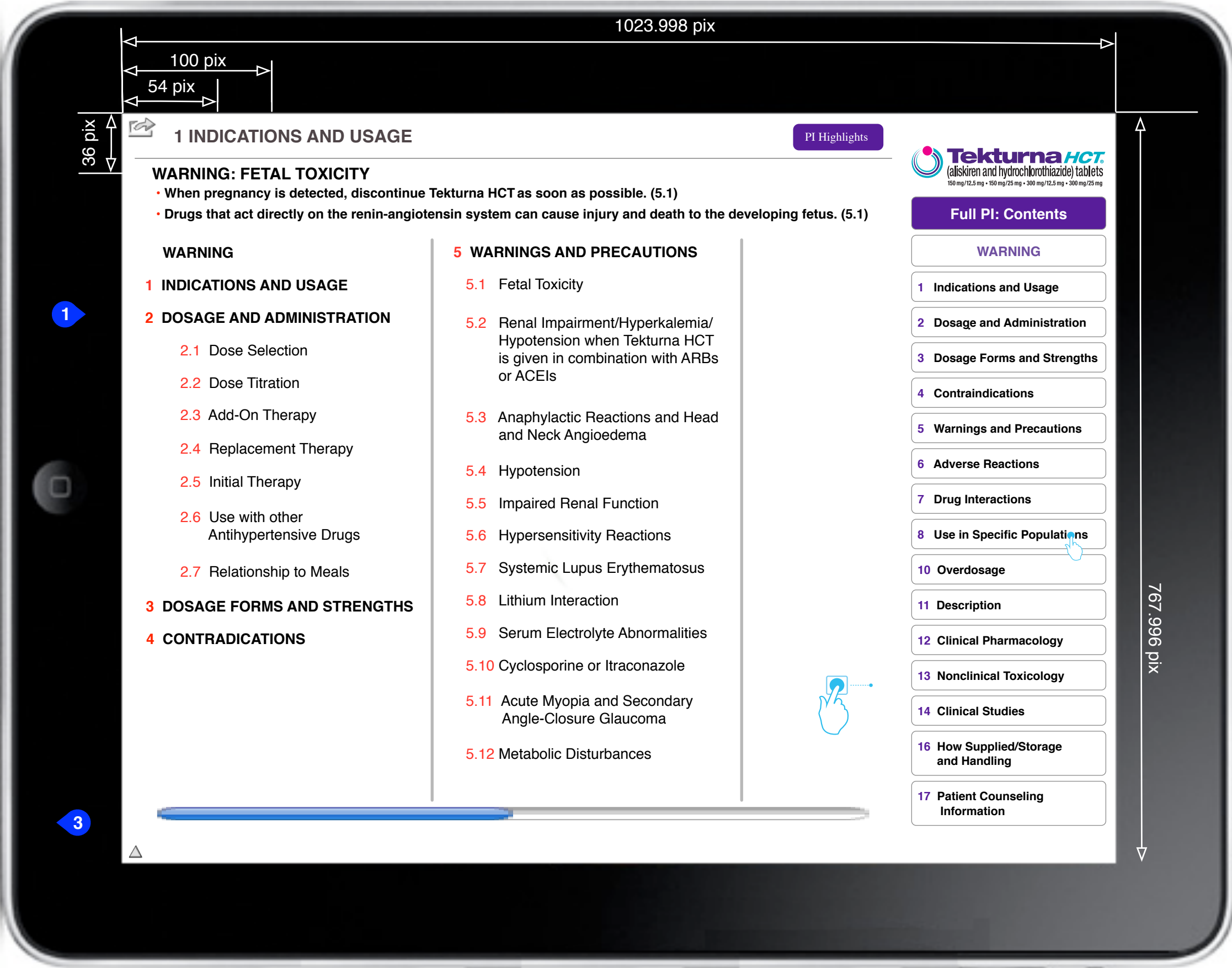


