blood vessels so blood can flow more easily, and the neprilysin inhibitor works with the ARB to help the heart pump blood to the body. The resulting medicine has been shown to work better in some people than an ACEI.*
11/7/2018	Sponsor Feedback	Again keep this page as an objective description of ARNI and not a c without constant reference or comparison to other medications	We respectfully disagree. As a decision aid, we must show comparisons, otherwise, it is just an advertisement. Please see our reply to the first two comments on page 1.
11/7/2018	Sponsor Feedback	“An ARNI may cause low blood pressure, high blood potassium levels, kidney problems, cough, dizziness and allergic reactions causing angioedema or swelling.”	We respectfully disagree; please see our reply to the first two comments on page 1. In order for this document to be considered a patient decision aid, descriptions of multiple options for this condition must be included.
11/7/2018	Sponsor Feedback	Under “What are the possible benefits of each?” “ARNI was studied in a heart failure trial of more than 8000 adults with heart failure for an average of two years. This study showed that ARNI reduced the risk of death due to heart related problems and heart failure hospitalizations.”	We will edit this section to include more specific information about the trial. The section will read: *“A study comparing and ACEI to an ARNI in more than 8000 adults with heart failure found:”* However, the comparative information will remain in the decision aid for reasons stated above
11/7/2018	Sponsor Feedback	Patients had a 20% relative reduction in hospitalization. 3% is the absolute number.	There is clear and strong evidence that relative risks are misunderstood by both patients and clinicians. Absolute event rates are recommended for patient communication in decision aids. http://ipdas.ohri.ca/resources.html
11/7/2018	Sponsor Feedback	The benefit of ARNI should be highlighted even more and this may	This document is meant to objectively highlight the pros and cons of taking an ARNI or ACEi to help patients decide

		not be the right location for it and the proper articulation of it. Simply put, "it helps HF patients stay alive and out of the hospital"	what is right for them. This is not meant to be a document that solely highlights the benefits of ARNI.
11/7/2018	Sponsor Feedback	Change title of page to “Other Considerations”	We respectfully disagree. The title reflects what patients told us.
11/7/2018	Sponsor Feedback	Scenarios should be based on the most common patient experience with insurance	Patients and providers found it helpful to highlight a range of cost experiences patients may face.
11/7/2018		In first paragraph, change “an ARNI can be much more expensive than an ACEI or ARB” to “an ARNI may be more expensive than an ACEI or ARB”	Agreed and changed.
11/7/2018	Sponsor Feedback	Suggested Patient B text: Medicare Part D Coverage (~65% of chronic heart failure patients) • Approximately 93% of Medicare Part D patients have preferred access* and pay the lowest branded co-pay fo ARNI o Average Preferred Co-pay is $39-$45 o Low-income subsidy, or Extra Help, patients pay only $0-$8.25 o More than half of approved ARNI Medicare Part D pharmacy claims have out-of-pockets costs of less than or equal to $10	We respectfully disagree. The purpose of showing the scenarios is to help an individual patient decide what is right for them. The fact that 93% have preferred access is not relevant to an individual. One of the major downsides of the ARNI is the extreme costs for patients who cannot pay and in a decision aid, this must be discussed. We believe that including percentages may make patients who are uninsured feel even more marginalized. Furthermore, patients have found the scenarios we included to be helpful. We have, however, included a sentence in the paragraph prior to the scenarios that reads, “Below are three scenarios showing patients that might be like you and their insurance plans. Of note: many patients will be able to find a way to cover most of the cost of the ARNI.” We have also updated the reported cost of the ARNI for these scenarios, with patient C’s projected cost equaling $39-$45 and patient A’s project cost equaling around $450 (per recent projections from the medication website GoodRx).
11/7/2018	Sponsor Feedback	Suggested patient C text: Commercial Insurance (~25% of chronic heart failure patients)	Please see reply to the previous suggestion for patient B text.

		• Approximately 70% of Commercially Insured patients have preferred access and pay the lowest branded co-pay for ARNI • Get each 30-, 60-, or 90-day supply of ARNI for as little as a $10 co-pay^	
11/7/2018	Sponsor Feedback	Suggested patient A text: Uninsured (less than 5% of chronic heart failure patients) • Patient has no prescription drug coverage and may pay full out-of-pocket costs. ARNI is priced around $400 per month.	Please see reply to the previous suggestion for patient B text.
11/7/2018	Sponsor Feedback	Suggest adding the following information somewhere on the page: *Preferred Access: Brand-name drugs that are covered at a lower tier/co-payment, and/or with fewer restrictions, than nonpreferred brands in the same pharmacologic class. ^$10 CO-PAY CARD available for eligible commercially insured patients, as prescribed by your doctor. Offer not valid under Medicare, Medicaid, or any other federal or state program.	We respectfully disagree—information regarding how to find lower costs is already included in a more general sense at the bottom of page 3. Additionally, this language is not simple.
11/7/2018	Sponsor Feedback	Recommend switching out “for comparison” section for the following text: Some insurance plans may require a prior authorization. Check with your health plan or local provider to learn more.	We respectfully disagree. A comparison to another medication available for the same form of treatment is necessary for this document to meet the decision aid standards.
11/7/2018	Sponsor Feedback	This section on affordability may cause hesitation to fill. Including the example below on Lisinopril, this says ARNI is simply expensive. This is not the case in all situations, given affordability programs available. When it comes to affordability, the perception or misperception on affordability needs to improve.	We respectfully disagree; please see our above response. Also please see our response to comments 1 and 2 on page one regarding the purpose of a patient decision aid. Emerging data suggest that ignoring cost data when prescribing is associated with high no-fill rates. For example, *JAMA*

			Cardiol. 2017;2(11):1217-1225 shows that out-of-pocket costs in the setting of high cost-sharing is the number one reason for prescription abandonment. In the case of ARNI, prescription abandonment is particularly problematic because the no therapy due to ARNI abandonment is worse than low-cost ACEi therapy.
11/7/2018	Sponsor Feedback	Change text for Option 1 to: "To figure out how much out of pocket you will have to pay for your ARNI prescription, you can call your insurance company or local retail pharmacy. Here are questions you may consider asking them: - Is it a preferred brand on formulary? - What will it cost me? - Is there a Prior authorization required? (as it will impact the costs of the medication) - If there is one, once the PA is approved, what would the out of pocket cost be?"	We respectfully disagree. The two scenarios laid out already cover much of this, but in a less high-literacy fashion.
11/7/2018	Sponsor Feedback	Rating tool - what is it for? What is based on? Not helpful if you don't know what you rate it against. Deletion recommended	We respectfully disagree. In order for a document to meet PtDA standards, it must elicit patient values and then encourage the patient to consider the trade-offs of treatment options as they map to values. This is based on a large psychology literature related to decision making.

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