

URSODIOL ROUNDTABLE



2018 PBC Conference

2002 PBCers Meeting

- Thomas Draime
 - Background –
 - URSO 250/Forte Product Manager/Liver franchise
 - New indications/formulations and authorized generic initiation
 - Healthcare consulting/Market Research/PR/Advertising
 - HCP/Patient marketing/advocacy
 - Liver - PBC/PSC/HCV/HCC
 - Other - CV/Hemophilia/ HSCT/NSCLC/mCRPC/mBC/Obesity/Immuno-oncology
 - Promoting patient-physician communication, information and advocacy



Objective of the Ursodiol Roundtable

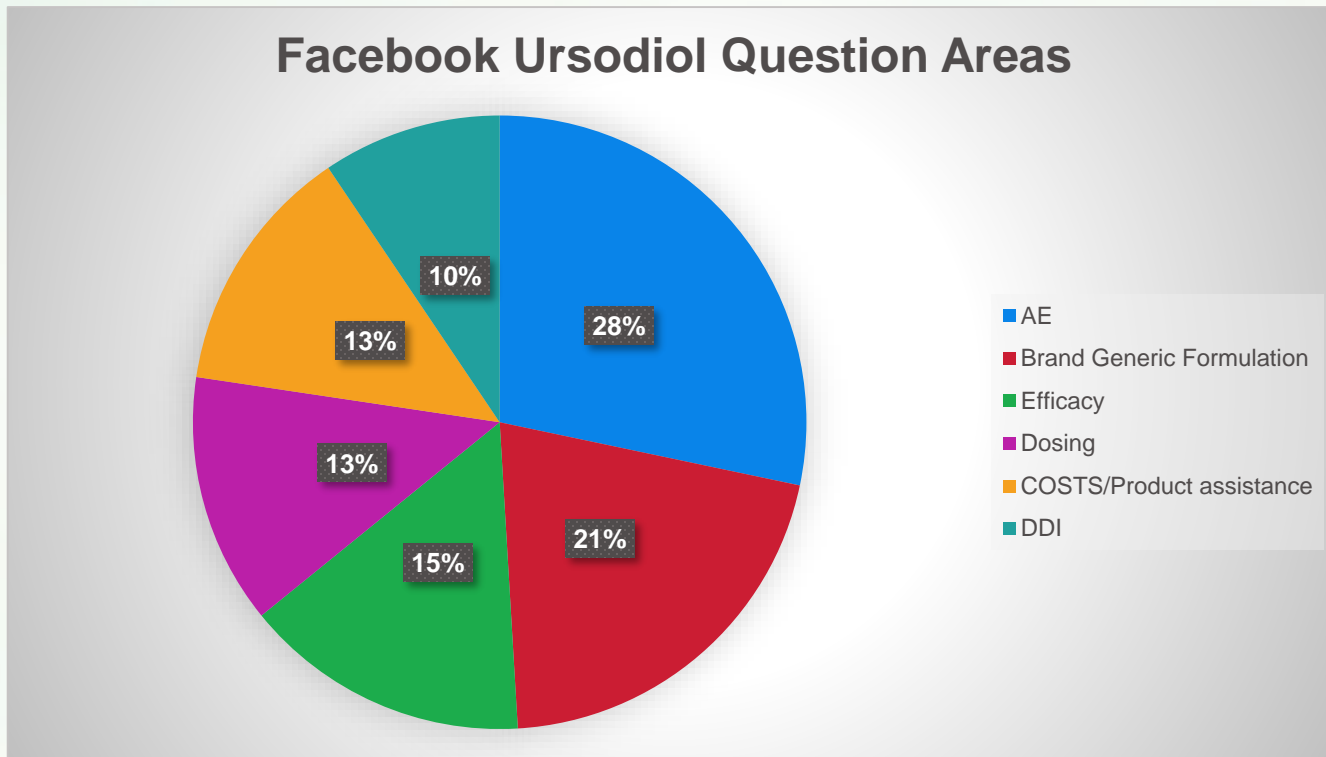
- Review some of the top questions and comments within the PBCers forums
 - This discussion is to inform people with PBC about some of the details on ursodiol to assist your conversation with your doctor
- Always consult with YOUR physician on any questions about YOUR treatment plan
 - Everyone is unique in her/his response to medications
- DO NOT make any changes to your treatments WITHOUT consulting your doctor



**Empower yourself with knowledge
and connections to live with PBC**

Areas of Facebook Questions

- What questions do you have about ursodiol?



What is Ursodiol?