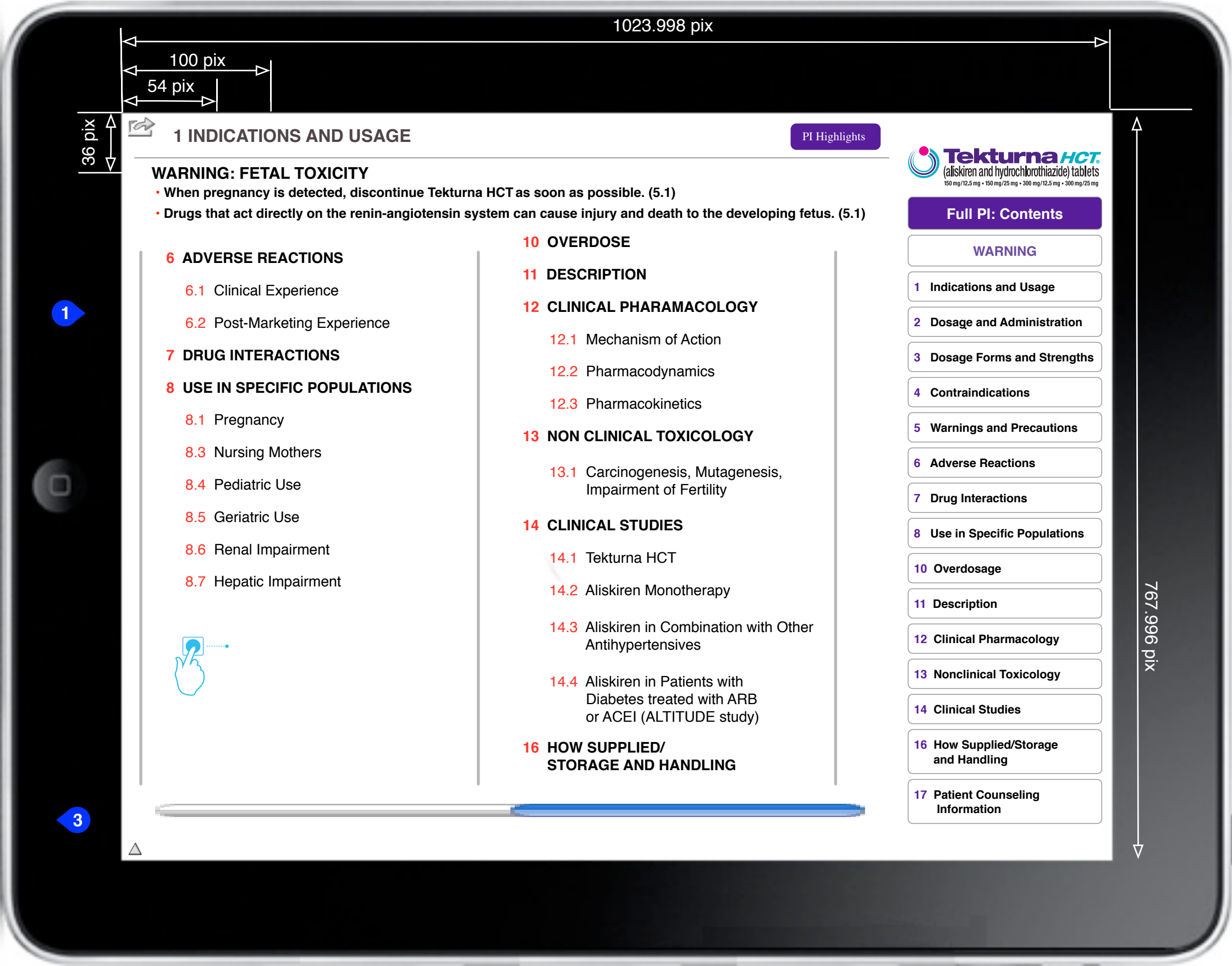
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