NOVARTIS

TEKTURNA® and TEKTURNA HCT ®

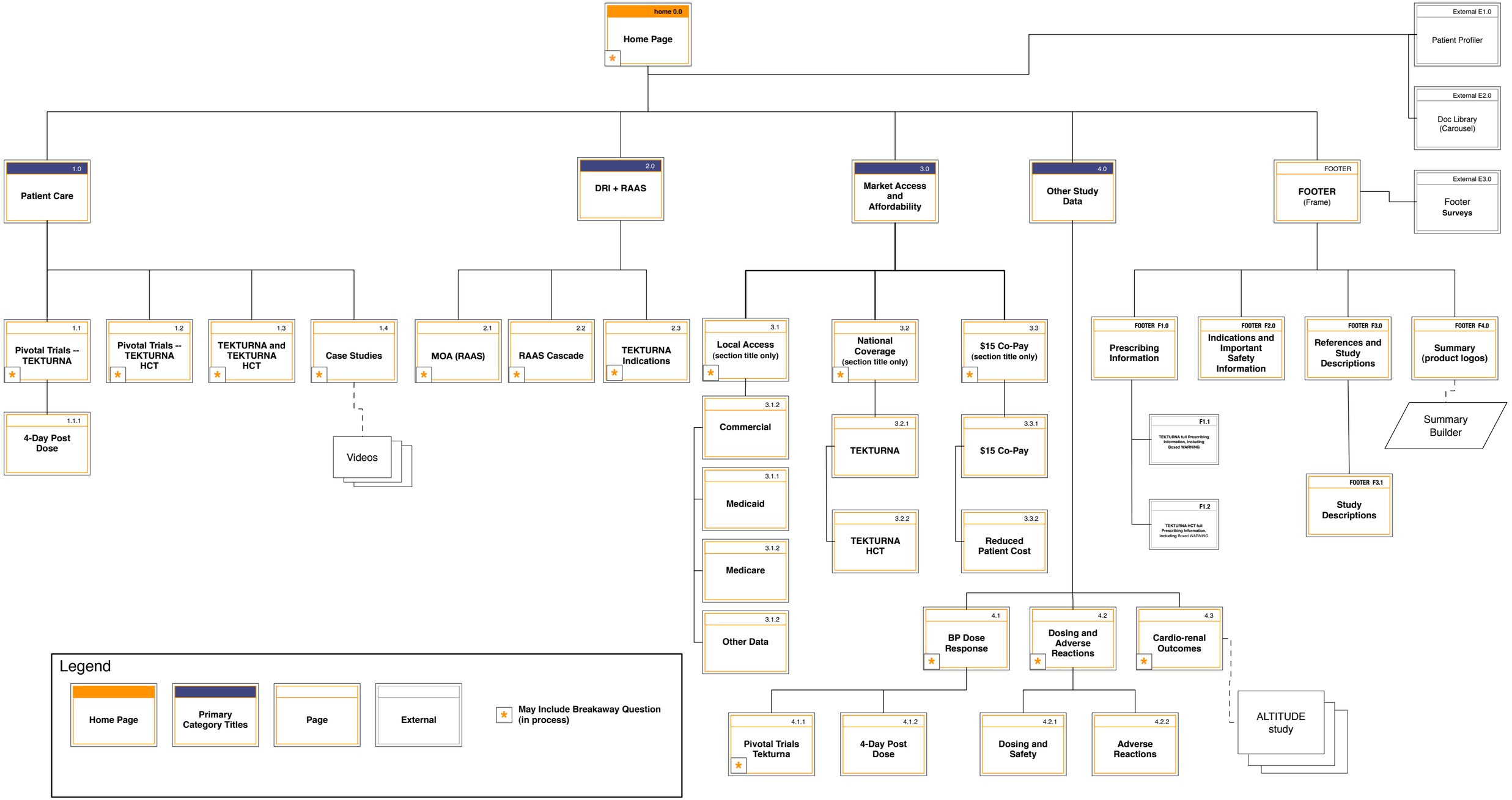
iPad Detail Aid Content Blocks

Tue Nov 27 2012

HAVAS LYNX

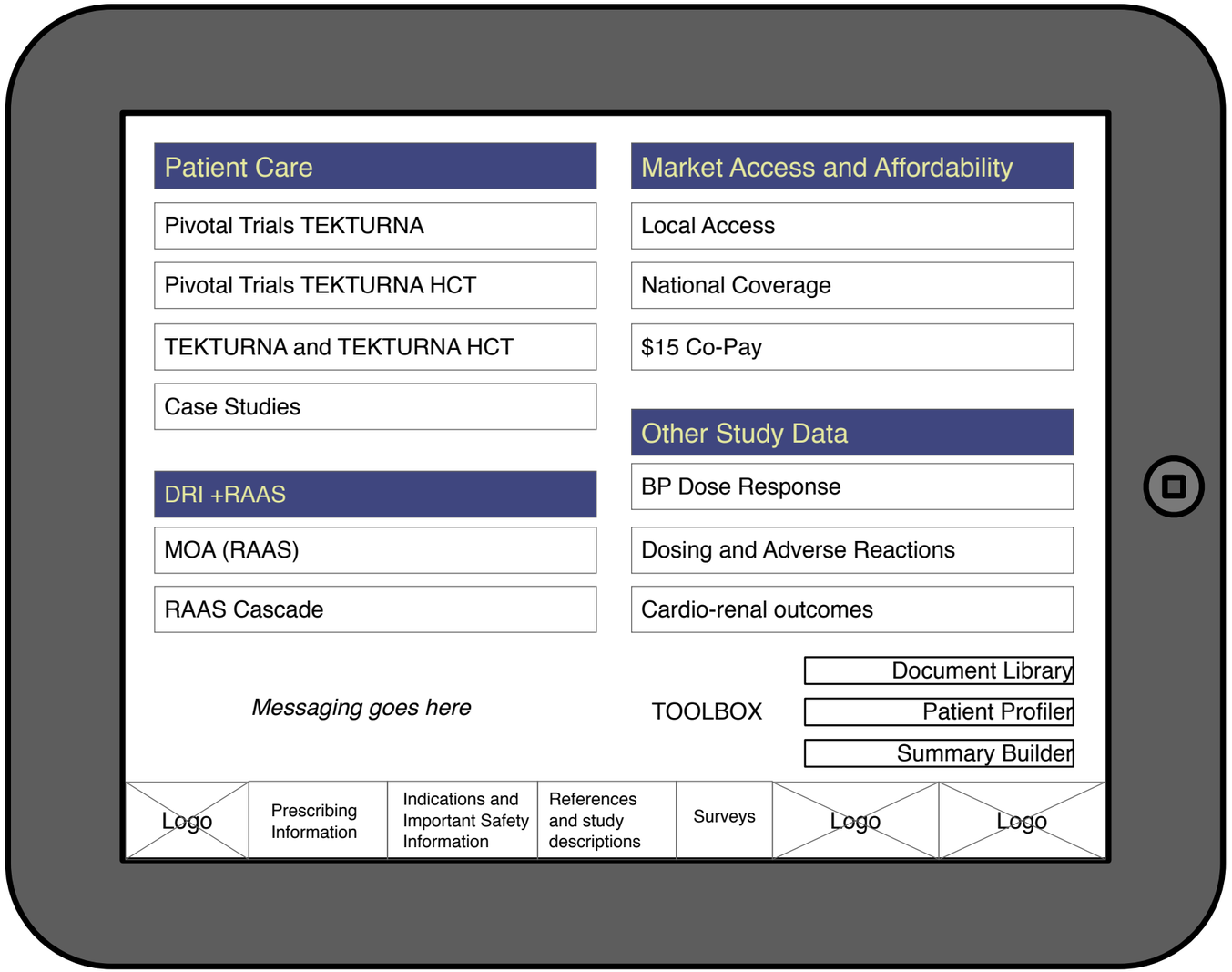
TEKTURNA® and TEKTURNA HCT® | Site Map

FINAL NOMENCLATURE TBD



TEKTURNA® and TEKTURNA HCT® Home Page Menu

Site Map ID#: 0.0



Notes:

Example Messaging: What can I discuss with you today that would help bring value to you and your practice?

Patient Care

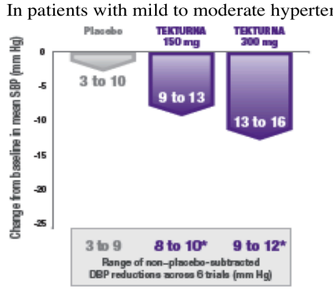
Site Map ID#: 1.1

Pivotal Trials-- Tekturna | Pivotal Trials-- Tekturna HCT | TEKTURNA and TEKTURNA HCT | Case Studies | ?

Pivotal trial data demonstrate BP-lowering efficacy

4-Day Post Dose

In patients with mild to moderate hypertension at baseline



1. In 6 randomized, double-blind, placebo-controlled, 8-week clinical trials, TEKTURNA was studied in patients with mild-to-moderate hypertension (msDBP 95-109 mm Hg)

* *P*<.05 vs placebo by ANCOVA with Dunnett's procedure for multiple comparisons in 4 studies. Black patients tended to have smaller reductions than Caucasians and Asians with TEKTURNA, consistent with what has been seen with ACEIs and ARBs.