- **First Line: Ursodeoxycholic Acid/Ursodiol (UDCA)**
- This medicine, also known as ursodiol (Actigall, Urso), is commonly used first. It helps move bile through your liver. UDCA doesn't cure primary biliary cholangitis, but it seems to improve liver function and reduce liver scarring.
- Everyone is different in their response to ursodio:
 - Responders
 - Non-responders
 - Intolerant

Differences Tablets vs Capsules

Actigall/Generic Capsules

- ▶ Indication – Dissolution of radiolucent, noncalcified gallstones <20 mm in diameter in patients who refuse cholecystectomy or are at increased risk during surgery. Prevention of gallstone formation in obese patients experiencing rapid weight loss.
- ▶ Dosage - Gallstone Dissolution: 8–10mg/kg per day in 2–3 divided doses. Prevention: 300mg twice daily
- ▶ Generics – launched ~2000
- ▶ Insurance – coverage based on ingredient vs indication (epocrates)

URSO250/Forte/Tablets 250/500 mg and Generic Tablets

- ▶ Indication – URSO 250 and URSO Forte (ursodiol) tablets are bile acids indicated for the treatment of patients with primary biliary cirrhosis
- ▶ Dosage - 13-15 mg/kg/day administered in two to four divided doses with food (trials 4 →2)
- ▶ Generics – launched ~2011
 - ▶ Different fillers to save on costs
- ▶ Bioequivalency –
 - ▶ Measure of drug
- ▶ Insurance – Coverage based on best price/rebate negotiations

- Each manufacturer and tablet/capsule is different – different bioequivalency, different fillers, different cost

Orange Book Approved Ursodiol Tablets/Capsules

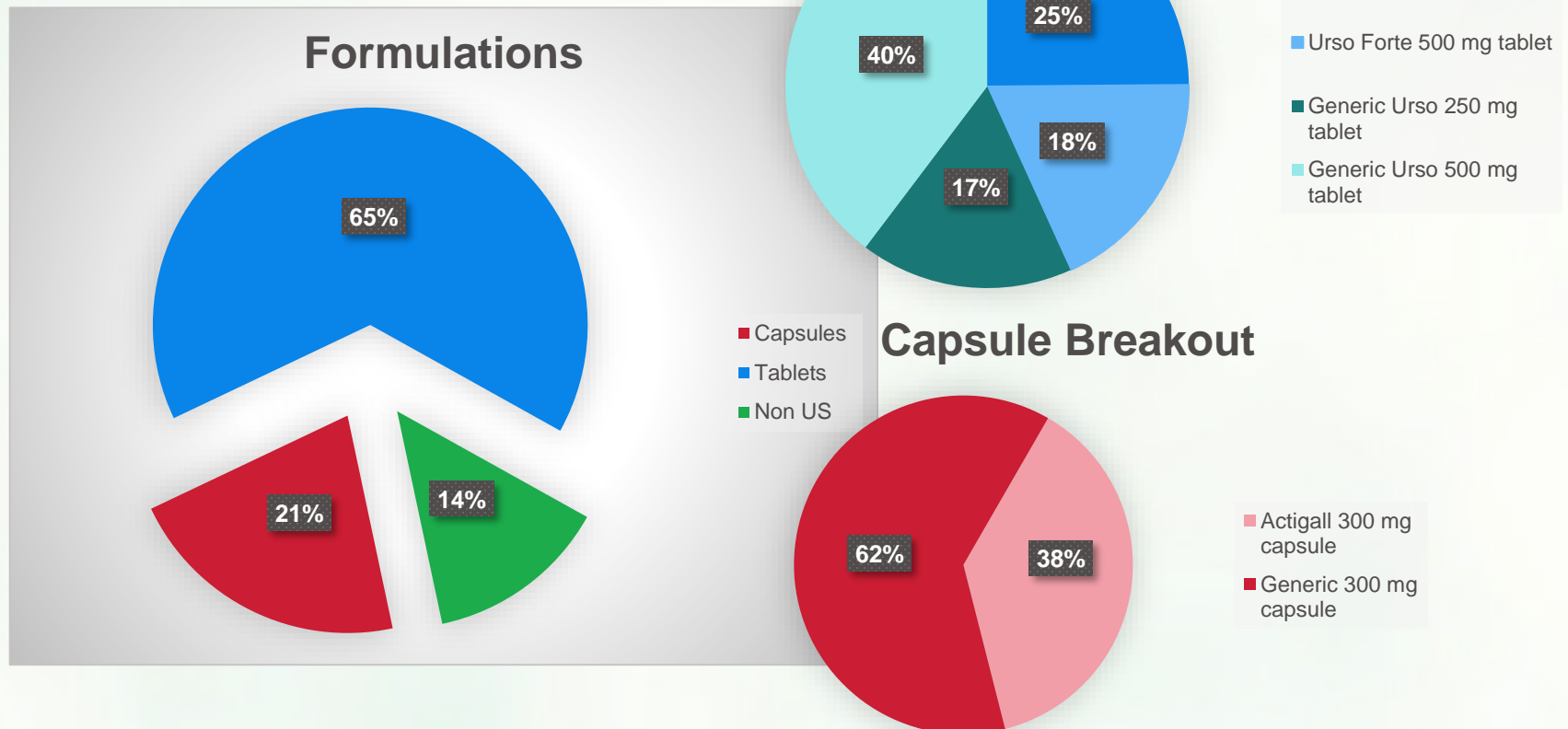
- Full list of generic listed products and manufacturers
- **RLD** – original Branded Products