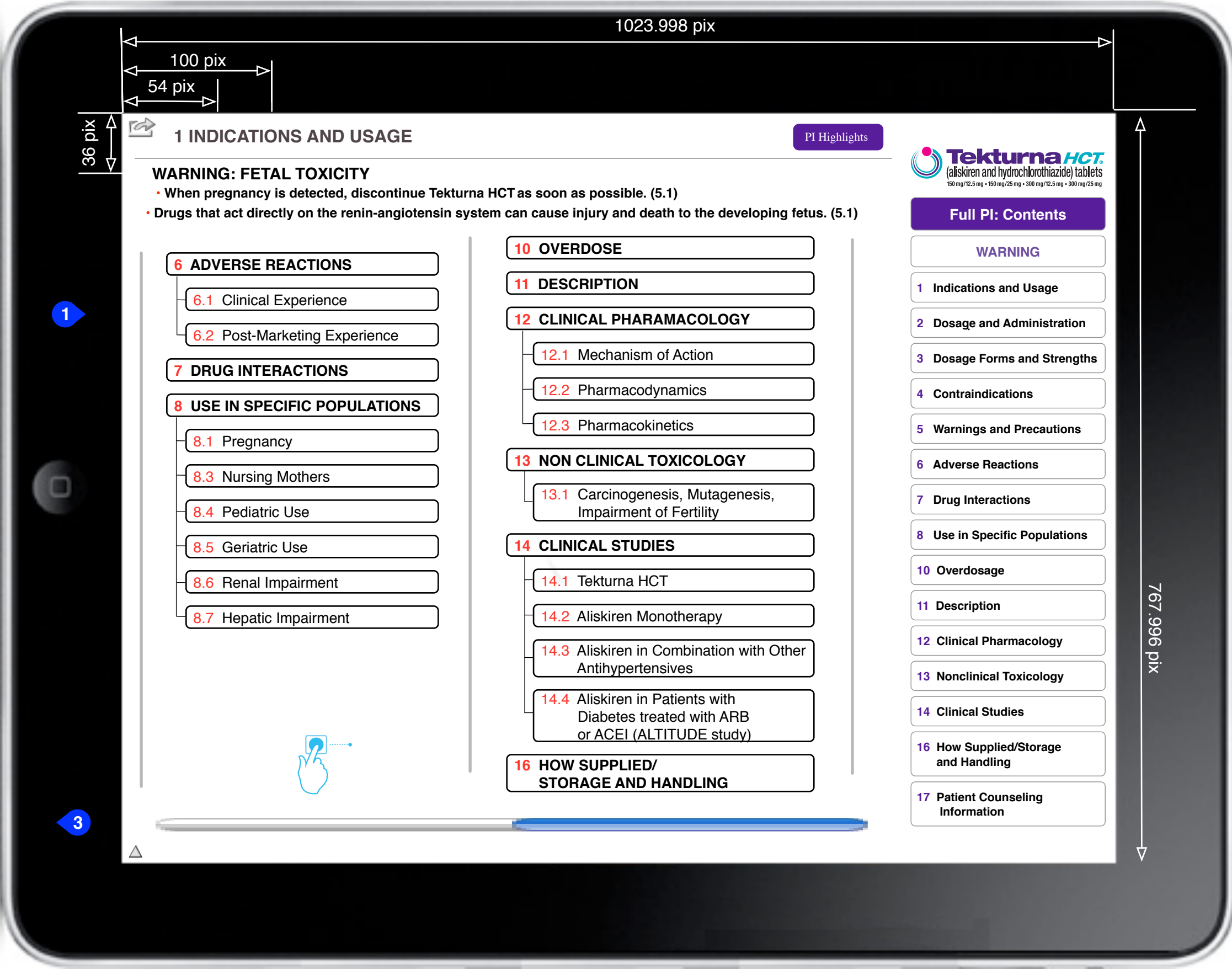