ISI and Indications

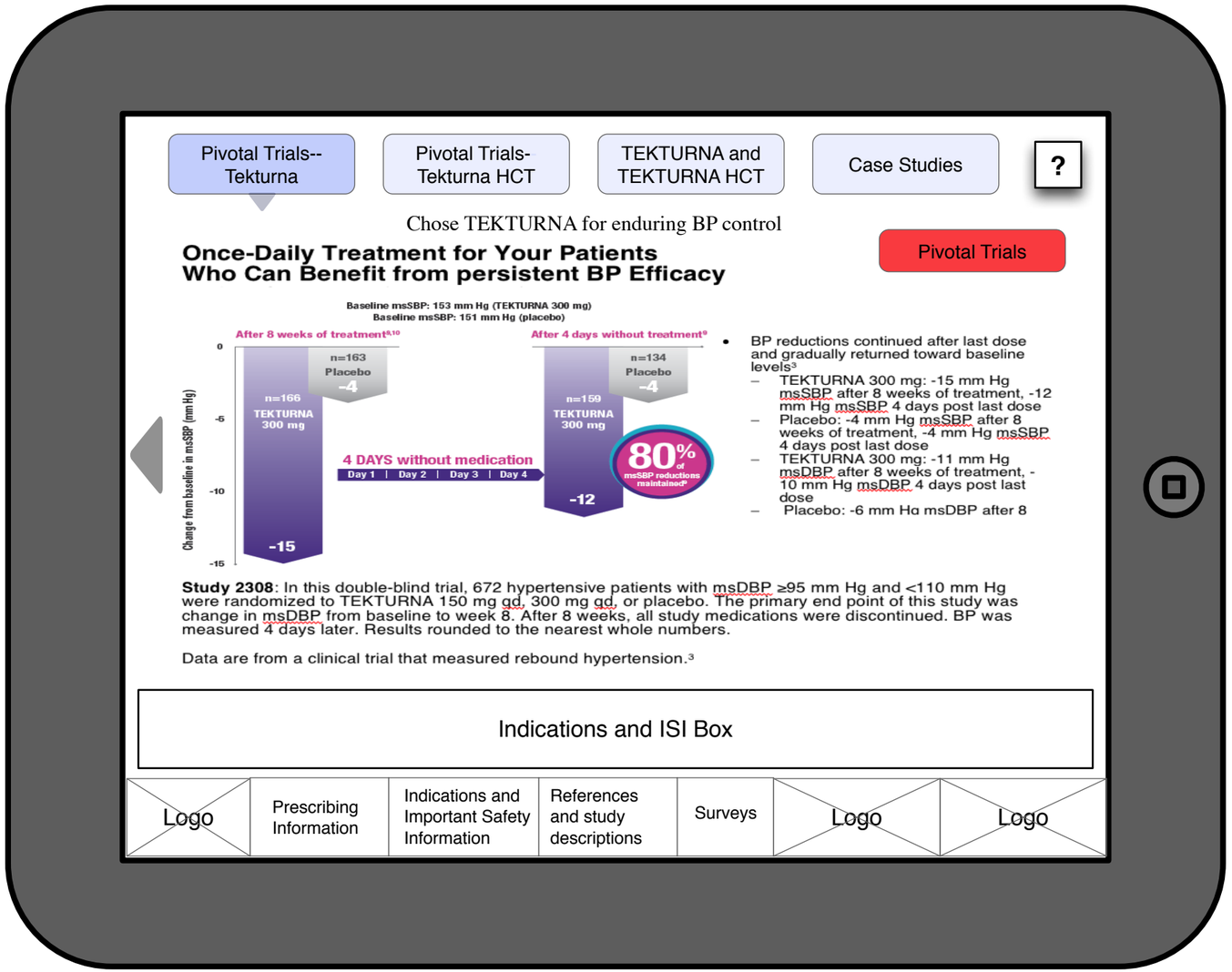
Logo | Prescribing Information | Indications and Important Safety Information | References and study descriptions | Surveys | Logo | Logo

Notes:

Animation will drop down.

Local navigation for 4-Day Post dose toggle is TBD.

Site Map ID#: 1.1.1

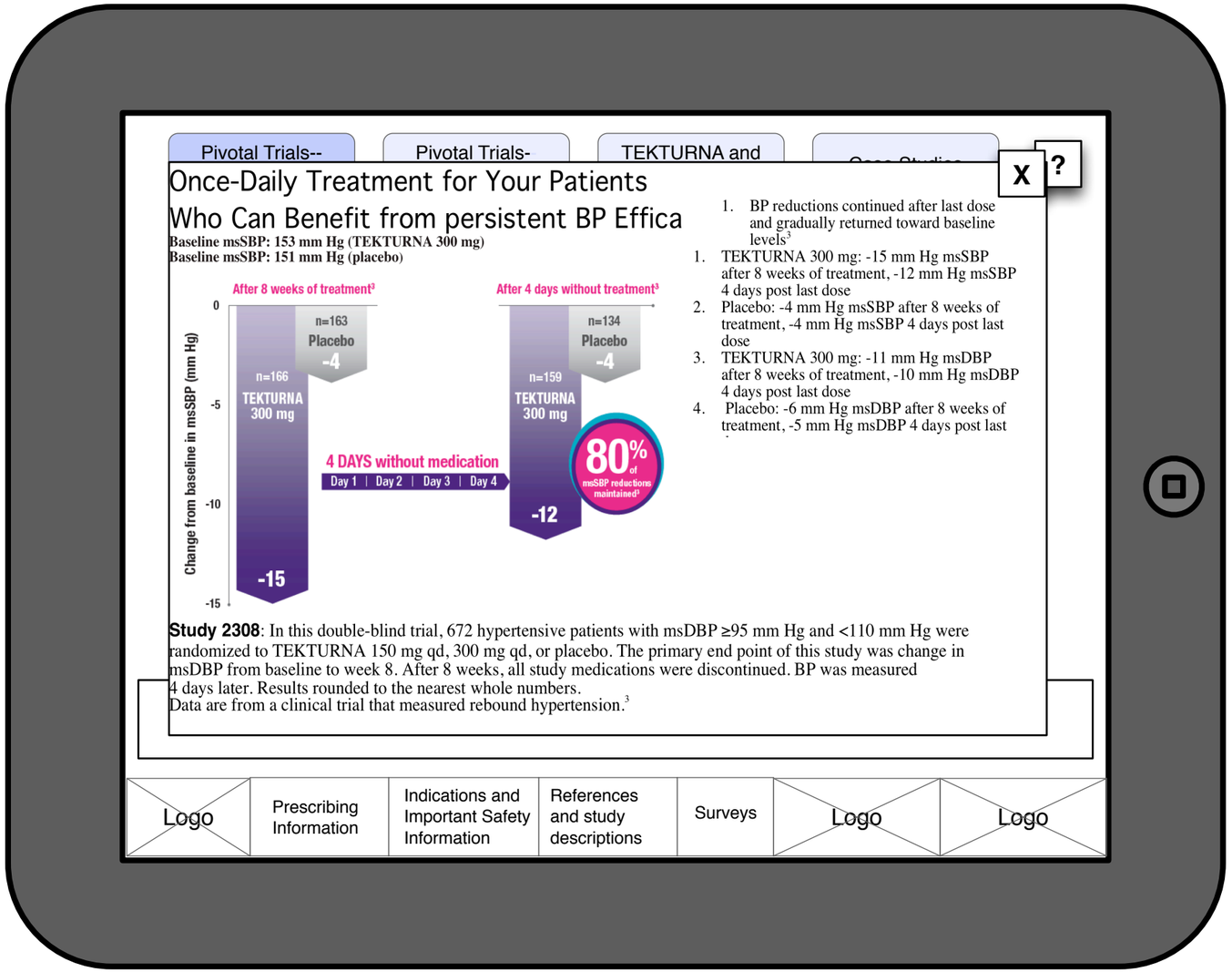


Notes:

We will require a build similar to EXALT study in EXFORGE, ie. 3 screens plus 80% conclusion overlay] (Please note: this 4-day post-dose chart and copy are identical to 4.1.2 on the site map).

Site Map ID#: 1.1.1

ALTERNATE: OVERLAY FOR 4-DAY POST DOSE



Notes:

Toggle TBD

Message TBD: Chose TEKTURNA for enduring BP control.

Site Map ID#: 1.2

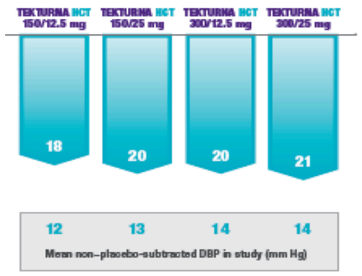
Notes:

Pivotal Trials-- Tekturna | Pivotal Trials-- Tekturna HCT | TEKTURNA and TEKTURNA HCT | Case Studies | ?