Mkt. Status	Active Ingredient	Proprietary Name	Appl No	Dosage Form	Route	Strength	TE Code	RLD	RS	Applicant Holder
RX	URSODIOL	ACTIGALL	N019594	CAPSULE	ORAL	300MG	AB	RLD	RS	ALLERGAN SALES LLC
RX	URSODIOL	URSODIOL	A075517	CAPSULE	ORAL	300MG	AB			EPIC PHARMA LLC
RX	URSODIOL	URSODIOL	A079082	CAPSULE	ORAL	300MG	AB			LANNETT HOLDINGS INC
RX	URSODIOL	URSODIOL	A090530	CAPSULE	ORAL	300MG	AB			MYLAN PHARMACEUTICALS INC
RX	URSODIOL	URSODIOL	A075592	CAPSULE	ORAL	300MG	AB			TEVA PHARMACEUTICALS USA
RX	URSODIOL	URSO 250	N020675	TABLET	ORAL	250MG	AB	RLD		FOREST LABORATORIES INC
RX	URSODIOL	URSO FORTE	N020675	TABLET	ORAL	500MG	AB	RLD	RS	FOREST LABORATORIES INC
RX	URSODIOL	URSODIOL	A090801	TABLET	ORAL	250MG	AB			GLENMARK GENERICS LTD
RX	URSODIOL	URSODIOL	A200826	TABLET	ORAL	250MG	AB			IMPAX LABORATORIES INC
RX	URSODIOL	URSODIOL	A202540	TABLET	ORAL	250MG	AB			PAR PHARMACEUTICAL INC
RX	URSODIOL	URSODIOL	A090801	TABLET	ORAL	500MG	AB			GLENMARK GENERICS LTD
RX	URSODIOL	URSODIOL	A200826	TABLET	ORAL	500MG	AB			IMPAX LABORATORIES INC
RX	URSODIOL	URSODIOL	A202540	TABLET	ORAL	500MG	AB			PAR PHARMACEUTICAL INC
DISCN	URSODIOL	ACTIGALL	N019594	CAPSULE	ORAL	150MG				ALLERGAN SALES LLC
DISCN	URSODIOL	URSODIOL	A077895	CAPSULE	ORAL	300MG				IMPAX LABORATORIES INC
DISCN	URSODIOL	URSODIOL	A079184	TABLET	ORAL	250MG				TEVA PHARMACEUTICALS USA INC
DISCN	URSODIOL	URSODIOL	A079184	TABLET	ORAL	500MG				TEVA PHARMACEUTICALS USA INC

https://www.accessdata.fda.gov/scripts/cder/ob/search_product.cfm

Which Formulation of Ursodiol are You On?

- 65% of survey respondents are on Tablet formulation
 - Of those, 57% are on a generic



Ursodiol Dosage and Efficacy

Optimal dosage for PBC is 13-15 mg/kg twice a day

Recommended adult dosage: 13-15 mg/kg/day administered in two to four divided doses with food (2.1)
Scored URSO Forte tablet: scored tablet can be broken in halves to provide recommended dosage

Clinical trials/approval is based on weight

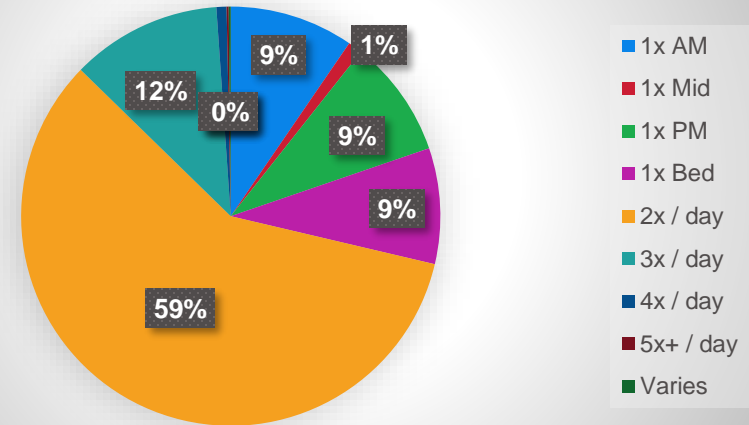
Efficacy above or below 13-15 mg/kg in clinical study dose ranging deemed not optimal