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Annotations

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Full PI: Contents	
WARNING	
1	Indications and Usage
2	Dosage and Administration
3	Dosage Forms and Strengths
4	Contraindications
5	Warnings and Precautions
6	Adverse Reactions
7	Drug Interactions
8	Use in Specific Populations
9	Overdosage
10	Description
11	Clinical Pharmacology
12	Nonclinical Toxicology
13	Clinical Studies
14	How Supplied/Storage and Handling
15	Patient Counseling Information



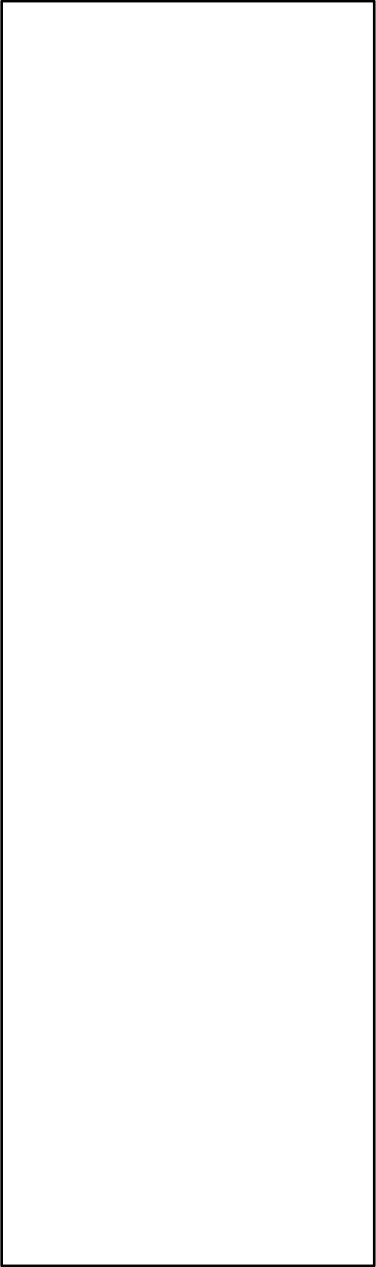
(aliskiren and hydrochlorothiazide) tablets
150 mg/12.5 mg • 150 mg/25 mg • 300 mg/12.5 mg • 300 mg/25 mg

Full PI: Contents	
WARNING	
1	Indications and Usage
2	Dosage and Administration
3	Dosage Forms and Strengths
4	Contraindications
5	Warnings and Precautions
6	Adverse Reactions
7	Drug Interactions
8	Use in Specific Populations
10	Overdosage
11	Description
12	Clinical Pharmacology
13	Nonclinical Toxicology
14	Clinical Studies
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WARNING	
1	Indications and Usage
2	Dosage and Administration
3	Dosage Forms and Strengths
4	Contraindications
5	Warnings and Precautions
6	Adverse Reactions
7	Drug Interactions
8	Use in Specific Populations
10	Overdosage
11	Description
12	Clinical Pharmacology
13	Nonclinical Toxicology
14	Clinical Studies
16	How Supplied/Storage and Handling
17	Patient Counseling Information



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8 USE IN SPECIFIC POPULATIONS

PI Highlights

Tekturna HCT

(aliskiren and hydrochlorothiazide) tablets

150 mg/12.5 mg • 150 mg/25 mg • 300 mg/12.5 mg • 300 mg/25 mg

Full PI: Contents

WARNING

1 Indications and Usage

2 Dosage and Administration

3 Dosage Forms and Strengths

4 Contraindications

5 Warnings and Precautions

6 Adverse Reactions

7 Drug Interactions

8 Use in Specific Populations

10 Overdosage

11 Description

12 Clinical Pharmacology

13 Nonclinical Toxicology

14 Clinical Studies

16 How Supplied/Storage and Handling

17 Patient Counseling Information

8.1 Pregnancy

Pregnancy Category D

Use of drugs that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death. Resulting oligohydramnios can be associated with fetal lung hypoplasia and skeletal deformations. Potential neonatal adverse effects include skull hypoplasia, anuria, hypotension, renal failure, and death. When pregnancy is detected, discontinue Tekturna HCT as soon as possible. These adverse outcomes are usually associated with use of these drugs in the second and third trimester of pregnancy. Most epidemiologic studies examining fetal abnormalities after exposure to antihypertensive use in the first trimester have not distinguished drugs affecting the renin- angiotensin system from other antihypertensive agents. Appropriate management of maternal hypertension during pregnancy is important to optimize outcomes for both mother and fetus.