TEKTURNA HCT pivotal trial data

Select TEKTURNA HCT for proven BP reductions

Mean baseline SBP 153-155 mm Hg (TEKTURNA HCT)



1. TEKTURNA HCT was studied in an 8-week, multicenter, randomized, double-blind, placebo-controlled, parallel-group, multifactorial study in patients with mild-to-moderate hypertension (msDBP 95-109 mm Hg)
2. The mean baseline SBP/DBP range was 153-155/99-100 mm Hg
3. The primary end point in these trials was change in msDBP from baseline to week 8

* *P*<.05 vs placebo by ANCOVA with Dunnett's procedure for multiple comparisons in 4 studies. Black patients tended to have smaller reductions than Caucasians and Asians with TEKTURNA, consistent with what has been seen with ACEIs and ARBs.

ISI

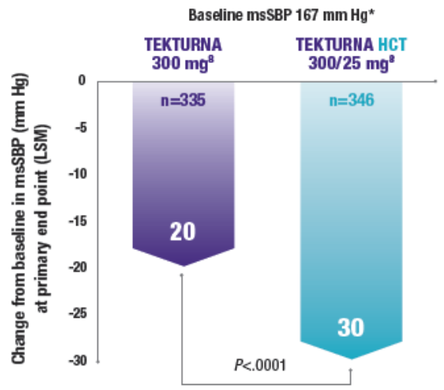
Logo | Prescribing Information | Indications and Important Safety Information | References and study descriptions | Surveys | Logo | Logo

Site Map ID#: 1.3

Notes:

Demonstrated efficacy for patients with stage 2 hypertension

Select TEKTURNA HCT for additional proven BP reductions[8,*]



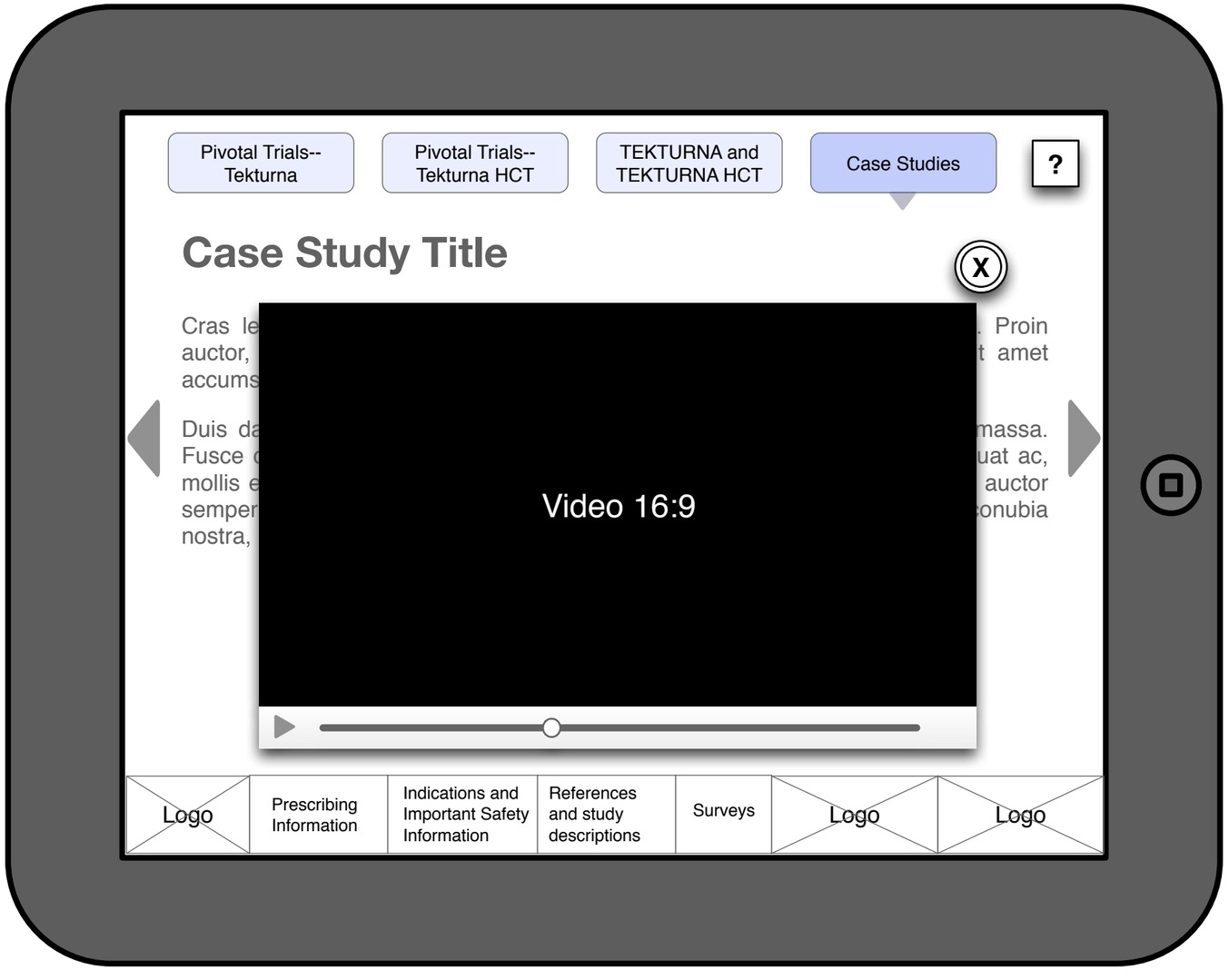
*Patients with stage 2 hypertension.

Study 2353

- A 12-week, double-blind, randomized, parallel-group, multicenter study to evaluate the efficacy and safety of the combination of aliskiren 300 mg and hydrochlorothiazide 25 mg compared to aliskiren 300 mg in patients with stage 2 hypertension
- The primary efficacy variable was the change from baseline (visit 2/day 1) in msSBP at end point
- For each patient, the last postbaseline measurement during the double-blind period was carried forward to week 12 as the end point measurement[8]
- At week 12, change from baseline in msDBP was -8 mm Hg for aliskiren 300 mg and -13 mm Hg for aliskiren 300 mg and HCTZ 25 mg

ISI

Site Map ID#: 1.4



Notes:

Case Studies TBD.

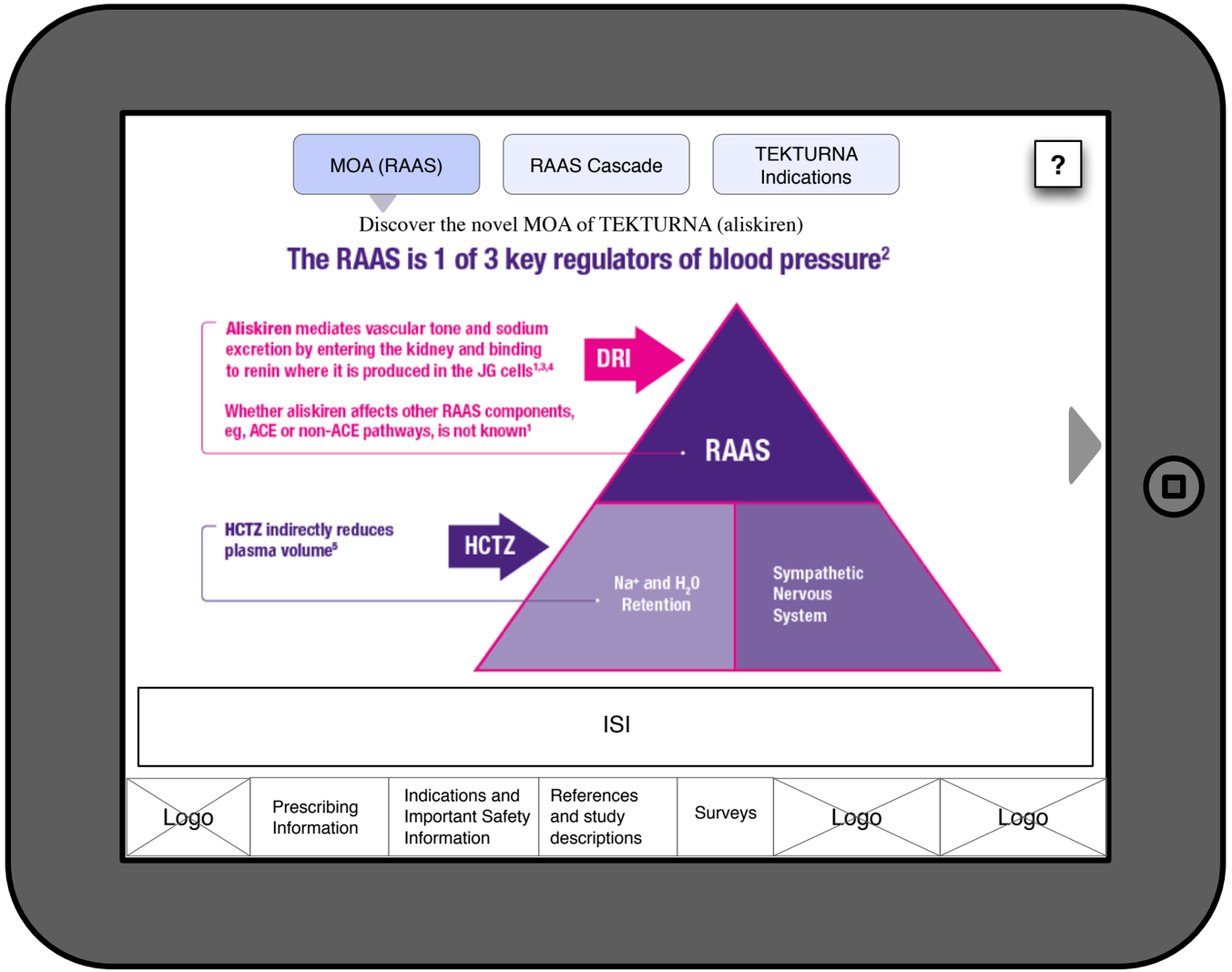
How to navigate from case study to case study.