Time of day: 2 to 4 times a day recommended
Actual PBCers time of day: 59% 2x a day

Efficacy based on stage: Range of stages studied (I-IV)

Food effect: Recommended to be taken with food

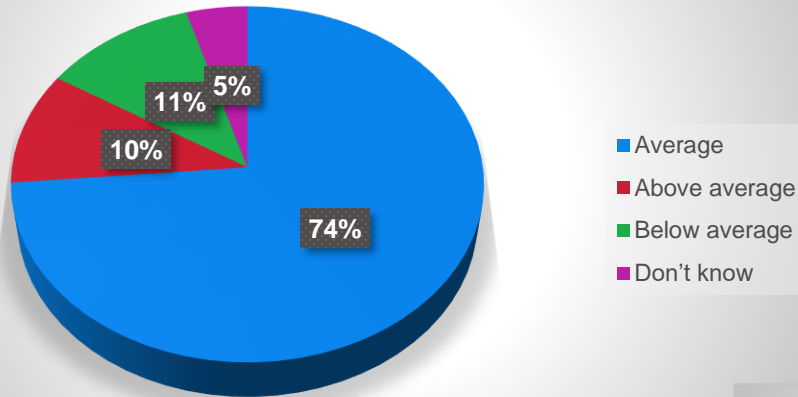
Dose Time/Frequency*



NOTE – Actigall Dosing for Gallstone Dissolution: 8–10mg/kg per day in 2–3 divided doses. Prevention: 300mg twice daily. (NOT PBC)

Am I on the Right Dose of Ursodiol?

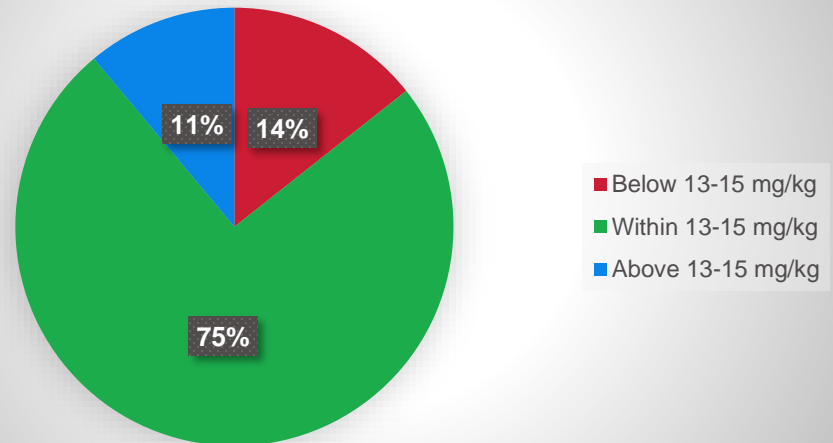
Perception of Correct Dosage*



74% have the perception they are on the right average dose (13-15mg.kg) of ursodiol based on weight

75% are approximately on the recommended dose (13-15mg.kg) of ursodiol based on weight

~ Within Recommended Dosage*



Under 100 lbs (45.36 kg)
100 - 150 lbs(45.46 - 68.04 kg)
150 - 200 lbs(68.04 - 90.72 kg)
200 - 250 lbs(90.72 - 113.40 kg)
Over 250 lbs(113.40 kg)
Survey Weight ranges (.45xlbs)

*Initial results of PBCers Survey 2018 (not complete)

Clinical and Post Marketing Side Effects / AE of Ursodiol

Original Reported Adverse Events from Clinical trials

The following table summarizes the adverse reactions observed in two placebo-controlled clinical trials.