In the unusual case that there is no appropriate alternative to therapy with drugs affecting the renin-angiotensin system for a particular patient, apprise the mother of the potential risk to the fetus. Perform serial ultrasound examinations to assess the intra-amniotic environment. If oligohydramnios is observed, discontinue Tekturna HCT, unless it is considered lifesaving for the mother. Fetal testing may be appropriate, based on the week of pregnancy. Patients and physicians should be aware, however, that oligohydramnios may not appear until after the fetus has sustained irreversible injury. Closely observe infants with histories of in utero exposure to Tekturna HCT for hypotension, oliguria, and hyperkalemia. [see Use in Specific Populations (8.4)]

Thiazides cross the placenta, and use of thiazides during pregnancy is associated with a risk of fetal or neonatal jaundice, thrombocytopenia, and possible other adverse reactions that have occurred in adults.

Reproductive toxicity studies of aliskiren hemifumarate did not reveal any evidence of teratogenicity at oral doses up to 600 mg aliskiren/kg/day (20 times the maximum recommended human dose[MRHD] of 300 mg/day on a mg/m² basis) in pregnant rats or up to 100 mg aliskiren/kg/day (seven times the MRHD on a mg/m² basis) in pregnant rabbits. Fetal birth weight was adversely affected in rabbits at 50 mg/kg/day (3.2 times the MRHD on a mg/m² basis). Aliskiren was present in placenta, amniotic fluid and fetuses of pregnant rabbits.

When pregnant mice and rats were given hydrochlorothiazide at doses up to 3000 and 1000 mg/kg/day, respectively (about 600 and 400 times the MRHD) during their respective periods of major organogenesis, there was no evidence of fetal harm.

Hydrochlorothiazide

Thiazides can cross the placenta, and concentrations reached in the umbilical vein approach those in the maternal plasma. Hydrochlorothiazide, like other diuretics, can cause placental hypoperfusion. It accumulates in the amniotic fluid, with reported concentrations up to 19 times higher than in umbilical vein plasma. Use of thiazides during pregnancy is associated with a risk of fetal or neonatal jaundice or thrombocytopenia. Since they do not prevent or alter the course of EPH (Edema, Proteinuria, Hypertension) gestosis (pre eclampsia), these drugs should not be used to treat hypertension in pregnant women. The use of hydrochlorothiazide for other indications (e.g. heart disease) in pregnancy should be avoided.

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8 USE IN SPECIFIC POPULATIONS

PI Highlights

8.3 Nursing Mothers

It is not known whether aliskiren is excreted in human milk, but aliskiren was secreted in the milk of lactating rats. Thiazides appear in human milk. Because of the potential for adverse effects on the nursing infant, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established. Neonates with a history of in utero exposure to Tekturna HCT:
If oliguria or hypotension occurs, direct attention toward support of blood pressure and renal perfusion. Exchange transfusions or dialysis may be required as a means of reversing hypotension and/or substituting for disordered renal function.

8.5 Geriatric Use

In the short-term controlled clinical trials of Tekturna HCT, 325 (19.6%) patients treated with Tekturna HCT were ≥65 years and 53 (3.2%) were ≥75 years.

No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

8.6 Renal Impairment

Safety and effectiveness of Tekturna HCT in patients with severe renal impairment (CrCl ≤ 30 mL/min) have not been established. No dose adjustment is required in patients with mild (CrCl 60-90 mL/min) or moderate (CrCl 30-60) renal impairment.

8.7 Hepatic Impairment

Aliskiren
No dose adjustment is necessary for patients with mild-to-severe liver disease.

Hydrochlorothiazide
Minor alterations of fluid and electrolyte balance may precipitate hepatic coma in patients with impaired hepatic function or progressive liver disease.

Tekturna HCT

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WARNING

1 Indications and Usage

2 Dosage and Administration

3 Dosage Forms and Strengths

4 Contraindications

5 Warnings and Precautions

6 Adverse Reactions

7 Drug Interactions

8 Use in Specific Populations

10 Overdosage

11 Description

12 Clinical Pharmacology

13 Nonclinical Toxicology

14 Clinical Studies

16 How Supplied/Storage and Handling

17 Patient Counseling Information

8.0

8.3

8.4

8.5

8.6

8.7

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