Video may live outside of DMV.

Bite sized video, under 30 seconds.

DRI + RAAS

Site Map ID#: 2.1



Notes:

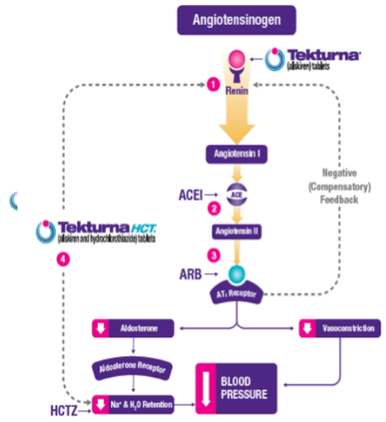
Chart should build in at least 3 steps

Site Map ID#: 2.2

MOA (RAAS) | RAAS Cascade | TEKTURNA Indications | ?

TEKTURNA works at the first and rate-limiting step of the RAAS[3]

The renin-angiotensin-aldosterone system[3,5,6]



1. Direct renin inhibition with TEKTURNA works at the first and rate-limiting step of the RAAS, limiting the formation of angiotensin I.[1,2]
2. Because DRI reduces angiotensin I levels, there is less angiotensin I available to be converted to angiotensin II.[1]
3. Reduced angiotensin II levels primarily decrease vasoconstriction and secondarily decrease aldosterone secretion and sodium/water retention.[2]
4. HCTZ in TEKTURNA HCT complements aliskiren and indirectly reduces plasma volume.[5]

The clinical implications of differences in effect on RAAS components are not known.[1]

Contraindications: Do not use aliskiren with angiotensin receptor blockers (ARBs) or ACE inhibitors (ACEIs) in patients with diabetes because of increased risk of renal impairment, hyperkalemia, and hypotension. Because of the HCTZ component, TEKTURNA HCT is contraindicated in patients with anuria or hypersensitivity to sulfonamide-derived drugs like HCTZ.

ISI/PI

Logo	Prescribing Information	Indications and Important Safety Information	References and study descriptions	Surveys	Logo	Logo

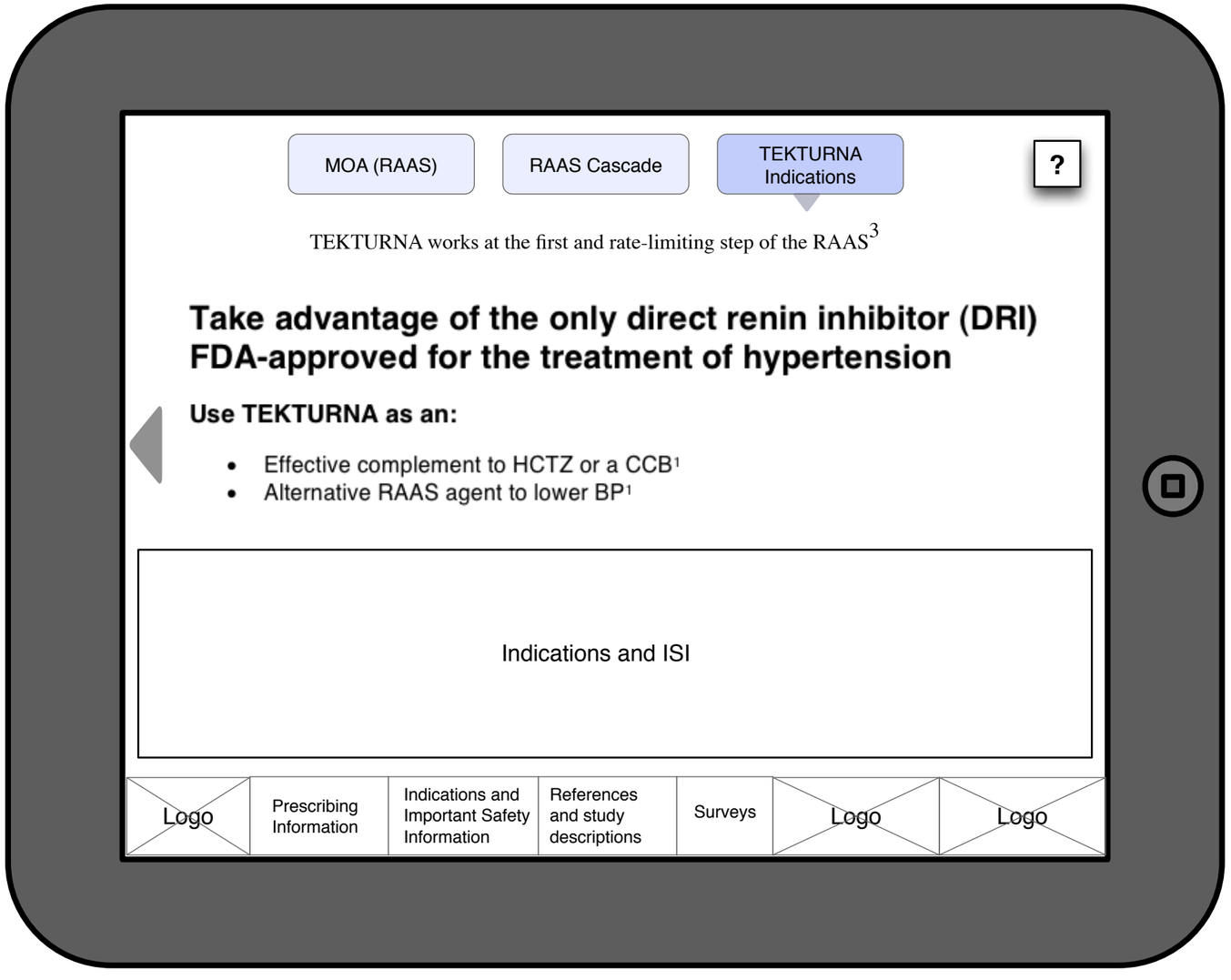
Notes:

3 or 4 part chart build;

Video/animation?

Site Map ID#: 2.3

Notes:



Market Access and Affordability

Site Map ID#: 3.1

Notes:

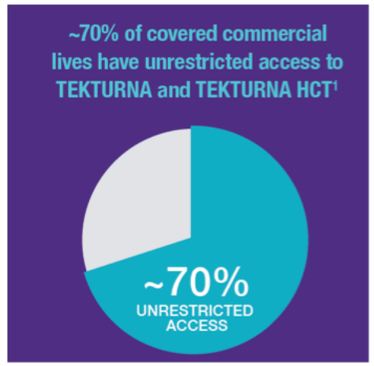
The top navigation, in order to be consistent with the other sections, should be Local Access, National Coverage, and $15 Co-Pay instead of Brand/Brand HCT. The brands would be tabs below the top nav. There is less screen real estate available when using this approach however.

This would result in one less click and avoids the practice of having users go back to the main menu and then down again in order to toggle between Market Access and Affordability subcategories.