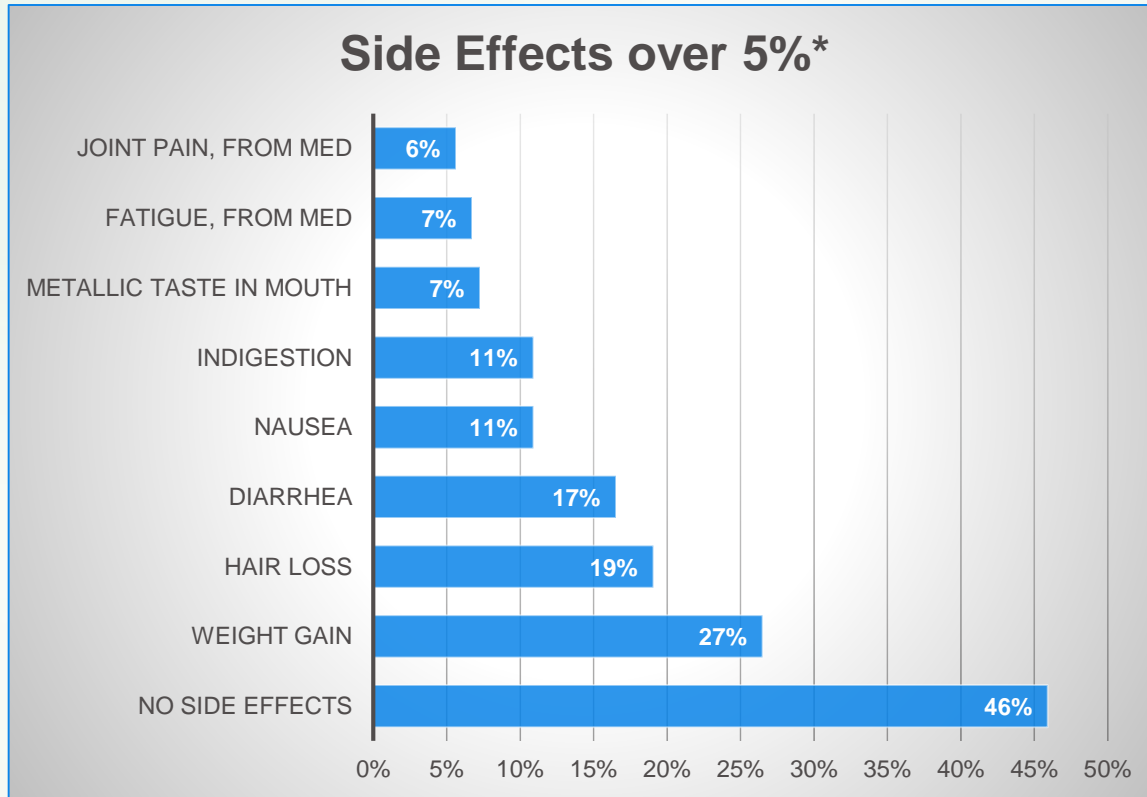
ADVERSE REACTIONS	VISIT AT 12 MONTHS		VISIT AT 24 MONTHS	
	UDCA n (%)	Placebo n (%)	UDCA n (%)	Placebo n (%)
Diarrhea	---	---	1 (1.32)	---
Elevated creatinine	---	---	1 (1.32)	---
Elevated blood glucose	1 (1.18)	---	1 (1.32)	---
Leukopenia	---	---	2 (2.63)	---
Peptic ulcer	---	---	1 (1.32)	---
Skin rash	---	---	2 (2.63)	---
Thrombocytopenia	---	---	1 (1.32)	---

Note: Those adverse reactions occurring at the same or higher incidence in the placebo as in the UDCA group have been deleted from this table (this includes diarrhea and thrombocytopenia at 12 months, nausea/vomiting, fever and other toxicity).
UDCA = Ursodeoxycholic acid = Ursodiol

Post Launch REPORTED Side Effects (ALL)

- Gastrointestinal disorders: abdominal discomfort, abdominal pain, constipation, diarrhea, dyspepsia, nausea, vomiting.
- General disorders and administration site conditions: malaise, peripheral edema, pyrexia.
- Hepatobiliary disorders: jaundice (or aggravation of preexisting jaundice).
- Immune System Disorders: Drug hypersensitivity to include facial edema, urticaria, angioedema and laryngeal edema.
- Abnormal Laboratory Tests: ALT increased, AST increased, blood alkaline phosphatase increased, blood bilirubin increased, γ -GT increased, hepatic enzyme increased, liver function test abnormal, transaminases increased.
- Musculoskeletal and connective tissue disorders: myalgia
- Nervous system disorders: dizziness, headache.
- Respiratory, thoracic and mediastinal disorders: cough.
- Skin and subcutaneous tissue disorder: alopecia, pruritus, rash

Side Effects / AE of Ursodiol Observed in Survey



38 people (out of 242, ~16%) in the PBCers Survey stopped ursodiol due to side effects

ALWAYS report any Side Effects with your Doctor! These need to be reported back to the pharmaceutical company.

*Other side effects 5% or below: Headache, Itching (from med), Weight loss, Urinary tract infection, Other

Long-Term use of Ursodiol

Results of long-term ursodiol treatment for patients with primary biliary cirrhosis

Roberta Jorgensen MS, RN, Paul Angulo MD, E Rolland Dickson MD & Keith D Lindor MD

American Journal of Gastroenterology 97,
2647-2650 (2002)
doi:10.1111/j.1572-0241.2002.06043.x
Download Citation

Received: 28 October 2001
Accepted: 19 April 2002
Published: 01 October 2002

CONCLUSIONS:

UDCA appears to be of most benefit when instituted in early stage disease. Although a substantial percentage of patients will achieve biochemical normalization on UDCA alone, there is a continued need for therapeutic options for others who have less complete biochemical responses.