Site Map ID#: 3.2

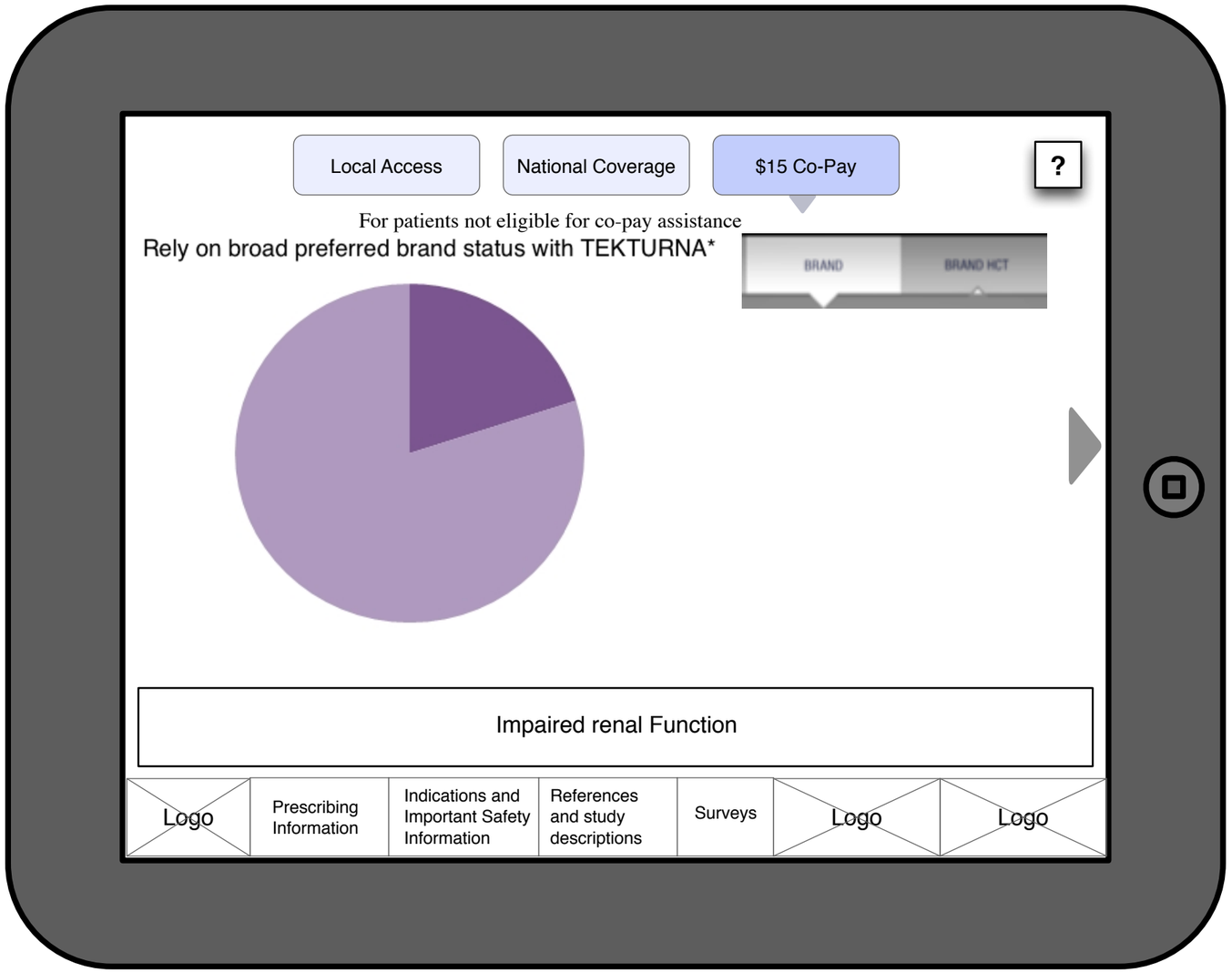
Notes:

There is no brand to compare. Could be a pie chart that reveals TEK coverage with toggle for TEK HCT coverage.



Site Map ID#: 3.3.1

ALTERNATE NAVIGATION

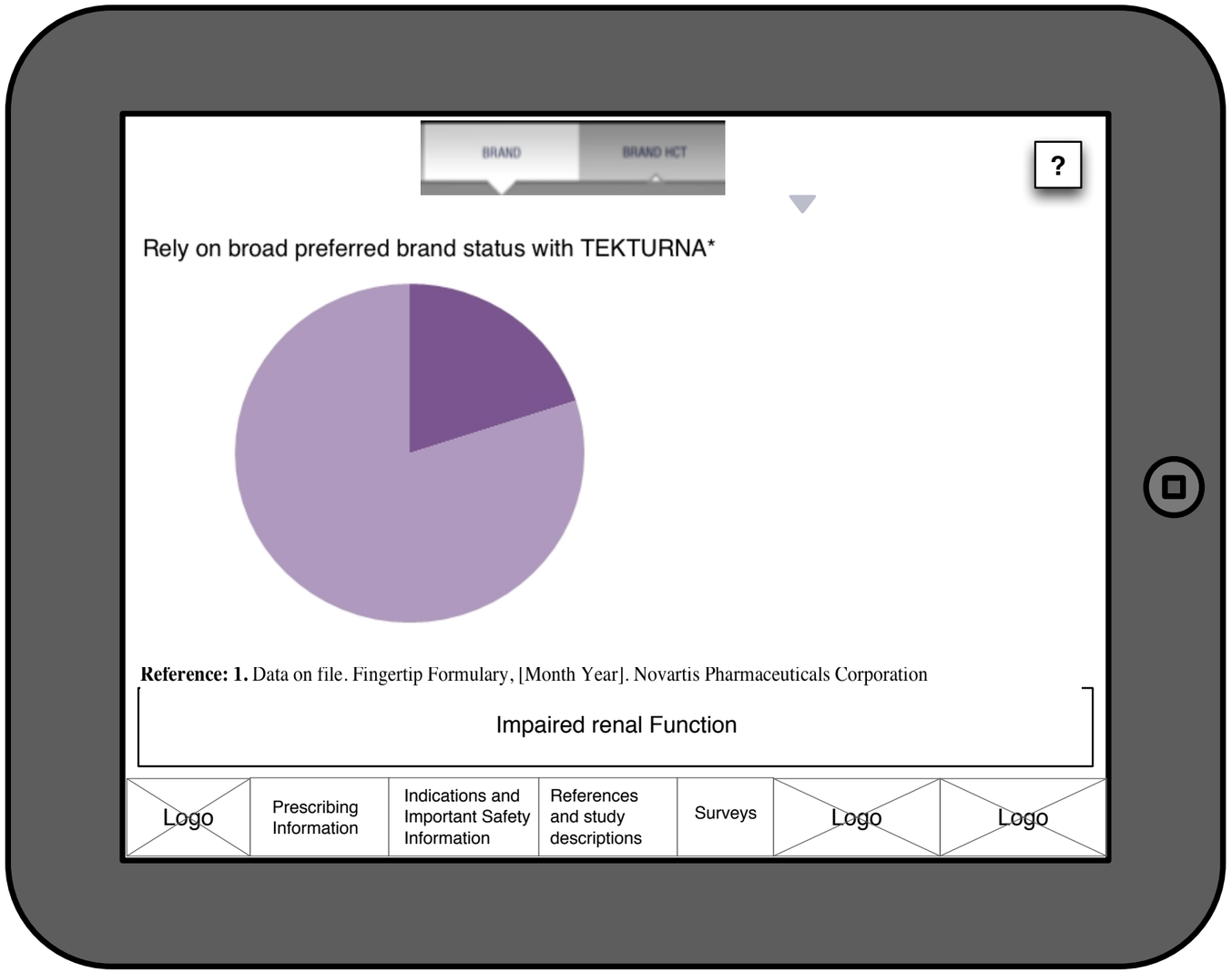


Notes:

(This chart is FPO = We will offer separate access data for TEK and TEK HCT. Headline will adjust.

Site Map ID#: 3.3.1

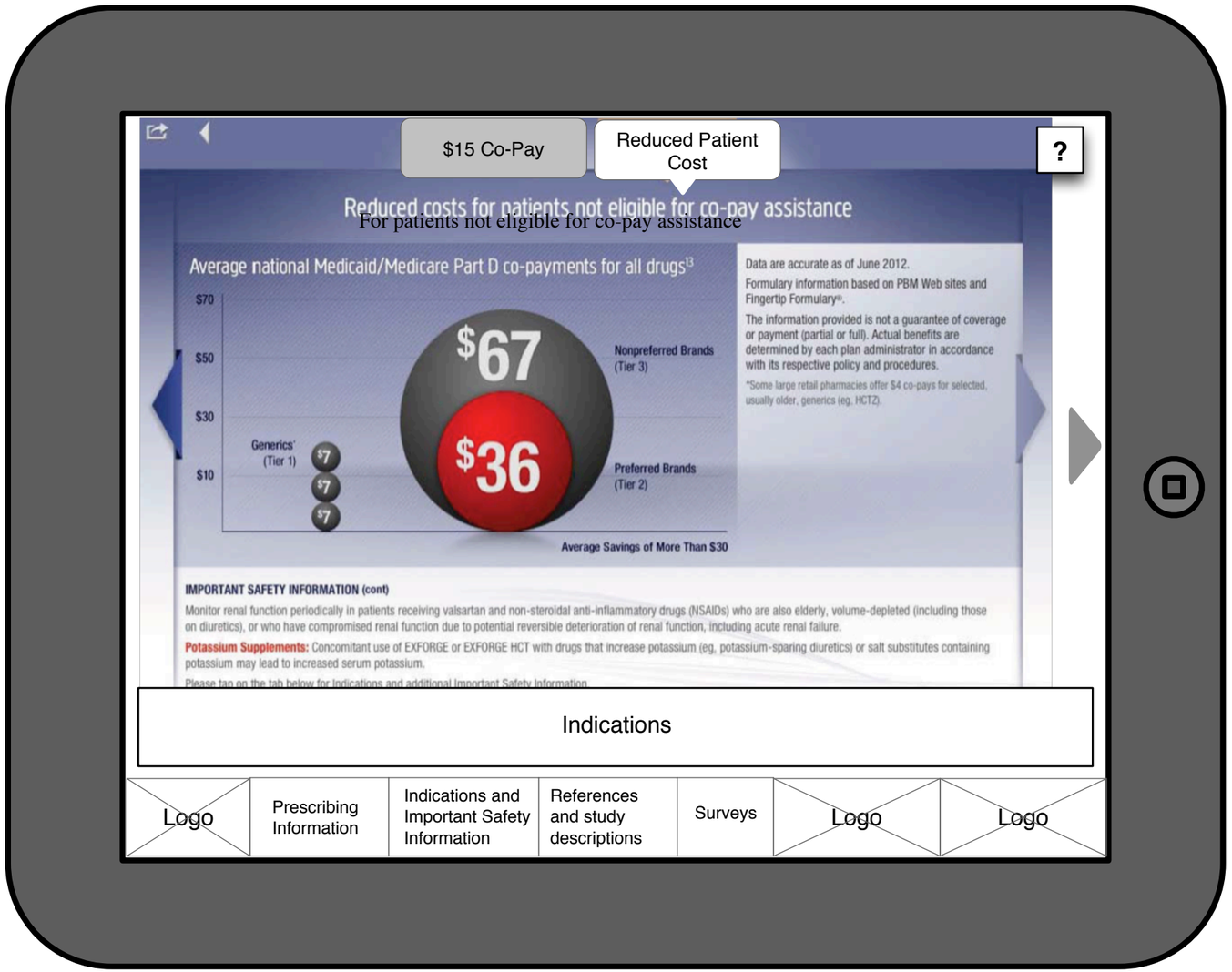
ALTERNATE NAVIGATION



Notes:

(This chart is FPO = We will offer separate access data for TEK and TEK HCT. Headline will adjust.

Site Map ID#: 3.3.2



Notes:

This FPO screen compares Generics vs Preferred and non-preferred brands [by tier level]. IT IS NOT SPECIFIC TO TEK or TEK HCT. We may have to include 2 levels of generics –as well as– preferred and non-preferred brands—in our update; this will be identical to the similar, updated screen on the EXFORGE LaunchPad.

Other Study Data

Site Map ID#: 4.1.1

BP Dose Response | Dosing and Adverse Reactions | Cardio-renal Outcomes | ?

Pivotal trial data demonstrate BP-lowering efficacy

Choose TEKTURNA for proven BP reductions

4-Day Post Dose

TEKTURNA pivotal trial data from 6 clinical trials in patients with mild-to-moderate hypertension[1,2]

	Placebo	TEKTURNA 150 mg	TEKTURNA 300 mg
SBP reductions*	3 to 10	9 to 13	13 to 16
DBP reductions†	3 to 9	8 to 10‡	9 to 12‡

Pivotal trials: TEKTURNA was studied in 6 randomized, double-blind, placebo-controlled, 8-week clinical trials in patients with mild-to-moderate hypertension (msDBP 95-109 mm Hg). The primary end point in these trials was change in msDBP from baseline to week 8.

*Change from baseline in mean SBP (mm Hg) from 0 to -25.

†Range of non–placebo-subtracted DBP reductions across 6 trials (mm Hg).

‡P<0.05 vs placebo by ANCOVA with Dunnett's procedure for multiple comparisons in 4 studies. Black patients tended to have smaller reductions than Caucasians and Asians with TEKTURNA, consistent with what has been seen with ACEIs and ARBs.

ISI and Warning Box

Logo | Prescribing Information | Indications and Important Safety Information | References and study descriptions | Surveys | Logo | Logo

Notes:

Please note: this is the tabular form of the pivotal trials data; it's an alternate way to talk about the data presented in 1.1 MAP requires an efficacy mention before we can detail Study 2308.

Site Map ID#: 4.1.2

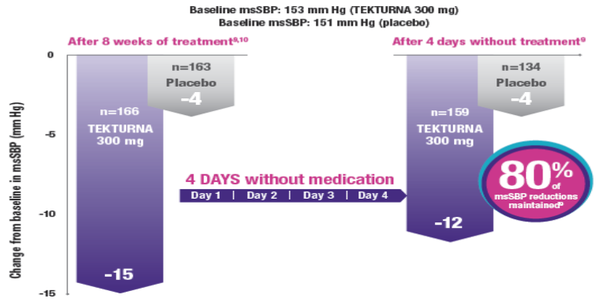
Notes:

Chart should build in at least 3 steps

BP Dose Response | Dosing and Adverse Reactions | Cardio-renal Outcomes | ?

Chose TEKTURNA for enduring BP control

Once-Daily Treatment for Your Patients Who Can Benefit from persistent BP Efficacy



- BP reductions continued after last dose and gradually returned toward baseline levels[3]
  - TEKTURNA 300 mg: -15 mm Hg msSBP after 8 weeks of treatment, -12 mm Hg msSBP 4 days post last dose
  - Placebo: -4 mm Hg msSBP after 8 weeks of treatment, -4 mm Hg msSBP 4 days post last dose
  - TEKTURNA 300 mg: -11 mm Hg msDBP after 8 weeks of treatment, -10 mm Hg msDBP 4 days post last dose
  - Placebo: -6 mm Hg msDBP after 8

Study 2308: In this double-blind trial, 672 hypertensive patients with msDBP ≥95 mm Hg and <110 mm Hg were randomized to TEKTURNA 150 mg qd, 300 mg qd, or placebo. The primary end point of this study was change in msDBP from baseline to week 8. After 8 weeks, all study medications were discontinued. BP was measured 4 days later. Results rounded to the nearest whole numbers.

Data are from a clinical trial that measured rebound hypertension.[3]

ISI

Logo	Prescribing Information	Indications and Important Safety Information	References and study descriptions	Surveys	Logo	Logo

Site Map ID#: 4.2.1

BP Dose Response | Dosing and Adverse Reacrions | Cardio-renal Outcomes

?

3

THE FLEXIBILITY OF MULTIPLE DOSAGE STRENGTH OPTIONS

TEKTURNA tablets are available in the following strengths:

TEKTURNA HCT tablets are available in the following strengths:

Samples shown are not actual size.

INDICATIONS

TEKTURNA and TEKTURNA HCT are indicated for the treatment of hypertension in adults, to lower blood pressure. Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions. Control of high blood pressure should be part of comprehensive cardiovascular risk management, including, as appropriate, lipid control, diabetes management, antithrombotic therapy, smoking cessation, exercise, and limited sodium intake. Many patients will require more than one drug to achieve blood pressure goals.

Use TEKTURNA HCT as initial therapy in patients who are likely to need multiple drugs to achieve their blood pressure goals. Switch a patient whose blood pressure is not adequately controlled with aliskiren or hydrochlorothiazide (HCTZ) monotherapy to TEKTURNA HCT.

TEKTURNA HCT may be substituted for its titrated components.

Safety and efficacy of aliskiren in pediatric patients have not been established.

Base the choice of TEKTURNA HCT as initial therapy on an assessment of potential benefits and risks. Individualize the decision to use a combination as initial therapy by weighing factors such as baseline blood pressure, the target goal, and the incremental likelihood of achieving goal with a combination compared to monotherapy.

IMPORTANT SAFETY INFORMATION

WARNING: FETAL TOXICITY
- **When pregnancy is detected, discontinue TEKTURNA or TEKTURNA HCT as soon as possible. (5.1).**
- **Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus. (5.1).**

Contraindications: Do not use aliskiren with angiotensin receptor blockers (ARBs) or ACE inhibitors (ACEIs) in patients with diabetes because of increased risk of renal impairment, hyperkalemia, and hypotension.

Because of the HCTZ component, TEKTURNA HCT is contraindicated in patients with anuria or hypersensitivity to sulfonamide-derived drugs like HCTZ. Hypersensitivity reactions may range from urticaria to anaphylaxis.

Anaphylactic Reactions and Angioedema: Hypersensitivity reactions such as anaphylactic reactions and angioedema of the face, extremities, lips, tongue, glottis and/or larynx have been reported in patients treated with aliskiren and have necessitated hospitalization and intubation. This may occur at any time during treatment and has occurred in patients with and without a history of angioedema with ACEIs or angiotensin receptor antagonists. Discontinue TEKTURNA or TEKTURNA HCT immediately in patients who develop anaphylactic reactions or angioedema, and do not readminister.