Angulo P, Batts KP, Therneau TM, Jorgensen RA, Dickson ER, Lindor KD. Long-term ursodeoxycholic acid delays histological progression in primary biliary cirrhosis. *HEPATOLOGY* 1999;29:644-647.

AASLD PRACTICE GUIDELINES

Primary Biliary Cirrhosis

Keith D. Lindor,¹ M. Eric Gershwin,² Raoul Poupon,³ Marshall Kaplan,⁴ Nora V. Bergasa,⁵ and E. Jenny Heathcote⁶

UDCA is widely used and has demonstrated the ability to produce a reduction in need for liver transplantation for this condition.^{1,2,3} The drug is used for patients with any stage of PBC as long as their liver biochemistries are abnormal. A liver biopsy is not required for the diagnosis for PBC in many settings, and the stage of biopsy does not determine whether UDCA should be used but may have an impact on developing treatment strategies.^{1,11} Patients with earlier histologic stage in general respond more favorably to UDCA, but even patients with advanced stage disease may derive improvement in survival or avoidance of need for liver transplantation with this therapy.^{4,2}



Comparison of Tablet Inactive Ingredients

Glenmark Generic	Par Pharmaceuticals	URSO 250	Impax Labs
Inactive Ingredients	INACTIVE INGREDIENTS	Inactive Ingredients	nactive Ingredients
Ingredient Name	Ingredient Name	Ingredient Name	Ingredient Name
CELLULOSE, MICROCRYSTALLINE	MEDIUM-CHAIN TRIGLYCERIDES (UNII: C9H2L21V7U)	microcrystalline cellulose	CELLULOSE, MICROCRYSTALLINE
POVIDONES	COPOVIDONE (UNII: D9C330MD8B)	povidone	SILICON DIOXIDE
SODIUM STARCH GLYCOLATE TYPE A POTATO	HYPROMELLOSES (UNII: 3NXW29V3WO)	sodium starch glycolate	POVIDONE
MAGNESIUM STEARATE	CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	magnesium stearate	MAGNESIUM STEARATE
ETHYLCELLULOSES	MAGNESIUM STEARATE (UNII: 70097M6130)	ethylcellulose	LACTOSE MONOHYDRATE
DIBUTYL SEBACATE	POLYDEXTROSE (UNII: VH2XOU12IE)	dibutyl sebacate	HYPROMELLOSES
CARNAUBA WAX	POLYETHYLENE GLYCOL 3350 (UNII: G2M7P15E5P)	carnauba wax	TITANIUM DIOXIDE
HYPROMELLOSES	SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	hydroxypropyl methylcellulose	SODIUM STARCH GLYCOLATE TYPE A POTATO
POLYETHYLENE GLYCOL 3350	TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	PEG 3350	POLYETHYLENE GLYCOL 400
POLYETHYLENE GLYCOL 8000	POVIDONE (UNII: FZ989GH94E)	PEG 8000	
CETYL ALCOHOL		cetyl alcohol	
SODIUM LAURYL SULFATE		sodium lauryl sulfate	
		hydrogen peroxide	

Similar yet ... different

Be aware of ingredients and how they affect YOU

Medium chain triglycerides are for dietary use in people whose bodies cannot digest certain foods properly. This includes people who are gluten or lactose intolerant, or who have unintended weight loss or need increased calories for other medical reasons.



URSO 250	Epic Pharma	Allergan	Lannett Company
Inactive Ingredients	INACTIVE INGREDIENTS	INACTIVE INGREDIENTS	INACTIVE INGREDIENTS
Ingredient Name	Ingredient Name	Ingredient Name	Ingredient Name
microcrystalline cellulose	STARCH, CORN (UNII: O8232NY3SJ)	Colloidal silicon dioxide	STARCH, CORN (UNII: O8232NY3SJ)
povidone	MAGNESIUM STEARATE (UNII: 70097M6I30)	Magnesium stearate	SILICON DIOXIDE (UNII: ETJ7Z6XBU4)
sodium starch glycolate	SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	starch (corn)	MAGNESIUM STEARATE (UNII: 70097M6I30)
magnesium stearate	D&C RED NO. 28 (UNII: 7671P0Y5NH)	ferric oxide	FD&C BLUE NO. 1 (UNII: H3R47K3TBD)
ethylcellulose	D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	gelatin	FD&C RED NO. 40 (UNII: WZB9127XOA)
dibutyl sebacate	FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	titanium dioxide	FD&C YELLOW NO. 6 (UNII: H77VEI93A8)
carnauba wax	FD&C BLUE NO. 2 (UNII: L06K8R7DQK)	black iron oxide	GELATIN (UNII: 2G86QN327L)
hydroxypropyl methylcellulose	FD&C RED NO. 40 (UNII: WZB9127XOA)		TITANIUM DIOXIDE (UNII: 15FIX9V2JP)
PEG 3350	GELATIN (UNII: 2G86QN327L)		SHELLAC (UNII: 46N107B71O)
PEG 8000	FERROSFERRIC OXIDE (UNII: XM0M87F357)		ALCOHOL (UNII: 3K9S98V90M)
cetyl alcohol	TITANIUM DIOXIDE (UNII: 15FIX9V2JP)		FERROSFERRIC OXIDE (UNII: XM0M87F357)
sodium lauryl sulfate	SHELLAC (UNII: 46N107B71O)		BUTYL ALCOHOL (UNII: 8PJ61P6TS3)
hydrogen peroxide	PROPYLENE GLYCOL (UNII: 6DC9Q167V3)		PROPYLENE GLYCOL (UNII: 6DC9Q167V3)
			METHYL ALCOHOL (UNII: Y4S76JW115)
			ALUMINUM OXIDE (UNII: LMI26O6933)
			FD&C BLUE NO. 2 (UNII: L06K8R7DQK)
			D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)



<https://dailymed.nlm.nih.gov>

Comparison of Capsule Inactive Ingredients

Actigall launched in 1987
Generics launched in 2000+

Comparison to raise awareness of what is in your tablet/capsule, not to compare efficacy.
Everyone responds differently!



Most Common Ursodiol Drug-Drug Interactions (DDI)

Most common side effects from clinical trials included:

DRUG INTERACTIONS

7.1 Bile Acid Sequestering Agents

Bile acid sequestering agents such as cholestyramine and colestipol may interfere with the action of URSO 250 and URSO Forte by reducing its absorption.

7.2 Aluminum-based Antacids

Aluminum-based antacids have been shown to adsorb bile acids in vitro and may be expected to interfere with URSO 250 and URSO Forte in the same manner as the bile acid sequestering agents.

7.3 Drugs Affecting Lipid Metabolism

Estrogens, oral contraceptives, and clofibrate (and perhaps other lipid-lowering drugs) increase hepatic cholesterol secretion and encourage cholesterol gallstone formation and hence may counteract the effectiveness of URSO 250 and URSO Forte.

Common medications **checked** in combination with Urso (ursodiol)

[Albuterol](#); [Calcium 600 D \(calcium / vitamin d\)](#); [Flonase \(fluticasone nasal\)](#); [gabapentin](#); [lactulose](#); [Lasix \(furosemide\)](#); [levothyroxine](#); [Nexium \(esomeprazole\)](#); [Omeprazole](#); [oxycodone](#); [prednisone](#); [Protonix \(pantoprazole\)](#); [spironolactone](#); [Symbicort \(budesonide / formoterol\)](#); [Synthroid \(levothyroxine\)](#); [trazodone](#); [Vitamin D2 \(ergocalciferol\)](#); [Vitamin D3 \(cholecalciferol\)](#); [Xanax \(alprazolam\)](#); [Zofran \(ondansetron\)](#)

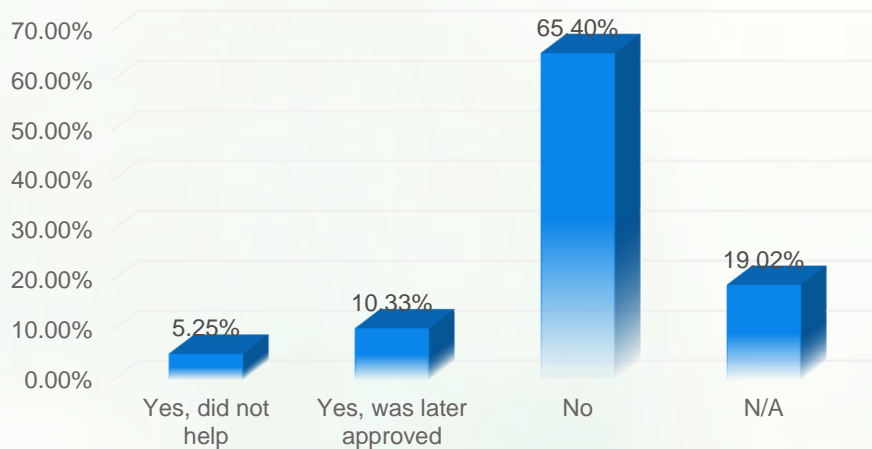
Cost and Formulary Coverage

Health Plan Name	Provider	Plan Type	Coverage
Actigall ⓘ			
Amerigroup (Texas)	Amerigroup	Managed Medicaid	Tier 1 Non-Preferred PA 93
BlueCross BlueShield Texas Basic	BlueCross BlueShield Texas	Commercial	Tier 3 Non-Preferred
CVS Caremark Performance Standard Control	CVS/Caremark	PBM	Tier 3 Non-Preferred
Humana Walmart Rx PDP	Humana	Medicare PDP	NC Not Covered
Silverscript Choice	SilverScript	Medicare PDP	NC Not Covered
Superior Health Plan	Superior HealthPlan	Managed Medicaid	Tier 1 Non-Preferred PA 93
UnitedHealthcare Advantage 3-Tier	United	Commercial	Tier 3 Non-Preferred
UnitedHealthcare Community Plan (Texas)	UnitedHealthcare Community Plan (TX)	Managed Medicaid	Tier 1 Non-Preferred PA 93
URSO Forte ⓘ			
Amerigroup (Texas)	Amerigroup	Managed Medicaid	Tier 1 Non-Preferred PA 93
BlueCross BlueShield Texas Basic	BlueCross BlueShield Texas	Commercial	Tier 3 Non-Preferred
CVS Caremark Performance Standard Control	CVS/Caremark	PBM	Tier 3 Non-Preferred
Humana Walmart Rx PDP	Humana	Medicare PDP	NC Not Covered
Silverscript Choice	SilverScript	Medicare PDP	NC Not Covered
Superior Health Plan	Superior HealthPlan	Managed Medicaid	Tier 1 Non-Preferred PA 93
UnitedHealthcare Advantage 3-Tier	United	Commercial	Tier 3 Non-Preferred
UnitedHealthcare Community Plan (Texas)	UnitedHealthcare Community Plan (TX)	Managed Medicaid	Tier 1 Non-Preferred PA 93
Ursodiol ⓘ			
Amerigroup (Texas)	Amerigroup	Managed Medicaid	Tier 1 Preferred
BlueCross BlueShield Texas Basic	BlueCross BlueShield Texas	Commercial	Tier 1 Preferred
CVS Caremark Performance Standard Control	CVS/Caremark	PBM	Tier 1 Preferred
Humana Walmart Rx PDP	Humana	Medicare PDP	Tier 3 Preferred 10
Silverscript Choice	SilverScript	Medicare PDP	Tier 4 Non-Preferred 10
Superior Health Plan	Superior HealthPlan	Managed Medicaid	Tier 1 Preferred
UnitedHealthcare Advantage 3-Tier	United	Commercial	Tier 1 Preferred
UnitedHealthcare Community Plan (Texas)	UnitedHealthcare Community Plan (TX)	Managed Medicaid	Tier 1 Preferred

COSTS/Product assistance

- Approximately 25% of respondents have difficulty covering Ursodiol co-pays for periods of time throughout the year
- 65% with difficulty paying for ursodiol co-pay have not reached out through the appeals process

USE OF APPEAL PROCESS*



*Initial results of PBCers Survey 2018 (not complete)

HealthWell Foundation Copay Program

This is a copay assistance program

Provided by: HealthWell Foundation

PO Box 220410
Chantilly, VA 20153-0410

Languages Spoken:
English, Others By Translation Service

TEL: 800-675-8416

[Program Website](#)

FAX: 800-282-7692

Ursodiol Coupon & Discounts

Save on Ursodiol at your pharmacy with the free discount below.

Ursodiol is a medication that is used to treat and prevent the formation of gallstones. Ursodiol can cost around \$150 for a month's supply. Use our free coupons to reduce the ursodiol pharmacy price by up to 64% when you fill your prescription. Our coupons are accepted in most pharmacies and they may be p... [Read more](#)



Ursodiol Discount

Savings with HelpRx discount up to:

64% Off
on Ursodiol

Privacy Protected
Never Expires

*The discount percent is an estimate based off recent cardholder data. Valid as of May 18, 2018.

Claim your free Ursodiol discount

- 1 Click the "Get free coupon" button to receive your free Ursodiol discount.
- 2 Print, email or text message your coupon
- 3 Present your coupon the next time you fill your prescription

[Get Free Coupon](#) →

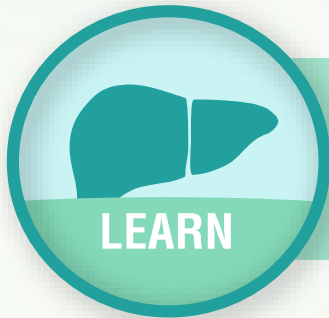
(No signup required!)



Closing Thoughts



**Reach out to PBCers members,
doctor's office and manufacturers**



**Learn about your treatments & talk
WITH your hep/gastro on plans**



**Empower yourself with knowledge
and connections to live with PBC**

Other Discussion Points



2018 PBC Conference

Breaker Sections



Connect with other PBC patients, family and friends.



Learn about PBC: History, current and future treatments & research



Empower yourself with knowledge and connections to live with PBC