Logo

Logo

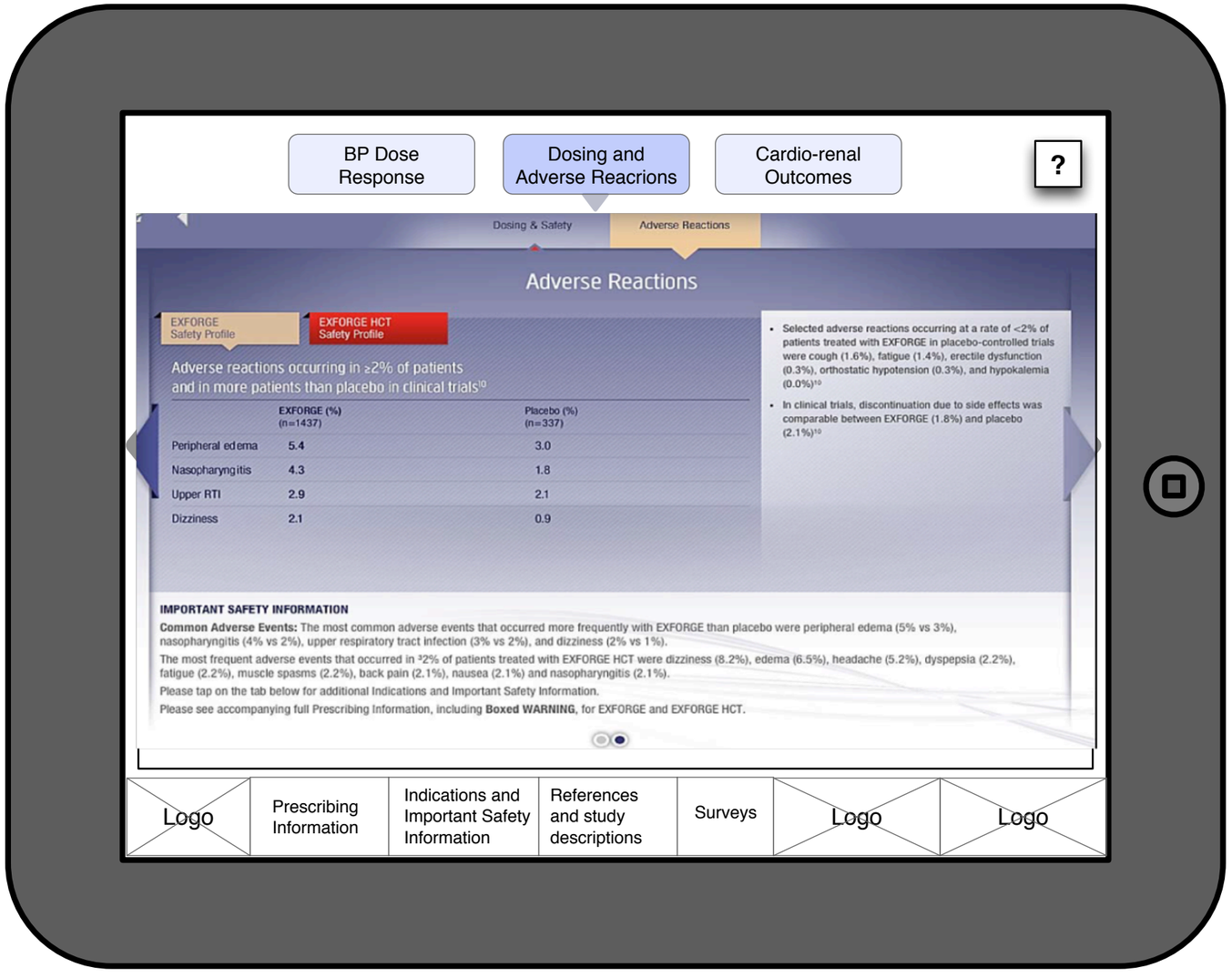
Notes:

3 or 4 part chart build;

Video/animation?

Site Map ID#: 4.2.2

EXFORGE EXAMPLE



Notes:

Please see EXFORGE pages for model = Need to tab between TEK and TEK HCT for Documented Adverse Reactions= table with TEK and TEK HCT values to come.

Site Map ID#: 4.2.2

EXFORGE HCT EXAMPLE

BP Dose Response | Dosing and Adverse Reacrions | Cardio-renal Outcomes | ?

Dosing & Safety | Adverse Reactions

Adverse Reactions

EXFORGE Safety Profile | EXFORGE HCT Safety Profile

Adverse reactions occurring in ≥2% of the EXFORGE HCT treatment group[12]

	EXFORGE HCT 10/320/25 mg (%) (n=582)	Valsartan/HTCZ 320/25 mg (%) (n=559)	Amlodipine/valsartan 10/320 mg (%) (n=566)	Amlodipine/HCTZ 10/25 mg (%) (n=561)
Dizziness	8.2	7.2	2.5	4.1
Edema	6.5	1.4	11.5	11.2
Headache	5.2	5.5	5.3	7.1
Dyspepsia	2.2	0.9	1.1	0.4
Fatigue	2.2	2.7	2.1	1.4
Muscle spasms	2.2	1.3	1.2	0.9
Back pain	2.1	2.3	0.9	2.1
Nausea	2.1	1.3	1.8	2.1
Nasopharyngitis	2.1	2.3	2.3	2.1

- Overall incidence of adverse reactions with EXFORGE HCT was similar between younger (<65 years) and older (≥65 years) patients[12]
- Orthostatic hypotension and postural dizziness were seen in 0.5% of patients treated with EXFORGE HCT 10/320/25 mg[12]
- In an active controlled trial, discontinuation because of adverse reactions occurred in 4.0% of patients treated with EXFORGE HCT 10/320/25 mg, 2.9% of patients treated with valsartan/HCTZ 320/25 mg, 1.6% of patients treated with amlodipine/valsartan 10/320 mg, and 3.4% of patients treated with amlodipine/HCTZ 10/25 mg[12]

Adverse reactions were generally mild and transient in nature and have only infrequently resulted in discontinuation.[12]

IMPORTANT SAFETY INFORMATION

Common Adverse Events: The most common adverse events that occurred more frequently with EXFORGE than placebo were peripheral edema (5% vs 3%), nasopharyngitis (4% vs 2%), upper respiratory tract infection (3% vs 2%), and dizziness (2% vs 1%).

The most frequent adverse events that occurred in ³2% of patients treated with EXFORGE HCT were dizziness (8.2%), edema (6.5%), headache (5.2%), dyspepsia (2.2%), fatigue (2.2%), muscle spasms (2.2%), back pain (2.1%), nausea (2.1%) and nasopharyngitis (2.1%).

Please tap on the tab below for additional Indications and Important Safety Information.

Please see accompanying full Prescribing Information, including **Boxed WARNING**, for EXFORGE and EXFORGE HCT.

Notes:

Site Map ID#: 4.3

BP Dose Response | Dosing and Adverse Reactions | Cardio-renal Outcomes | ?

Aliskiren Trial in Type 2 Diabetes Using Cardio-renal End Points

Hypertension was not part of inclusion criteria[1]

Inclusion criteria:

- Type 2 diabetes
- Male or female patients ≥35 years of age
- Patients remained concomitantly on prior, conventional ACEI or ARB therapy without any treatment adjustments for ≥4 weeks prior to randomization
- Patients with one or more of the following:
  - –Persistent macroalbuminuria or microalbuminuria
  - –Diabetic nephropathy
  - –History of cardiovascular disease

Additional parameters:

- Study patients were high risk at baseline
- Majority of patients had adequately controlled BP at baseline

Patients (n=8600)* randomized to receive either:

Aliskiren 300 mg tablets qd + an ARB or ACEI (n=4300)

or

Placebo qd + an ARB or ACEI (n=4300)

Primary end point was not BP lowering[1]

Primary composite end point included the first occurrence of one of the following events:

- CV or resuscitated sudden death
- Nonfatal MI or stroke
- Unplanned hospitalization for HF
- Doubling of baseline serum creatinine concentration to above the ULN (sustained for ≥1 month)
- Onset of ESRD or renal death

Indications and ISI

Logo | Prescribing Information | Indications and Important Safety Information | References and study descriptions | Surveys | Logo | Logo

Notes:

Build chart from left to right

OBJECTIVE: To assess benefits of combination treatment of aliskiren + an ARB or ACEI on CV and renal morbidity and mortality[1]

Site Map ID#: 4.3.1

Notes:

Build chart from left to right

BP Dose Response | Dosing and Adverse Reactions | Cardio-renal Outcomes | ?

Aliskiren Trial in Type 2 Diabetes Using Cardio-renal End Points

4.3.1

Study results–incidence of selected AEs[2]

	Aliskiren n=4283		Placebo n=4296	
	SAEs† (%)	AEs (%)	SAEs† (%)	AEs (%)
Renal impairment‡	4.7	12.4	3.3	10.4
Hypotension§	2.0	18.6	1.7	14.8
Hyperkalemia‖	1.1	36.9	0.3	27.1

The risk of stroke (2.7% aliskiren vs 2.0% placebo) and death (6.9% aliskiren vs 6.4% placebo) were also numerically higher in aliskiren-treated patients.[2]

Label implications from ALTITUDE[2]

- A contraindication against combined use of aliskiren-based products with ARBs or ACEIs in patients with diabetes
- A warning against the use of aliskiren-based products in patients with moderate renal (kidney) impairment (eGFR <60 ml/min) who are also taking an ARB or ACEI

*Assuming a screenings failure rate of 60%.[1]
†SAE is defined as an event which is fatal or life-threatening, results in persistent or significant disability/incapacity, constitutes a congenital anomaly/birth defect, requires inpatient hospitalization or prolongation of existing hospitalization, or is medically significant (ie, defined as an event that jeopardizes the patient or may require medical or surgical intervention to prevent one of the outcomes previously listed).[2]
‡Renal failure, renal failure acute, renal failure chronic, or renal impairment.[2]
§Dizziness, dizziness postural, hypotension, orthostatic hypotension, presyncope, or syncope.[2]
‖Given the variable baseline potassium levels of patients with renal insufficiency on dual RAAS therapy, reporting hyperkalemia was at the discretion of the investigator.[2]

IMPORTANT SAFETY INFORMATION (cont)

Anaphylactic Reactions and Angioedema: Hypersensitivity reactions such as anaphylactic reactions and angioedema of the face, extremities, lips, tongue, glottis and/or larynx have been reported in patients treated with aliskiren and have necessitated hospitalization and intubation. This may occur at any time during treatment and has occurred in patients with and without a history of angioedema with ACEIs or angiotensin receptor antagonists. Discontinue TEKTURNA immediately in patients who develop anaphylactic reactions or angioedema, and do not readminister.

Hypotension: In patients with an activated renin-angiotensin-aldosterone system (RAAS), such as volume- and/or salt-depleted patients receiving high doses of diuretics, symptomatic hypotension may occur in patients receiving RAAS blockers. Correct these conditions before administering TEKTURNA, or start the treatment under close medical supervision.

Site Map ID#: 4.3.2

Notes:

BP Dose Response | Dosing and Adverse Reactions | Cardio-renal Outcomes | ?

Aliskiren Trial in Type 2 Diabetes Using Cardio-renal End Points

TEKTURNA is approved for patients with mild-to-moderate hypertension[2]

The data below are not derived from the ALTITUDE study

Discontinuation rates due to AEs comparable to placebo

TEKTURNA	**2.2%** of study population vs 3.5% placebo[2]

Hyperkalemia (increases in serum potassium >5.5 mEq/L) was infrequent with TEKTURNA alone

TEKTURNA	**0.9%** of study population vs 0.6% placebo[2]

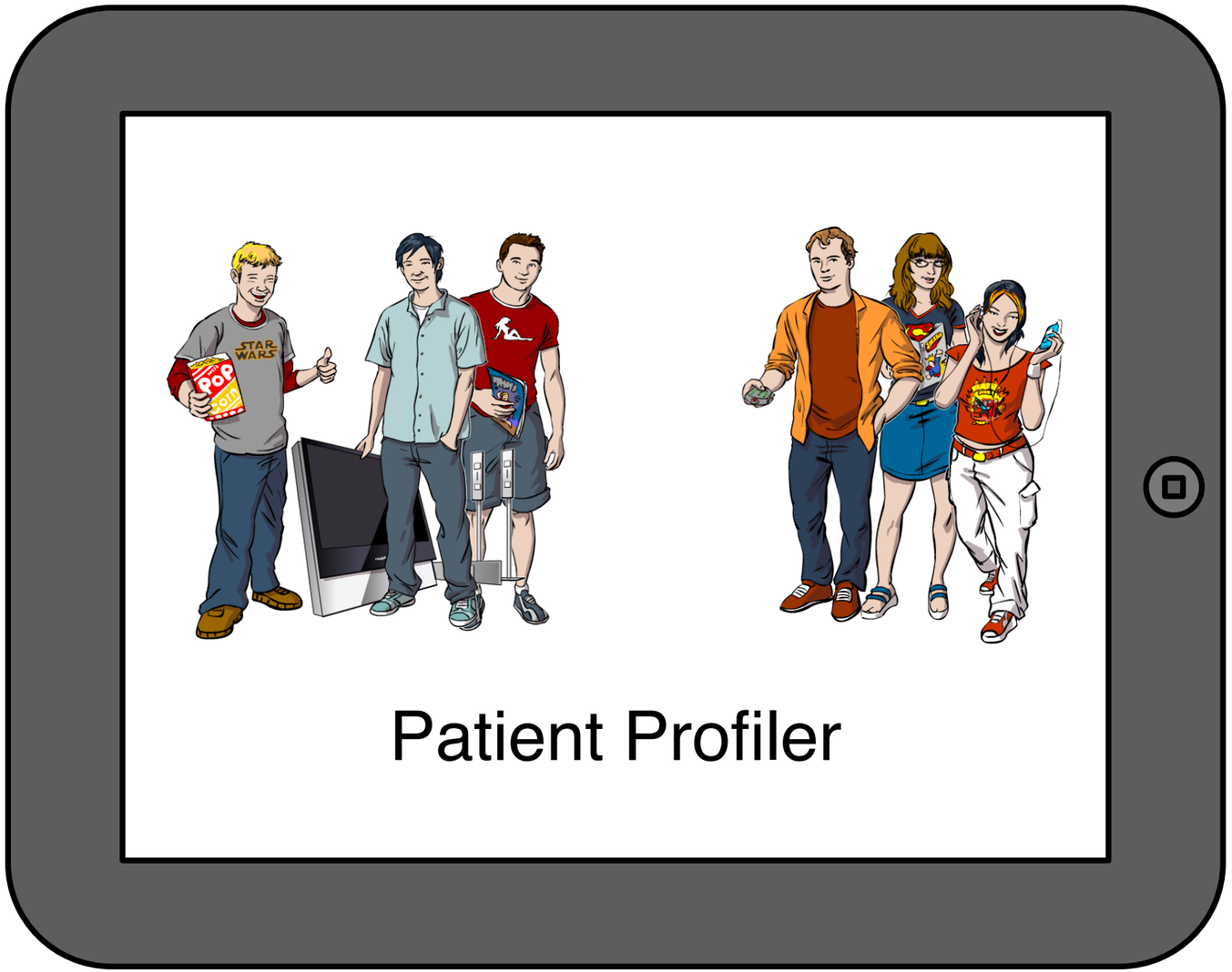
Hyperkalemia: Monitor serum potassium periodically in patients receiving aliskiren. Drugs that affect the RAAS can cause hyperkalemia. Risk factors for the development of hyperkalemia include renal insufficiency, diabetes, and combination use of aliskiren with ARBs or ACEIs, NSAIDs, potassium supplements, or potassium-sparing diuretics.

The safety of TEKTURNA has been evaluated in more than 6000 patients[2]

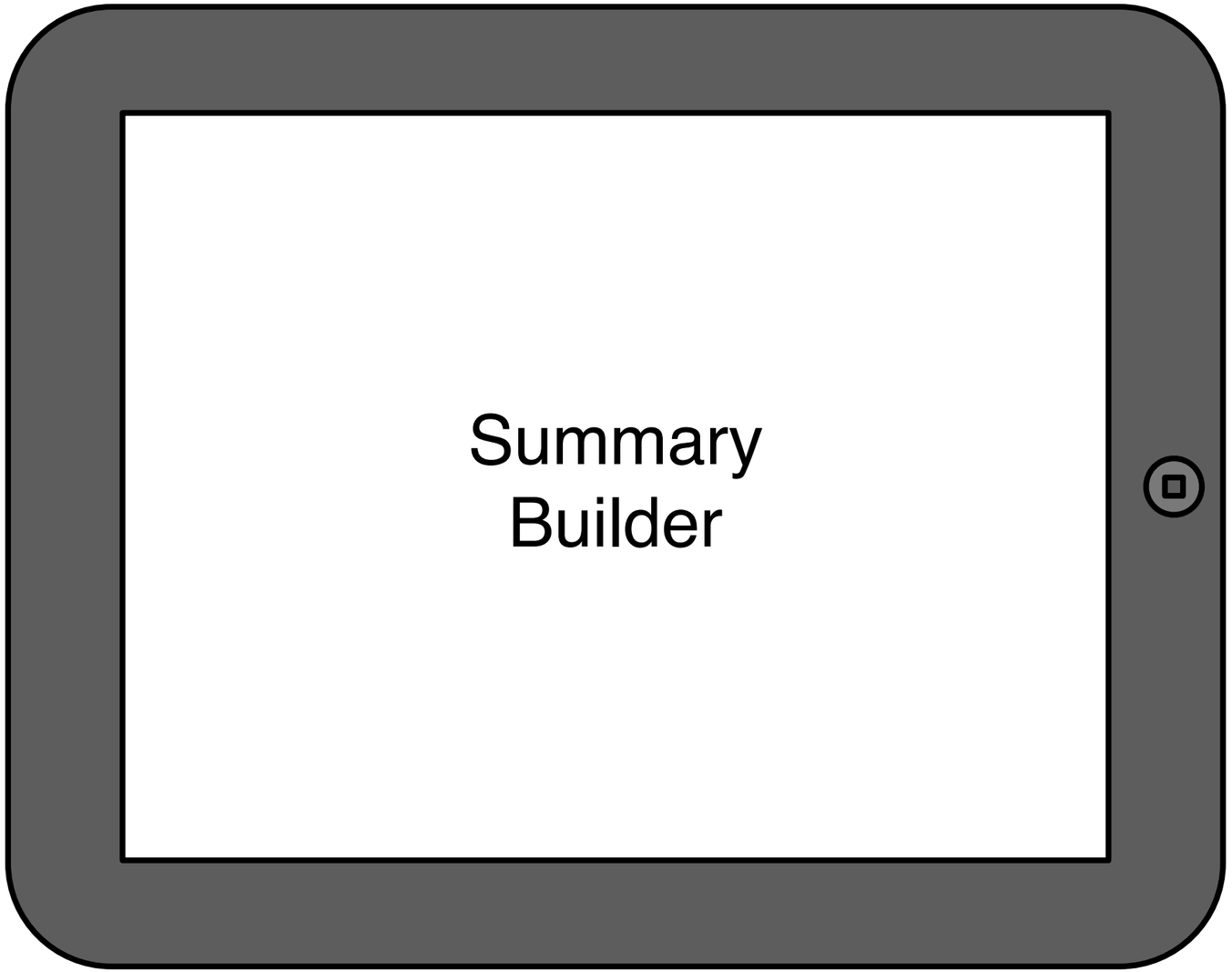
Logo | Prescribing Information | Indications and Important Safety Information | References and study descriptions | Surveys | Logo | Logo

Site Map ID#: E1.0

Notes:



Site Map ID#: TBD



Notes:

One bullet summary per screen for Rep's view only

Site Map ID#: E2.0

Notes: